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The influence of fat thickness on the human epicardial bipolar electrogram characteristics: measurements on patients undergoing open-heart surgery

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Aims Reference values exist for endocardial but not for epicardial (EPI) substrate mapping in cases of cardiomyopathy-associated ventricular tachycardia. We sought to establish such values for EPI electrogram voltage, including areas with overlying fat.

Methods and results Ten patients (six males) undergoing cardiac surgery were studied. After opening the pericardium, the distal bipole of an electrophysiology catheter was placed tangential to the EPI surface to obtain an electrogram recording. The bipole was tangentially rotated 90° and the higher of the two amplitudes (mV) was taken as the local amplitude. Recordings were taken from normal left and right ventricular myocardium ($n = 26$ data points each), over thick ($\geq$0.5 cm) fat at both ventricular bases ($n = 16$) and thin ($<$0.5 cm) fat at the mid-ventricular level ($n = 32$). A total of 100 recordings (mean 10/patient) were analysed. Four patients underwent valvular surgery, three bypass surgery, and three combined procedures. Mean age was 61.7 $\pm$ 10.4 years and mean left ventricular ejection fraction was 46 $\pm$ 12%. Electrogram amplitude was inversely related to EPI fat thickness. Over thick fat, 31% of recordings were $<$0.5 mV.

Conclusion Human EPI electrogram amplitude varies by ventricular chamber and significantly by EPI fat thickness. A cut-off of 0.5 mV to define 'scar' will include normal areas with thick overlying fat. EPI substrate maps should include data on EPI fat thickness for higher specificity.

Keywords Epicardial • Electrogram amplitude • Ventricular tachycardia • Epicardial fat • Ablation

Introduction

Cardiomyopathy, both ischaemic and non-ischaemic, is frequently associated with malignant ventricular tachyarrhythmias. As more patients survive longer with the advent of the implantable cardioverter-defibrillator, ablative therapy for ventricular tachycardia (VT) is assuming a more central role in the management of such patients.[1] Substrate-guided approaches to VT ablation have evolved, particularly when dealing with haemodynamically unstable rhythms.[2] While endocardial scarring is more prominent in ischaemic cardiomyopathy,[3] non-ischaemic cardiomyopathy is characterized by an equal distribution of endocardial and epicardial (EPI) electrogram abnormalities.[4] Recent data indicate that sustained VT originates from the epicardium in a substantial proportion of patients with non-ischaemic cardiomyopathy.[3,5–8] Substrate mapping for VT relies on identifying myocardial scar to guide therapy. Endocardial data collected from six healthy volunteers[2] and from swine[9] provide the basis for using the currently accepted cut-offs to define normal and abnormal myocardium, and the borderline zone in between.

Epicardial VT ablation utilizes the same concept as the endocardial procedure, but the percutaneous technique for pericardial access and epicardial mapping was only introduced by Sosa *et al.*[7] in 1996.

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In patients with non-ischaemic cardiomyopathy and sustained VT, the endocardial substrate is mainly located in the basal regions of the left ventricle[10] and abnormal, low-voltage EPI electrograms have been demonstrated in such patients to be more extensive than endocardial scarring,[8,11] often involving the base of the heart. However, fat thickness is particularly more pronounced at the base of the heart, raising concerns about the accuracy of current epicardial mapping techniques. No reference values exist for epicardial surface electrograms despite the different nature of the epicardial mapping procedure compared with endocardial mapping, namely, the absence of a blood pool and the presence of, frequently thick, epicardial fat.

This study seeks to establish reference values for the epicardial bipolar electrogram over non-scarred myocardium of both ventricles as well as overlying epicardial fat of varying thickness.

Methods

The study was approved by the institutional review board and all subjects gave written informed consent. Ten patients (six males) undergoing cardiac surgery were asked to participate in the study. After the parietal pericardium was opened and before the patient was placed on cardiopulmonary bypass, the distal bipole of a sterile, 6 Fr electrophysiology catheter, distal electrode 1 mm, proximal electrode 2 mm, and 5 mm inter-electrode distance (Explorer 360^{TM}, Boston Scientific Corp., Natick, MA, USA), connected to a pacing system analyzer (Model 2090, Medtronic Inc., Minneapolis, MN, USA), was gently placed by the surgeon tangential to the EPI surface (*Figure 1*). The recording catheter was connected to a quadripolar connector (Model TJ-101, Nexus Inc., Stanford, CT, USA), the distal bipole of which was connected via pacing cables to the pacing system analyzer. A stable, 'unfiltered' (frequency response 0.5–250 Hz on paper) analogue electrogram recording was obtained. Then, the bipole was rotated 90°, tangential to the EPI surface, and the higher of the two peak-to-peak amplitudes (mV) was taken as the local electrogram amplitude. As the amplitude of a bipolar electrogram is influenced by the direction of wavefront propagation,[12] we made two bipolar recordings at each site, one perpendicular to the other but both tangential to the EPI surface, and recorded the higher of the two readings as the local electrogram amplitude. The orientation of the catheter, as shown in *Figure 1*, was perpendicular to the AV groove then rotated up to 90° to become parallel with the AV groove. Peak-to-peak electrogram amplitude was reported automatically by the pacing system analyzer and confirmed manually in 20 (20%) randomly selected recordings for accuracy. The thickness of the epicardial fat layer was assessed by the surgeon guided by the electrophysiologist. A sterile ruler was placed perpendicular to the surface of the heart at the level of the edge of the fat layer, which represented the thinnest part, and a measurement of its thickness made. The electronic calipers of the pacing system analyzer were used to measure electrogram duration. The minimum distance between two markers was 5 ms at a paper speed of 100 mm/s, thus measurements were made in increments of 5 ms. We used only one type of catheter for consistency.

Statistical analysis

All analyses were performed using SAS® 8.0 statistical software (SAS Institute Inc., Cary, NC, USA). ANOVA was used to test for differences between the means of continuous variables and a two-tailed *P*-value <0.05 was considered statistically significant. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

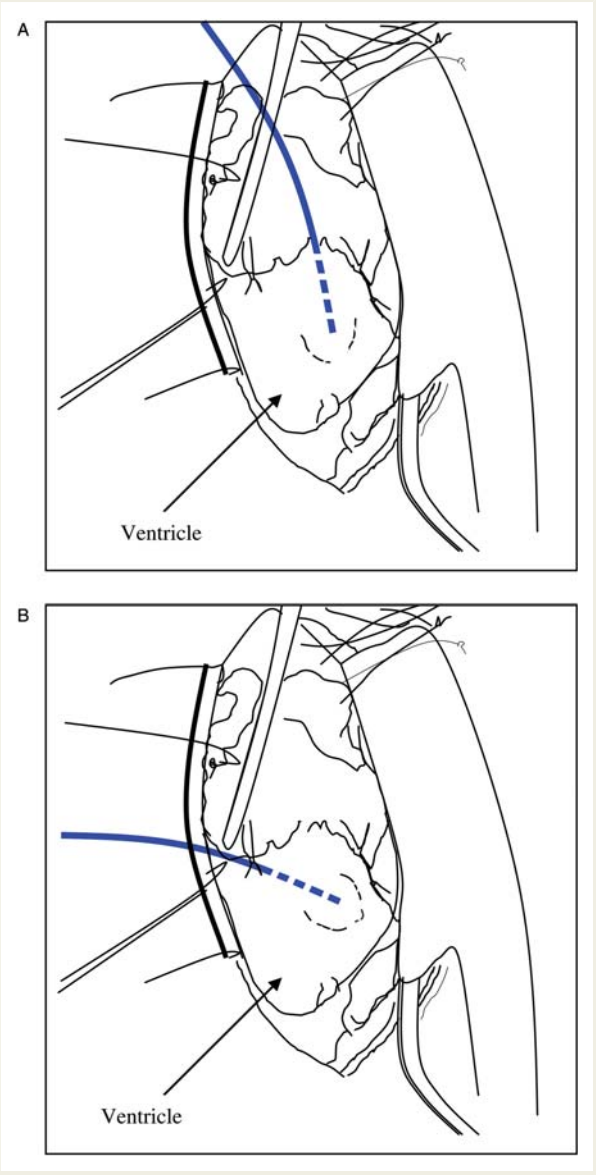

Figure 1 Schematic depicting a quadripolar electrophysiology catheter (in blue) placed by the surgeon tangential to the exposed epicardial surface, in this case of the right ventricle. (*A*) The catheter is perpendicular to the atrioventricular groove. (*B*) The same patient but the catheter has been rotated to a position more parallel to the atrioventricular groove, depicted here at approximately 60° to the original position. Rotation of the catheter did not markedly affect electrogram amplitude as discussed in the text.

Results

Four patients underwent valvular surgery, three coronary artery bypass surgery, and three combined procedures. The mean age was 61.7 ± 10.4 years. The mean left ventricular ejection fraction

Table 1 Patient characteristics

Patient no.	Sex	Age (years)	LVEDD (mm)	EF (%)	QRS duration (ms)	Underlying disease
1	M	57	64	35	154	Severe MR, NICM
2	M	52	60	35	106	CAD, ICM
3	M	51	70	35	100	CAD, ICM, Severe MR
4	F	57	37	50	86	Severe MR
5	M	74	59	30	98	CAD, ICM, Severe MR
6	F	68	50	55	116	CAD, Severe AS
7	M	51	46	40	96	CAD
8	F	71	44	60	86	CAD
9	F	79	40	60	70	Severe MR
10	M	57	53	60	100	Severe MR

M, male; F, female; LVEDD, left ventricular end-diastolic dimension; EF, ejection fraction; MR, mitral regurgitation; NICM, non-ischaemic cardiomyopathy; CAD, coronary artery disease; ICM, ischaemic cardiomyopathy; AS, aortic stenosis.

Table 2 Epicardial electrogram voltage and duration

	Left ventricle (mid/basal ventricle; $n = 26$)	Right ventricle (mid/basal ventricle; $n = 26$)	Thin fat (mid-ventricle; <0.5 cm; $n = 32$)	Thick fat (basal ventricle; ≥0.5 cm; $n = 16$)	ANOVA, *P*-value
Mean electrogram amplitude (mV)	15.6 ± 7.6	11.1 ± 6.0	6.4 ± 3.2	1.9 ± 1.4	<0.0001*
Mean electrogram duration (ms)	44.4 ± 7.4	47.1 ± 9.0	43.6 ± 8.2	45.8 ± 6.4	0.46

*P-value for all inter-group comparisons <0.05.

was 46 ± 12%, and the mean left ventricular end-diastolic dimension was 52.3 ± 11.0 mm. Nine patients were in sinus rhythm (see *Table 1* for detailed patient characteristics). Recordings were taken from the epicardial surface of left and right ventricular myocardium ($n = 26$ data points per ventricle) adjacent to but not overlying the basal fat at a basal or mid-ventricular level, as well as over thick (≥0.5 cm) fat at both ventricular basal regions ($n = 16$; nine over RV and seven over LV) and thin (<0.5 cm) fat at the mid-ventricular level ($n = 32$, equally distributed over both ventricles). A total of 100 electrogram recordings (mean 10 per patient) were available for analysis, and to avoid over-representation of a particular patient, we recorded relatively equally (range 9–12 samples) from all patients. Rotation of the catheter tangential to the EPI surface did not markedly affect electrogram amplitude, with variation below 10% observed. The pacing system analyzer used provides output on graded paper (increments of 5 mV). The peak-to-peak amplitude of the raw signal was automatically measured in all readings and independently confirmed by manual measurement with calipers against the scale on the paper in 20 randomly selected recordings. We found the automatic measurement to be highly accurate, with no changes made to the automatic reading as a result of discrepancy.

Electrogram amplitude varied significantly by ventricular chamber; mean electrogram amplitude was 15.6 ± 7.6 mV over the left ventricle compared with 11.1 ± 6.0 mV over the right ventricle ($P = 0.02$). Electrogram amplitude was found to be inversely related to EPI fat thickness; mean electrogram amplitude was 6.4 ± 3.2 mV over thin fat compared with 1.9 ± 1.4 mV over thick fat ($P < 0.0001$). Over thick fat, 5 of 16 (31%) recordings were <0.5 mV. These recordings over thick fat had zero amplitude, where no signal was obtained.

Importantly, electrogram duration did not vary by chamber over which sampling was performed or the underlying fat thickness, nor was there evidence of electrogram fractionation overlying areas of thick or thin fat (*Tables 2* and *3*).

Discussion

To our knowledge, this is the first report of epicardial electrogram amplitude and duration, measured under direct visualization, in a group of patients without a history of VT and with relatively preserved left ventricular systolic function, undergoing open-heart surgery. We used a standard quadripolar electrophysiology catheter with 5 mm inter-electrode spacing. The mapping catheter was placed tangential to the EPI surface of normal myocardial tissue as assessed by the surgeon, guided by the electrophysiologist (M.M.S.). No patient had Q waves on 12-lead ECG and only one patient had regional hypokinesis of the inferior wall on echocardiography, an area that was not sampled to avoid transmurally scarred myocardium. Our data show that EPI electrogram amplitude varies

Table 3 Epicardial electrogram amplitude values according to each sampled site in milliVolts ($n = 100$ points)[a]

Left ventricle (mid/basal ventricle; $n = 26$)	Right ventricle (mid/basal ventricle; $n = 26$)	Thin fat (mid-ventricle; <0.5 cm; $n = 32$)	Thick fat (basal ventricle; ≥0.5 cm; $n = 16$)
5.8	3.8	3.1	0.0
6.0	5.1	3.1	0.0
6.0	5.3	3.1	0.0
6.4	6.1	3.2	0.0
6.5	7.3	3.4	0.0
7.4	8.0	3.5	2.3
8.5	8.1	3.5	2.3
9.0	8.1	3.5	2.5
10.1	8.5	3.5	2.5
11.4	8.5	4.2	2.5
12.5	8.6	4.2	2.5
13.4	8.8	4.6	2.6
13.9	8.9	5.1	3.1
16.4	9.2	5.1	3.3
17.2	9.2	5.4	3.6
17.5	9.6	5.4	3.8
18.7	10.0	5.4	
20.7	10.0	6.0	
21.4	12.1	6.1	
22.3	12.9	6.7	
23.0	13.8	7.1	
23.4	14.0	7.6	
23.6	19.6	7.9	
26.9	21.7	8.3	
27.4	25.1	8.4	
29.9	27.5	8.5	
		9.4	
		9.5	
		11.2	
		12.5	
		13.1	
		14.6	

[a]Values are arranged in ascending order.

significantly by the ventricular chamber mapped (LV > RV) and by EPI fat thickness (thick fat < thin fat). Electrogram duration, however, did not vary by chamber or fat thickness. Of particular importance is the observation that thick fat (≥0.5 cm), generally located at basal right and left ventricular regions, is associated with dramatically attenuated electrogram amplitudes. This is despite the use of a catheter with a 5 mm inter-electrode distance, which is more likely to register far-field signals than a catheter with a shorter inter-electrode spacing. We acquired 'unfiltered' signals to render as pure an electrogram as possible. With this frequency-response setting, the low-pass filter is similar to that used clinically, but the high-pass filter (set at 0.5 Hz) would allow for lower frequency components than those recorded clinically and may affect electrogram duration but would not significantly affect electrogram amplitude. Notably, raising the high-pass filter to 30 Hz did not alter electrogram characteristics, but removed baseline wander.

Epicardial mapping in cases of VT has a long history. In 1978, Spielman *et al.*[13] published the results of endocardial and epicardial mapping in dogs and showed discrepancies between endocardial site of VT origin and epicardial breakthrough sites, and in 1980 Josephson *et al.*[14] published their experience with pre-operative endocardial mapping followed by intraoperative epicardial and endocardial mapping in humans and highlighted the limitations of epicardial-only intraoperative mapping, which was the standard at that time. Their work, however, focused on locating the VT site of origin rather than describing the electrogram characteristics of the epicardial surface and its relationship to fat thickness.

Given that patients with non-ischaemic cardiomyopathy tend to have endocardial scar in basal regions[2] and the same group of patients has a predilection to EPI VT components,[3,5–8,11] it is critical to improve our mapping techniques in order to better characterize the epicardial substrate in this subgroup of patients. d'Avila *et al.*[15] showed in an animal model the effect of epicardial fat on epicardial lesion formation using radiofrequency energy. In areas with overlying epicardial fat, there was a clear attenuating effect on lesion depth. They concluded that cooled-tip RF ablation generates epicardial lesions more effectively than standard RF ablation and was particularly important in areas with overlying epicardial fat.

A reliance on current techniques and cut-off values would overestimate the extent of epicardial abnormal tissue, particularly in the basal regions. In fact, based on our data, even if 0.1 mV was used to define scar, inaccurate information would be obtained about the presence of scar.

Therefore, knowledge of the location and thickness of epicardial fat, along with attention to electrogram characteristics such as prolonged duration and fractionation, will increase the specificity of epicardial substrate maps and potentially improve epicardial VT ablation outcomes.

Limitations

The study group represented consecutive patients, without significant comorbidities, undergoing cardiac surgery and this is reflected in the lower than normal mean left ventricular ejection fraction. Although a limitation from the standpoint of establishing cut-off values of 'normal' patients, we believe such data to be quite representative of the patient population seen in everyday practice.

We used only one catheter type with 5 mm inter-electrode spacing for this study. The possibility that the difference in size between the distal and proximal electrodes of commercially available catheters used for both mapping and ablation may influence local electrogram characteristics, and thus render our findings less applicable to current mapping techniques, cannot be excluded, but is unlikely. The accuracy of fat thickness measurements is a limiting factor. While there would exist some overlap at the 0.5 cm cut-off, we feel confident that this cut-off segregated the thick basal fat from the mid-myocardial fat layer that generally occurred

in the epicardial coronary vessel vicinities, providing evidence for a clear inverse relationship between fat thickness and epicardial electrogram amplitude.

Interestingly, we did not record any electrograms >0.0 mV and <1.5 mV over thick or thin fat. Therefore, we cannot provide separate percentages of electrogram amplitudes in the range of 0.5–1.5 mV or <0.5 mV over thick fat. Our raw data (*Table 3*) show the lowest electrogram amplitudes over thick fat. There are recordings of 0 mV, all of which were made over thick basal fat and from different patients. It may be possible that such areas with such very low amplitude electrograms require amplification beyond the capabilities of the recording system used. We did not perform metabolic imaging of the myocardium to exclude the presence of myocardial scar underlying the areas of thick epicardial fat and thus contributing to electrogram attenuation, as this was considered a remote possibility.

Conclusions

Human epicardial electrogram amplitude, but not duration, varies by ventricular chamber and significantly by epicardial fat thickness. Epicardial substrate maps should include data on epicardial fat thickness for higher specificity.

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Conflict of interest: none declared.

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