ESC European Society of Cardiology

Europace (2019) **21**, 813–821
doi:10.1093/europace/euy304

BASIC SCIENCE

Omnipolarity applied to equi-spaced electrode array for ventricular tachycardia substrate mapping

Andreu Porta-Sánchez[1,2†], Karl Magtibay[2†], Sachin Nayyar[2], Abhishek Bhaskaran[2], Patrick F.H. Lai[2], Stéphane Massé[2], Christopher Labos[3], Beiping Qiang[2], Rocco Romagnuolo[2], Hassan Masoudpour[2], Labonny Biswas[4], Nilesh Ghugre[4], Michael Laflamme[2], Don Curtis Deno[5], and Kumaraswamy Nanthakumar[2*‡]

[1]Dept de Medicina, Universitat de Barcelona, Barcelona and Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain; [2]Department of Medicine, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada; [3]Office for Science and Society, McGill University, Montreal, Quebec, Canada; [4]Sunnybrook Research Institute, Toronto, Ontario, Canada; and [5]Applied Research, Abbott Laboratories, St Paul, MN, USA

Received 28 August 2018; editorial decision 26 November 2018; accepted 4 December 2018; online publish-ahead-of-print 4 February 2019

Aims Bipolar electrogram (Bi_{EGM})-based substrate maps are heavily influenced by direction of a wavefront to the mapping bipole. In this study, we evaluate high-resolution, orientation-independent peak-to-peak voltage (Vpp) maps obtained with an equi-spaced electrode array and omnipolar EGMs (OT_{EGMs}), measure its beat-to-beat consistency, and assess its ability to delineate diseased areas within the myocardium compared against traditional Bi_{EGMs} on two orientations: along (AL) and across (AC) array splines.

Methods and results The endocardium of the left ventricle of 10 pigs (three healthy and seven infarcted) were each mapped using an Advisor^{TM} HD grid with a research EnSite Precision^{TM} system. Cardiac magnetic resonance images with late gadolinium enhancement were registered with electroanatomical maps and were used for gross scar delineation. Over healthy areas, OT_{EGM} Vpp values are larger than AL bipoles by 27% and AC bipoles by 26%, and over infarcted areas OT_{EGM} Vpp values are 23% larger than AL bipoles and 27% larger than AC bipoles ($P < 0.05$). Omnipolar EGM voltage maps were 37% denser than Bi_{EGM} maps. In addition, OT_{EGM} Vpp values are more consistent than bipolar Vpps showing less beat-by-beat variation than Bi_{EGM} by 39% and 47% over both infarcted and healthy areas, respectively ($P < 0.01$). Omnipolar EGM better delineate infarcted areas than traditional Bi_{EGMs} from both orientations.

Conclusion An equi-spaced electrode grid when combined with omnipolar methodology yielded the largest detectable bipolar-like voltage and is void of directional influences, providing reliable voltage assessment within infarcted and non-infarcted regions of the heart.

Keywords Electroanatomic mapping • Omnipolar • Bipolar • Unipolar • Voltage • Electrogram • Myocardial infarction • Porcine

* Corresponding author. Tel: (416) 340 4442; fax: (416) 340 4457. *E-mail address:* Kumar.Nanthakumar@uhn.ca

† These authors are co-first authors.

‡GW 3-522, 150 Gerrard St. W, Toronto, Ontario, M5G 2C4, Canada.

What's new?

- Bipolar EGMs (Bi_{EGM}) are significantly influenced by direction of the propagating wavefront to recording bipolar axis, especially in diseased myocardium.
- The new methodology of Omnipolar EGMs (OT_{EGMs}) when coupled to a fixed equi-spaced array provides for voltage measurements that are physiological and have been validated *ex vivo* previously. Omnipolar voltage assessment can be visualized in real time and is void of directional influences and in this manuscript has been validated *in vivo* in diseased myocardium.
- Here, we demonstrate that *in vivo* substrate mapping of a swine model of myocardial infarction with OT_{EGMs} provides higher peak to peak voltages than Bi_{EGMs} and more consistent measurements with less beat-to-beat variability.
- Those findings may indicate their ability to detect surviving bundles of myocardial tissue and may be an important tool for VT substrate assessment.

Introduction

The directional dependency of bipolar electrograms (Bi_{EGMs}) and voltage assessment for detection of non-healthy myocardium have been recently highlighted in multiple publications.[1–4] An orientation agnostic voltage assessment would allow for a consistent physiological description of the myocardium being interrogated. Recently, Deno *et al.*[5] introduced the concept of omnipoles which are bipolar-like EGMs that are catheter-orientation independent and could potentially alleviate the limitations of traditional direction-dependent bipolar recordings. Omnipolar methodology (OT) determines the direction of a traveling wave (TW) along the myocardial plane by interrogating its electric field (E-field).[6] Another advantage of omnipoles is that it can survey all possible bipolar electrode orientations without the need for catheter rotation. Previous *ex vivo* studies by Massé *et al.*,[6] Haldar *et al.*,[7] and Magtibay *et al.*[8] in isolated animal and human hearts introduced omnipolar EGM (OT_{EGM}), an OT_{EGM} with the largest voltage peak-to-peak (Vpp), an OT_{Vmax}, value along the myocardial plane which was used to create consistent, physiologically relevant voltage maps of the myocardial substrate both in healthy and diseased conditions. However, especially in the endocardium, substrate evaluation *in vivo* with OT_{EGM} has not been undertaken.

Previously, it has been shown that within diseased areas, surviving myocardial tracts produces heterogeneous scar substrates.[9] Omnipolar EGM could provide the largest Vpp value along the maximal bipole direction independent of catheter orientation which could potentially better reflect the physiological condition of the near field myocardium.

We conducted *in vivo* studies to generate electroanatomical maps of the left ventricle (LV) of infarcted pigs using both OT_{EGMs} and Bi_{EGMs} along two orientations within a grid catheter of 16 equally spaced electrodes. The objectives of our work are as follows: (i) evaluate orientation-independent OT_{EGM}-based voltage maps compared with traditional Bi_{EGM}-based voltage maps, along two bipole orientations; (ii) assess mapping densities of OT_{EGM}-based voltage maps; (iii) measure beat-to-beat consistency of Vpp values from both Bi_{EGM} and OT_{EGM}; and finally, (iv) assess OT's capability to delineate infarcted areas within the myocardium. Thus, we hypothesize that an equi-spaced electrode array coupled with OT could provide higher resolution, physiologically relevant, and consistent voltage maps of the endocardium.

Methods

Swine infarct model

Animal procedures were approved by the Animal Care Committee at Sunnybrook Health Sciences Centre and at University Health Network, both in Toronto, Ontario, Canada. Details are provided in the Supplementary material online, *File*.

Cardiac magnetic resonance imaging

Approximately 3 weeks following myocardial infarction (MI), each pig underwent cardiac magnetic resonance imaging with late gadolinium enhancement (LGE). Details of the imaging protocol used in this study were described by Ghugre *et al.*[10] elsewhere and are detailed in the Supplementary material online, *File*.

Electroanatomic mapping procedure

Endocardial mapping was performed 4 weeks after MI using an Advisor™ HD grid (*Figure 1A*) and a research version of EnSite Precision™ mapping system (Abbott Laboratories, St Paul, MN, USA). A quadripolar catheter was advanced in to the right ventricular apex and another within the inferior vena cava for electrical unipolar reference. Surface electrocardiograms (ECGs) were used for timing reference. Initially a 3D volume was created with the Advisor™ HD grid of both the aortic root and the LV endocardium with care in reconstructing the entire LV surface. Local activation time (LAT) maps were also created during sinus rhythm and during right ventricular pacing with annotation based on absolute $+dV/dt$ (Supplementary material online). Post-procedure, MRI-segmented surfaces, as described above, were registered with the electroanatomical 3D surface using anatomical landmarks that included the LV apex, the aortic root and the mitral ring, which was available for two pigs. Macrohistology was available for two post-MI hearts. After inclusion in formaldehyde, 5 mm cuts were used to grossly correlate the areas of MI and fibrosis with our electroanatomical maps and MRI findings (Supplementary material online). No precise electroanatomical comparison measures of healthy vs. infarcted tissue was done with histology due to the change in size of the cardiac surfaces after formaldehyde inclusion (*Figure 2*).

Bipolar voltage mapping with Advisor™ HD grid

Bipolar electrograms were filtered at 30–300 Hz and were measured from two orientations within the Advisor™ HD grid: along- (AL) and across (AC) splines as shown in *Figure 1A*. Bipolar electrogram Vpp values were plotted at the centre of a hypothetical line segment between adjacent electrodes of each bipolar orientation. For each mapped area, there were a total of 24 Bi_{EGM} Vpp values, 12 from each orientation. Voltage cut-off used to define low voltage was <1.5 mV. These values were minimally interpolated to create continuously coloured voltage maps of the LV using a triangular-mesh-based interpolation method available within the EnSite Precision™ mapping system.

Omnipolar voltage mapping with Advisor™ HD grid

Technical details of OT have been previously described by Deno *et al.*[5] The method for derivation of OT_{EGMs} used for voltage mapping has also

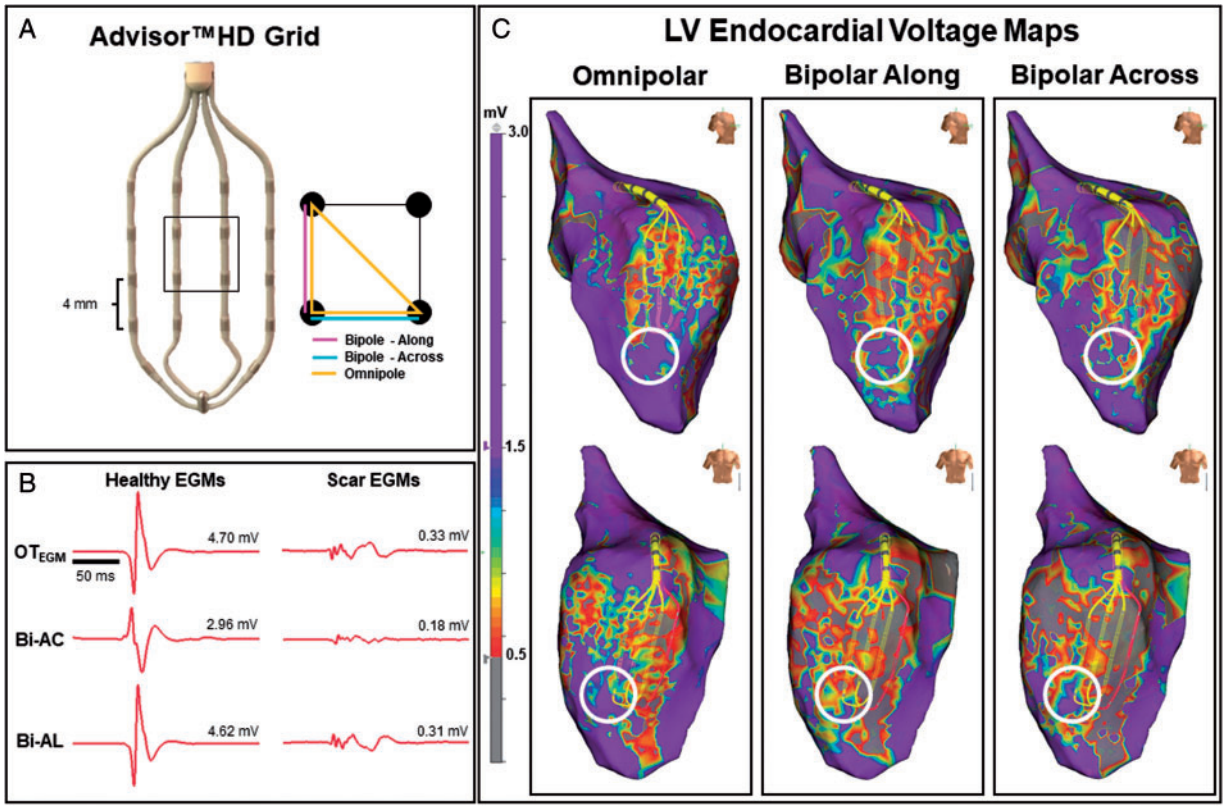

Figure 1 Voltage mapping with Advisor™ HD grid. (*A*) The specifications of an Advisor™ HD grid as well as the configuration of the bipoles and omnipoles are shown. Each electrode along and across the splines of the catheter are 4 mm apart, unrestricted. Bipoles were calculated AL and AC the splines while omnipoles (OT_{Vmax}) were derived from a right triangle clique. Within a square area, we can derive four OT_{Vmax} values and two bipolar AL and two bipolar AC values. Constituent bipoles and omnipoles were matched later for analysis. (*B*) Sample EGMs calculated using OT and its paired bipolar electrode splines over healthy and scarred areas are shown. Sensitivity of bipoles to electrode orientation is clearly shown between the two bipoles calculated within an area. OT_{EGMs} exhibits an EGM with the largest Vpp which is similar—but larger—to the largest measurable traditional bipole. This is true for both healthy and scarred areas. (*C*) The comparison of resultant voltage maps from OT_{Vmax}, bipolar AL, and bipolar AC is shown. Electrode orientation dependence of bipoles is exacerbated when translated in to maps providing different low-voltage zone map profiles. Omnipolar maps, on the other hand, provides voltage maps with larger voltages as well as better defined boundaries. White circles highlight the specific differences in the voltage maps between bipolar AL and AC and OT_{Vmax}. AC, across; AL, along; EGM, electrograms; LV, left ventricle; OT, omnipolar methodology; OT_{EGMs}, omnipolar electrograms; Vpp, voltage peak-to-peak.

been previously described by Haldar *et al.*[7] and Magtibay *et al.*[8] In brief, OT is derived from the E-field of a uniform TW that is sensed by at least three closely spaced unipolar electrodes (cliques) lying along the plane of the myocardium. In this work, we used in real-time right triangle cliques within the Advisor™ HD grid which allowed for relatively higher resolution mapping as an alternative to the originally proposed square cliques[5] (36 vs. 9 mapping points). Omnipolar EGMs were filtered at 30–300 Hz. As with previous works, Vpp of OT_{EGMs} (OT_{Vmax}) were mapped at the centre of each triangle clique and projected on to previously made LV endocardial geometry to create voltage maps. Similar to bipolar voltage mapping, standard voltage cut-offs used to define low voltages was <1.5 mV. OT_{Vmax} values were interpolated using triangular-mesh-based interpolation method available within the EnSite™ Precision™ mapping system.

Quantitative analysis

For each pig, voltage data were collected over both healthy and infarcted areas identified using MR-LGE images as described above. Time segments during sinus rhythm were qualified for analysis only when the HD grid™ is close to the surface of the LV endocardial shell (<4 mm), when EGMs are time stable for at least 10 beats, and when the Advisor™ HD grid splines are unrestricted so that the interelectrode distances AL and AC the catheter splines are similar and consistent between the two bipolar orientations. Furthermore, OT_{EGM} and OT_{Vmax} values from each clique were paired with their constituent Bi_{EGM} and Bi_{EGM} Vpp values from both AL and AC orientations.

Voltage mapping with bipolar electrograms vs. omnipolar electrograms

First, to illustrate the dependence of Bi_{EGM} Vpp values on electrode orientation, we quantified the mean absolute difference of Vpp values between Bi_{EGM} Vpps from AL and AC orientations. Second, we calculated how much the mean absolute difference OT_{Vmax} values are larger than measured traditional Bi_{EGM} Vpp values to demonstrate its orientation independence and its potential for more accurate physiological

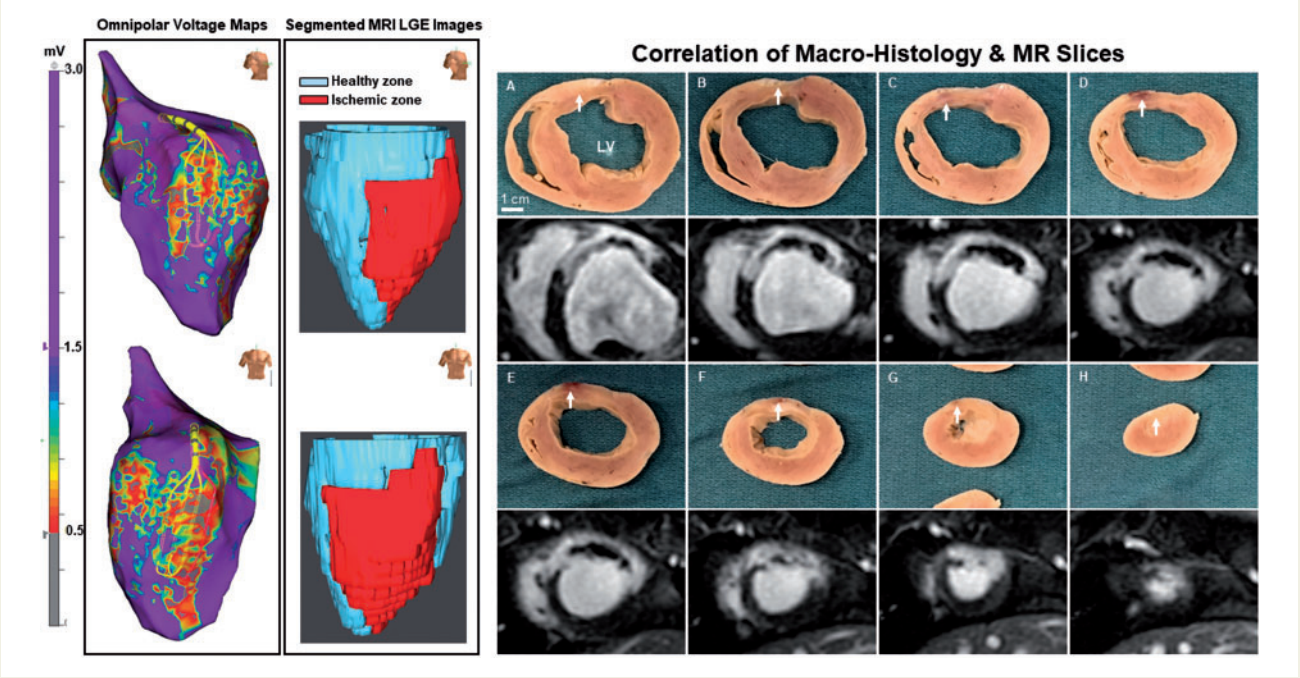

Figure 2 Omnipolar voltage map comparison to LGE-MR images. This figure shows the comparison of the detected low-voltage areas in an omnipolar voltage map compared with the segmented shells of MR images with LGE taken from a sample infarcted porcine heart. LGE shows the general areas of no-reflow and intramyocardial haemorrhage frequently seen in 3–4-week-old myocardial infarction following a patchy pattern. For reference, we show the general location of the infarcted zones within an LV with respect to the location of the low-voltage areas in an omnipolar substrate map using segmented portions of the MR-LGE images coloured in red. We verify the location of the infarcted zones by comparing the macro-histological slices of the whole heart. White arrows point to the infarcted zones as shown from *A* (base) to *H* (apex), respectively. LGE, late gadolinium enhancement; LV, left ventricle; MR, magnetic resonance.

measurement. Third, we measured how similar and how much larger the mean absolute difference of OT_{Vmax} values were compared with the largest measurable Bi_{EGM} Vpp from either AL or AC orientations (Max-Bi). Furthermore, for a single beat, we calculated for the correlation of OT_{Vmax} and Max-Bi values and the morphologies of their corresponding EGMs, OT_{EGM} vs. Max-Bi_{EGM}, for all pigs.

Voltage mapping density: omnipolar vs. bipolar voltage maps

We defined mapping density as the number of points per square centimetre (pts/cm^2). In order to quantify the mapping density of both omnipolar and bipolar voltage maps, random areas within the LV endocardial shell were chosen and were enclosed with an arbitrary surface polygon with areas readily calculated by the EnSite Precision^{TM} system. Within these areas, the number of OT_{Vmax} values and Bi_{EGM} Vpp values projected on to the shell were counted. It is important to note that there was no repetition of points within a 3 mm radius of each point. We then divided the counted points with the area of the arbitrary surface polygon to obtain mapping density values for each mapping method.

Beat-by-beat consistency between omnipoles and bipoles

We calculated beat-by-beat variations between OT_{Vmax} and Bi_{EGM} Vpp values by measuring their coefficient of variation (CoV) over 10 beats, while the catheter array was in a stable position. CoV values that approach one and above are not consistent throughout beats, while CoV values that approach values near 0 have better consistency throughout beats.

Comparison of low-voltage areas from electroanatomical maps and infarcted areas from magnetic resonance late gadolinium enhancement images

After registration, previously calculated surface areas of the infarcted regions of the endocardial LV based off MR-LGE images were compared with the low-voltage areas (<1.5 mV) of voltage maps generated from both bipolar orientations, AL and AC, and OT_{Vmax} for two pigs. We referred to the MR-LGE images as reference and surface areas were calculated as described above. The surface area of low-voltage areas from all three substrate map types were readily obtained from EnSite Precision^{TM} mapping system.

Results

Bipolar maps are qualitatively but not quantitatively sensitive to electrode orientation

Bipolar voltage maps created from AL and AC bipolar orientations differ visually from each other for all pigs from both healthy and

Table 1 Summary of quantitative analysis of voltage mapping data

	Healthy	Infarcted
A. Vpp of bipoles		
AL (mV), avg ± std err	4.87 ± 0.95	0.53 ± 0.09
AC (mV), avg ± std err	4.94 ± 0.95	0.51 ± 0.09
Δ |AL − AC| (mV), p (HME)	0.07 ± 0.23, NS	0.02 ± 0.06, NS
B. Vpp of omnipoles		
OT_{Vmax} (mV), avg ± std err	6.64 ± 0.95	0.69 ± 0.09
Δ |OT_{Vmax} − AL| (mV), p (HME)	1.77 ± 0.23, S	0.17 ± 0.06, S
Δ |OT_{Vmax} − AC| (mV), p (HME)	1.70 ± 0.23, S	0.19 ± 0.06, S
C. OT_{Vmax} vs. maximal (AL or AC) bipole Vpp		
Correlation − r (avg)	0.99	0.99
Max-Bi (mV), avg ± std err	5.99 ± 0.95	0.64 ± 0.08
Δ |OT_{Vmax} − Max-Bi| (mV), p	0.65 ± 0.23, S	0.06 ± 0.06, NS
D. Beat-by-beat variation (CoV)		
Bipole, avg ± std	0.32 ± 0.16	0.31 ± 0.13
OT_{max}, avg ± std	0.17 ± 0.12	0.19 ± 0.11
P-value (paired *t*-test)	$P < 0.01$	$P < 0.01$

Section A shows the average and standard error of both bipolar types, AL and AC and their absolute difference, within the Advisor™ HD Grid in both healthy and infarcted areas of the left ventricle. Although, there is no quantitative difference between the bipolar voltage values from two different orientations their corresponding maps shown in *Figure 1C* that orientation is a determining factor for voltage map profiles. *Section B* shows the average and standard error of OT_{Vmax} and its difference to both bipolar voltage from AL and AC orientations in both healthy and infarcted areas. OT_{Vmax} provides larger voltage values compared with any bipolar voltage values from any orientations as shown in their absolute differences. *Section C* illustrates that even obtaining the bipolar voltage with the largest value from any orientation, OT_{Vmax} still provides larger values than any bipolar values as shown by the absolute difference of their average and standard error. *Section D* shows that OT_{Vmax} values have greater temporal consistency compared with traditional bipolar values as shown by their contrasting CoV. We used a HME with Random Intercept (RI) model test for Sections A–C to determine statistical significance of the absolute differences of voltage values. **S** indicates that there is a statistically significant difference between voltage values while **NS** indicates that there is not. For Section D, we used a standard paired *t*-test to assess the statistical difference between the CoV values of bipolar and omnipolar values with a 95% confidence interval. Comparisons with *P*-values that were below 0.05 ($P \leq 0.05$) have significant differences.

AC, across; AL, along; CoV, coefficient of variation; HME, hierarchical mixed effect; OT_{Vmax}, omnipolar voltage values; std err, standard error; Vpp, voltage peak-to-peak.

infarcted areas. Absolute Vpp difference between bipolar AL (4.88 ± 0.95 mV) and bipolar AC (4.94 ± 0.95 mV) was calculated as (0.07 ± 0.23 mV) over healthy areas. Absolute Vpp difference between bipolar AL (0.53 ± 0.09 mV) and bipolar AC (0.52 ± 0.09 mV) was calculated as (0.02 ± 0.06 mV) over infarcted areas. Although the numerical differences between bipolar AL and AC Vpps for both comparisons were statistically non-significant, *Figure 1B* and *C* illustrates sample bipolar AL and AC EGMs over healthy and scar area as well as the visual differences between voltage maps created with bipolar AL and AC configuration, i.e. maps obtained with different bipolar configurations with identical electrode spacing will look different from each other despite mapping the exact same substrate. *Table 1* (Section A) shows a summary of the numerical findings.

OT_{Vmax} provide higher voltage peak-to-peak values than traditional bipoles

OT_{Vmax} substrate maps have larger Vpp values than the substrate maps individually derived from AL and AC bipolar orientations over both healthy and infarcted areas for all pigs. Over healthy areas, OT_{Vmax} Vpp values are larger than AL bipoles by 27% (6.64 ± 0.95 mV vs. 4.87 ± 0.95 mV) and AC bipoles by 26% (6.64 ± 0.95 mV vs. 4.94 ± 0.95 mV). Over infarcted areas, OT_{Vmax} Vpp values are also larger than AL bipoles by 23% (0.69 ± 0.08 mV vs. 0.53 ± 0.08 mV) and AC bipoles by 27% (0.69 ± 0.08 mV vs. 0.51 ± 0.08 mV). Numerical differences between bipolar AL and AC Vpps and OT_{Vmax} were determined to be statistically significant within a 95% confidence interval which shows that OT_{Vmax} values do provide higher Vpp values than traditional bipoles. Sample EGMs for both OT and bipoles are shown in *Figure 1B* and their corresponding voltage maps in *Figure 1C*. A summary of the numerical results are shown in *Table 1* (Section B).

OT_{Vmax} values are larger and correlated to Max-Bi

OT_{Vmax} Vpp values are highly correlated with Max-Bi obtained from either AL or AC configurations, for all pigs. Correlations between OT_{Vmax} Vpp values and Max-Bi Vpp values were calculated as 0.99 over both healthy and infarcted areas as shown in *Table 1* (Section C). Importantly, OT_{Vmax} Vpp values are still larger than Max-Bi Vpp values over healthy areas by 10% (6.64 ± 0.95 mV vs. 5.99 ± 0.95 mV) and over infarcted areas by 8% (0.69 ± 0.08 mV vs. 0.64 ± 0.08 mV). Scatter plots for both myocardial conditions as shown in *Figure 3* illustrates this relationship.

Omnipoles provide better beat-to-beat voltage consistency than traditional bipoles

During sinus rhythm for an average of 10 beats from all pigs, mean CoV values of omnipoles are lower than those of bipoles by 47% in healthy areas (0.17 ± 0.12 vs. 0.32 ± 0.16, $P < 0.01$) and by 39% in infarcted areas (0.19 ± 0.10 vs. 0.31 ± 0.13, $P < 0.01$) as shown in *Figure 4* and *Table 1* (Section D). This indicates that OT_{Vmax} exhibit more consistent beat-to-beat Vpp values than traditional bipoles.

Substrate maps derived from omnipoles are denser than substrate maps from along and across bipoles

Recorded mapping segments have an average duration of 37.7 ± 9.3 min. Within each pig and for same mapping duration, OT_{Vmax} substrate maps are denser compared to traditional bipolar substrate maps. OT_{Vmax} maps are denser by 36.7% than bipolar maps (32.74 ± 5.24 points/cm^2 vs. 20.71 ± 4.72 points/cm^2) for all pigs as shown in *Figure 5*. This finding is inherent to the number of mapping points obtained in each acquisition during mapping.

Omnipolar substrate maps better delineate infarcted areas maps than bipolar substrate maps

Table 2 summarizes the comparison between the measurements of the surface area of infarction from MR-LGE images and low-voltage areas of substrate maps created from both bipolar orientations, AL and AC, and OT_{Vmax} for two pigs. We show that low-voltage areas from OT_{Vmax}-based substrate maps were closer in value with the surface area of endocardial infarction based on MR-LGE images compared with either bipolar substrate maps in both pigs. These results indicate that OT_{Vmax}-based substrate maps could better delineate infarcted areas within the endocardium compared with traditional orientation-dependent bipolar substrate maps which could overestimate the span of infarction and hence produce larger low-voltage areas. Supplementary material online, *Figure S3* illustrates the concept and the ability of OT_{Vmax} to detect surviving endocardial bundles.

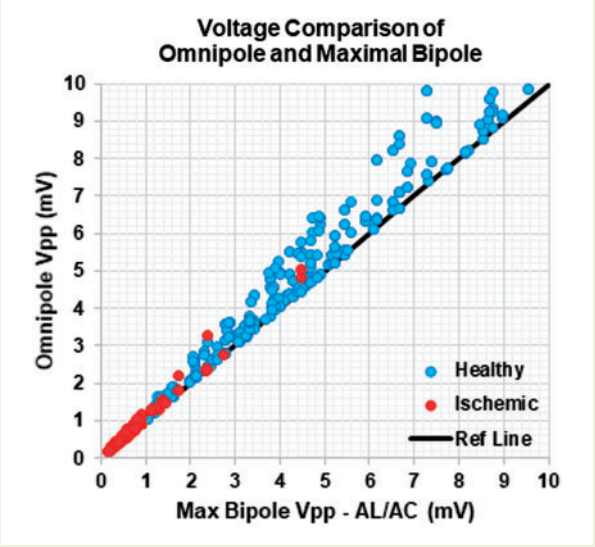

Figure 3 Relationship of OT_{Vmax} and Max-Bi. A scatter plot shows the correlation between OT_{Vmax} values and the Max-Bi values from any orientation, AL or across AC, within the Advisor™ HD Grid over both healthy and infarcted areas. As shown in *Table 1*, Section C, that OT_{Vmax} still offers an advantage (by over 10% on healthy areas and 8% on infarcted areas) over traditional bipolar voltage values even if the Max-Bi was chosen for mapping. AC, across; AL, along; Max-Bi, maximum bipolar; Vpp, voltage peak-to-peak.

Discussion

Our main findings from *in vivo* porcine studies using OT with an equispaced catheter array are as follows: (i) OT_{Vmax} has larger Vpp values compared with conventional Bi_{EGM} along any direction; (ii) beat-by-beat, OT_{EGMs} and OT_{Vmax} are more consistent than Bi_{EGMs} and Max-Bi; (iii) OT_{Vmax}-based substrate maps have higher mapping point densities, hence greater mapping resolution, than Bi_{EGM}-based substrate maps from any orientation; and lastly, (iv) OT could potentially provide better estimation of the span of endocardial infarcted areas compared to traditional bipolar mapping.

Novel omnipolar vs. traditional bipolar mapping

Bipolar-electrograms have been shown to be extremely susceptible to the angle of incidence of a wavefront with respect to recording electrodes while OT_{EGMs} have been previously shown to provide catheter/wave orientation-independent measurements. The key difference between conventional Bi_{EGMs} and OT_{EGMs} lies in the fact that OT takes advantage of the local E-field generated along the endocardial surface using equally spaced electrodes to obtain physiologically reproducible measurements. OT generates information similar to an ECG QRS vectorcardiogram only it is specific and local to areas within the myocardium.

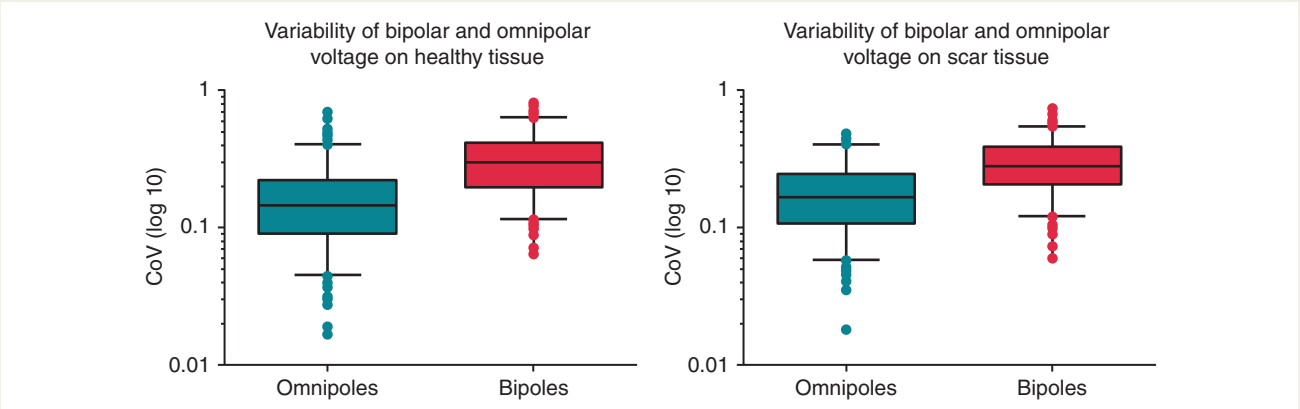

Figure 4 Beat-by-beat value of OT_{Vmax} is less variable compared with traditional bipoles. Boxplots showing comparison of the CoVs for OT_{Vmax} and traditional bipolar voltage values from any orientation for over 10 beats over healthy and infarcted areas. OT_{Vmax} offer less variable values over time compared with traditional bipoles which we have previously shown to be greatly influenced by catheter orientation. CoV, coefficient of variation.

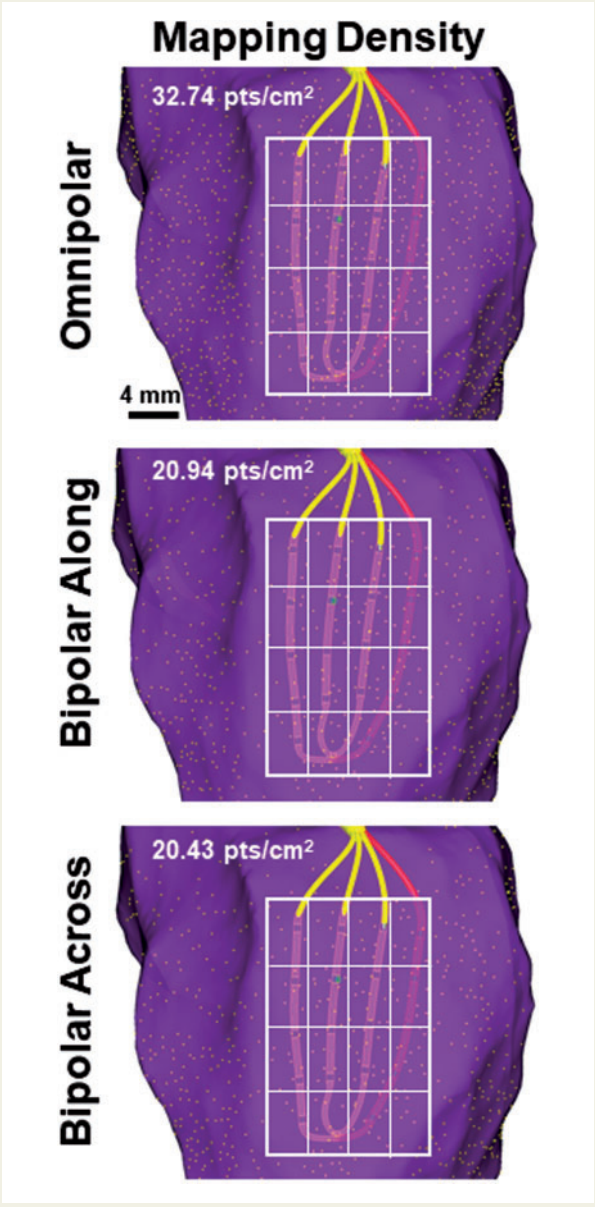

Figure 5 Omnipolar methodology provides denser voltage maps compared with traditional bipoles using the Advisor™ HD Grid. Over the same mapping areas and the same mapping time, compared to traditional bipoles, omnipoles provides greater number of mapping points availing denser voltage maps which could give extra details about the myocardium being mapped. On average, omnipolar maps provide 36% denser maps than both bipolar maps, from either direction using the Advisor™ HD Grid. Bipoles from any direction only uses a maximum of 12 mapping points while omnipoles could provide a maximum of 36 mapping points because of the clique arrangements within the catheter grid.

Specific to this work, the overall differences in Vpp between the AC and AL Bi_{EGMs} were found to be non-significant which may be counterintuitive. The reason for this is as follows. In an ideal case, where a catheter has a fixed position and senses a wavefront along a specific direction, Bi_{EGM} Vpps AL and AC will give different values, as has been shown with mathematical models by Beheshti *et al.*[11]; however, when mapping an entire heart chamber with catheter positions always changing with respect to a wavefront, the population of AL and AC Bi_{EGMs} Vpp measurements will be similar to each other yielding non-statistically significant difference.

The importance of having OT_{EGMs} and OT_{Vmax} is underscored by the following observations made on Bi_{EGM} maps derived from AL and AC. Highlighted in *Figure 1* are specific areas in which Bi_{EGM} Vpps greatly differ. Bi_{EGMs} at one orientation could erroneously indicate that certain areas of the substrate are diseased but if examined at another orientation they are not. This, coupled with the ever-changing position of catheters within a heart chamber, could produce highly inconsistent substrate maps. Therefore, interpretation of such maps and a clinician's treatment strategy could be heavily influenced by catheter orientation. Omnipolar EGMs, and its corresponding OT_{Vmax} values, could aid to improve substrate mapping by providing physiologically relevant and consistent measurements independent of catheter orientation. This is supported by the fact that on the same areas of the OT_{EGM}-based substrate maps, only the higher Vpp values are mapped, if not the highest. We validate this claim by presenting Max-Bi_{EGM}, a directly measured Bi_{EGM} with the largest Vpp, Max-Bi, from any orientation to be maximally correlated to both OT_{EGMs} and OT_{Vmax}. This type of an approach could help identify channels of conduction into the dense scar critical for sustaining VT. Furthermore, beat-to-beat consistency of OT_{Vmax} values ensure that substrate map profiles are maintained.

OT was originally introduced by Deno *et al.*[5] to utilize four-electrode cliques within the Advisor™ HD Grid to provide a total of nine measurement points at particular areas at any time. This is to establish the theoretical concept of OT with a model of a uniform TW. However, we proposed the use of three-electrode cliques to maximize the use of catheter grid arrays under the OT paradigm, providing a total of 36 measurement points. This is a still valid approach since the examination of a 3D E-field requires a minimum of three points. This allowed us to significantly increase the mapping resolution of OT used with an equi-spaced electrode array, completely mapping the endocardium in less time compared to its four-electrode clique version and its linear catheter counterparts.

Another traditional tool for substrate analysis is a LAT map which allows for global tracking of wave propagation within the heart chamber. Here, we provide additional comparison of LAT maps generated from Bi_{EGMs} and OT_{EGMs} LAT maps generated using traditional Bi_{EGMs}, when compared with LAT maps generated with OT_{EGMs} show similar profiles as shown in Supplementary material online, *Figure S2*. This is because OT_{EGMs} are bipole-like EGMs, that they provide local information only they are orientation independent. Unlike unipolar EGMs, which are also orientation-independent, OT_{EGMs} are more resilient to far-field noise which could greatly influence the creation of unipole-based LAT and substrate maps.[12–15] The ability of OT_{EGMs} to depict the 3D intramural structure of the scar remains to be proven at this time as the normal projection of the E-field to perform such task needs further testing and validation *ex vivo* first and then *in vivo* thoroughly.

Table 2 Area comparison between low-voltage areas from electroanatomical maps and MR-LGE images of infarcted areas maps

	Total endocardial scar area (cm^2)	Total low-voltage area from OT (cm^2)	Total low-voltage area from Bi-AL (cm^2)	Total low-voltage area from Bi-AC (cm^2)
Pig 1	18.8	23.0	30.2	32.9
Pig 2	7.7	12.6	17.0	16.7

The total measured area of endocardial scars from segmented MR images are closer in value with the measured low-voltage area from orientation independent, OT-based voltage maps compared with those from any of the two orientations of bipolar-based voltage maps for both sample pigs.
AC, across; AL, along; LGE, late gadolinium enhancement; MR, magnetic resonance; OT, omnipolar methodology.

Multi-electrode vs. linear mapping catheters

A wide variety of linear mapping catheters are currently used in cardiac mapping practice with different electrode and shaft configurations, electrode spacing, and electrode size. It has been shown in a number of studies[11,16–18] that bipolar electrode spacing and electrode size could greatly influence substrate mapping profiles, hence the interpretation of the substrate and corresponding appropriate treatment strategies.[19] The authors attempted to minimize this effect by representing conventional linear mapping catheters with a spline within the Advisor™ HD Grid array. This ensures that the Bi_{EGM} and OT_{EGM} measurement comparisons are fair such that electrode size and electrode spacing are consistent across all studies.

Electrode spacing and detection of low voltage

Within the Advisor™ HD Grid array there are four orientations along which Bi_{EGMs} can be derived: AL, AC, and two opposite diagonals in-between splines. In our study, we limited our analysis only between OT_{EGMs} and AL and AC Bi_{EGMs} and their corresponding Vpp values to maintain a consistent electrode spacing (4 mm, centre-to-centre). We have not used the 'HD wave' software for any of our analysis. We did not include the Bi_{EGMs} from the two opposite diagonals in-between splines since their interelectrode spacing is different. It is important to note that OT measurements are based on E-fields, which are in the units of mV/mm and are scaled by average interelectrode distances among the bipolar electrode pairs within a clique as previously introduced by Haldar *et al.*[7] and Magtibay *et al.*[8]

Re-examination of the Bi_{EGM} Vpp threshold for determining diseased areas within the ventricular myocardium as many new types of catheters (multielectrode or linear, large or small electrodes) are created is of importance. The case of Advisor™ HD Grid array with the OT methodology is no different. Magtibay *et al.*[8,20] attempted to adopt a new voltage threshold specifically for OT_{Vmax} values derived from a 56-channel (2-mm interelectrode spacing) grid array used in *ex vivo* fixed epicardial mapping of isolated porcine hearts. They came up with OT_{Vmax} values $\geq$2.0 mV for healthy tissues, between 1.5 mV and 2.0 mV for tissues at the scar border, and $\leq$1.5 mV for dense scar. However, the authors followed the standard <1.5 mV voltage threshold for this *in vivo* study since a voltage threshold for a 4-mm equi-spaced grid array has not been previously determined. Using this threshold value, we showed that an OT_{Vmax}-based substrate map depicts a closer representation of the endocardial span of the infarcted areas compared with the traditional Bi_{EGM}-Vpp-based substrate maps from any orientation.

Limitations

As with any multielectrode catheter, tissue-electrode contact could be an issue with the Advisor™ HD Grid array. However, in keeping with *ex vivo* findings where catheter contact was standardized the *in vivo* findings of this work still show the same results. As for the derivation of OT in this case, it is robust such that OT_{Vmax} retains its maximal value since the interelectrode distances within an OT clique is taken in to consideration when measuring E-field parameters. We did not pursue analysis of the normal projection of the E-field for 3D mapping capabilities of OT in this manuscript.

Correlations between MR-LGE images of scar and substrate maps were calculated only from two out of the seven pigs with MI mapped. Majority of the MR data collected from pigs were not sufficient for proper registration with corresponding electroanatomical maps since they lacked robust landmarks (i.e. aortic root and/or valves). Furthermore, a histological examination of the MI was not performed as a trade-off to maintain the size and shape of the heart slices so that they are comparable and easily matched with their corresponding MR-LGE image slices. Future *in vivo* studies should involve detailed histological analysis of the MI substrate to detect surviving myocardial tissues within diseased areas to compare with areas of OT_{Vmax}- and Bi_{EGM}-Vpp-based substrate maps.

Conclusions

In an *in vivo* pig infarct model, substrate mapping with OT using an equi-spaced electrode grid array produces local, orientation-independent, physiologically relevant electrograms which may improve delineation of diseased areas and aid to optimize treatment strategies for ventricular arrhythmias.

Supplementary material

Supplementary material is available at *Europace* online.

Acknowledgements

The authors would like to thank Antonio Berruezo and Lluis Serra for the help provided by analyzing our MRI data with ADAS VT.

Funding

This work was funded by Abbott Laboratories, St. Paul, MN, USA.

Conflict of interest: D.C.D. is an employee of Abbott Laboratories. K.N. and S.M. have received consultant honoraria from Abbott Laboratories and Biosense Webster. M.L. is one of the owners of BlueRock Therapeutics. A.P.S. has received consultant honoraria from Abbott Laboratories. K.M, S.N., A.B., P.F.H.L., C.L., B.Q., R.R., H.M., L.B., and N.G., have no disclosures.

References

1. Anter E, Josephson ME. Bipolar voltage amplitude: what does it really mean? *Heart Rhythm* 2016;**13**:326–7.
2. Josephson ME, Anter E. Substrate mapping for ventricular tachycardia. *JACC Clin Electrophysiol* 2015;**1**:341–52.
3. Tung R, Josephson ME, Bradfield JS, Shivkumar K. Directional influences of ventricular activation on myocardial scar characterization: voltage mapping with multiple wavefronts during ventricular tachycardia ablation. *Circ Arrhythm Electrophysiol* 2016;**9**:e004155.
4. Sacher F, Field ME. Activation wavefront direction and the voltage map: a matter of perspective? *Circ Arrhythm Electrophysiol* 2016;**9**:e004448.
5. Deno DC, Balachandran R, Morgan D, Ahmad F, Massé S, Nanthakumar K. Orientation-independent catheter-based characterization of myocardial activation. *IEEE Trans Biomed Eng* 2017;**64**:1067–77.
6. Massé S, Magtibay K, Jackson N, Asta J, Kusha M, Zhang B *et al.* Resolving myocardial activation with novel omnipolar electrograms. *Circ Arrhythm Electrophysiol* 2016;**9**:e004107.
7. Haldar SK, Magtibay K, Porta-Sanchez A, Massé S, Mitsakakis N, Lai PFH *et al.* Resolving bipolar electrogram voltages during atrial fibrillation using omnipolar mapping. *Circ Arrhythm Electrophysiol* 2017;**10**:e005018.
8. Magtibay K, Masse S, Asta J, Kusha M, Lai PFH, Azam MA *et al.* Physiological assessment of ventricular myocardial voltage using omnipolar electrograms. *J Am Heart Assoc* 2017;**6**:e006447.
9. Soejima K, Stevenson WG, Maisel WH, Sapp JL, Epstein LM. Electrically unexcitable scar mapping based on pacing threshold for identification of the reentry circuit isthmus: feasibility for guiding ventricular tachycardia ablation. *Circulation* 2002;**106**:1678–83.
10. Ghugre NR, Pop M, Thomas R, Newbigging S, Qi X, Barry J *et al.* Hemorrhage promotes inflammation and myocardial damage following acute myocardial infarction: insights from a novel preclinical model and cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2017;**19**:50.
11. Beheshti M, Magtibay K, Massé S, Porta-Sanchez A, Haldar S, Bhaskaran A *et al.* Determinants of atrial bipolar voltage: interelectrode distance and wavefront angle. *Comput Biol Med* 2018;**102**:449–57.
12. Nguyen UC, Maffessanti F, Mafi-Rad M, Conte G, Zeemering S, Regoli F *et al.* Evaluation of the use of unipolar voltage amplitudes for detection of myocardial scar assessed by cardiac magnetic resonance imaging in heart failure patients. *PLoS One* 2017;**12**:e0180637.
13. Chrispin J, Keramati AR, Assis FR, Misra S, Zghaib T, Berger RD *et al.* Correlation of right ventricular multielectrode endocardial unipolar mapping and epicardial scar. *Pacing Clin Electrophysiol* 2018;**41**:345–52.
14. Venlet J, Piers SRD, Kapel GFL, de Riva M, Pauli PFG, van der Geest RJ *et al.* Unipolar endocardial voltage mapping in the right ventricle: optimal cutoff values correcting for computed tomography-derived epicardial fat thickness and their clinical value for substrate delineation. *Circ Arrhythm Electrophysiol* 2017;**10**:e005175.
15. Polin GM, Haqqani H, Tzou W, Hutchinson MD, Garcia FC, Callans DJ *et al.* Endocardial unipolar voltage mapping to identify epicardial substrate in arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Heart Rhythm* 2011;**8**:76–83.
16. Tschabrunn CM, Roujol S, Dorman NC, Nezafat R, Josephson ME, Anter E. High-resolution mapping of ventricular scar: comparison between single and multielectrode catheters. *Circ Arrhythm Electrophysiol* 2016;**9**:e003841.
17. Anter E, Tschabrunn CM, Josephson ME. High-resolution mapping of scar-related atrial arrhythmias using smaller electrodes with closer interelectrode spacing. *Circ Arrhythm Electrophysiol* 2015;**8**:537–45.
18. Berte B, Relan J, Sacher F, Pillois X, Appetiti A, Yamashita S *et al.* Impact of electrode type on mapping of scar-related VT. *J Cardiovasc Electrophysiol* 2015;**26**:1213–23.
19. Acosta J, Penela D, Andreu D, Cabrera M, Carlosena A, Vassanelli F *et al.* Multielectrode vs. point-by-point mapping for ventricular tachycardia substrate ablation: a randomized study. *Europace* 2018;**20**:512–9.
20. Magtibay K, Massé S, Asta J, Lai PFH, Azam MA, Porta-Sanchez A *et al.* Isthmus and lesion gap: the incremental value of omnipoles over high density mapping. *Heart Rhythm* 2017;**14**:S528. (Abstract).