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Original Article

A new mapping method to estimate exit sites of ventricular arrhythmias using intracardiac echocardiography and M-mode for catheter ablation

Osamu Inaba, MD[a,b,c,*], Junichi Nitta[a], Syunsuke Kuroda[a], Masahiro Sekigawa[a], Masahito Suzuki[a], Yukihiro Inamura[a], Akira Satoh[a], Mitsuaki Isobe[b], Kenzo Hirao[c]

[a] Department of Cardiology, Saitama Red Cross Hospital, Japan
[b] Department of Cardiology, Tokyo Medical and Dental University, Japan
[c] Heart Rhythm Center, Tokyo Medical and Dental University, Japan

ABSTRACT

Background: Catheter ablation of premature ventricular complexes (PVCs) has been used as a curative therapy in many cases. Intracardiac ultrasound with a magnetic sensor probe has recently become available for catheter ablation. In this study, we assessed a new mapping method, contraction mapping, for determining the optimal ablation sites using intracardiac ultrasound and M-mode. This study sought to assess the accuracy of the new mapping method using intracardiac echocardiography.
Methods: Eighteen patients (10 males and eight females; mean age, 63 ± 12 years) with 104 mapping points diagnosed as idiopathic PVCs were included in this study. At the mapping points, the time interval from the onset of the QRS to the onset of the contraction (QRS-c-time) and the local activation time were measured using M-mode with an intracardiac echo probe and using the conventional method. The correlation between the QRS-c-time and local activation time were studied.
Results: The QRS-c-time was significantly correlated with the local activation time (activation time $= -66.8 + 0.882 *$ QRS-c-time, $R2 = 0.728$, $p < 0.0001$).
Conclusions: Contraction mapping could help determine the local activation time without the delivery of a catheter to the mapping points.
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1. Introduction

Frequent premature ventricular complexes (PVCs) occasionally induce reversible left ventricular dysfunction and adverse hemodynamic alterations [1,2], even in the absence of patient symptoms of palpitations [3]. Catheter ablation of idiopathic PVCs has been reported as a curative and more effective therapy than anti-arrhythmic medications for many cases in retrospective and prospective studies [4,5], and sometimes as an adjunct therapy in patients who have received implantable cardioverter-defibrillators or cardiac resynchronization therapy devicesand in whom non-idiopathic and fatal PVCs are reported [6–9]. For PVC ablation, three-dimensional (3D) electro-anatomical mapping systems havepreviously been available in addition to the use of conventional methods such as activation mapping and pace mapping for identifying optimal ablation sites. Furthermore, the efficacy and safety of ablation of PVCs guided by two-dimensional (2D) intracardiac echocardiography (ICE) with electroanatomical mapping has also been previously reported [10–13]. The usage of ICE

during PVC ablation procedures can enable a baseline survey of apatient's anatomy;an easier assessment of the local wall motion and abnormal structure;better identification of the catheter tip location, contact, and level of stability; and improved monitoring of complications. With the help of these devices and methods, we devised a new supplemental mapping technique, called contraction mapping, to estimate the target area for PVC ablation. This technique was based on using ICE integrated with electroanatomical mapping (CARTOSound™ system, Biosense Webster, Irvine, CA, USA) and M-mode ultrasound imaging, which istypically used for assessing cardiac contractile function, valvular disease, and abnormal intracardiac structures. The present study described the reliability of the particular method using contraction mapping to estimate a local activation time.

2. Material and methods

2.1. Methods of the contraction mapping

This mapping method was based on the hypothesis of excitation-contraction coupling, in which the ventricle muscle that contracts earlier also activates earlier electrically, so that the

* Corresponding author at: Department of cardiology, Tokyo Medical and Dental University, 1–5-45 Yushima, Bunkyo-ku, Tokyo 113-0034, Japan. Fax: +81358030133.
E-mail address: oinbcvm@tmd.ac.jp (O. Inaba).

earliest activation site can be estimated by the earliest contraction of that site. If the patients had been prescribed any antiarrhythmic drugs, they were discontinued for at least one week prior to the sessions. During the procedure, a 3D anatomical map of the ventricle was first constructed using a novel CARTOound™ (Biosense Webster, Irvine, CA, USA) technology after the insertion of an electrode catheter (Fig. 1A). An ICE probe with a CARTO navigation sensor (SOUNDSTAR®, Biosense Webster, Irvine, CA, USA) was positioned in the right atrium or right ventricle, and 3D shells of the right and left ventricles were constructed during a PVC rhythm. The second step involved identifying the time from the onset of the QRS to the onset of the local contraction (QRS-c-time) of each mapping point. The M-mode interrogation line was obtainable with 2D echocardiography concurrently with the construction of the ventricle shell (Fig. 1B). The M-mode beam was swept to map the points, and the QRS-c-time of each point was measured when PVCs appeared (Fig. 2). The onset of contraction was defined as the timing of the beginning of the myocardium movement on M-mode (Fig. 2, left, arrow). The time of data collection of the QRS-c-time of each patient was limited to 15 min after the construction of the ventricle shell. At the mapped points, landmarks were placed on the 3D anatomical map to measure the local activation time of the same points in the next step.

2.2. Activation mapping of each point

After measuring the QRS-c-time of each point, conventional activation mapping of all mapped points, of which the QRS-c-time had been measured, was performed using an ablation catheter with a navigation sensor (ThermoCool® SF, Biosense Webster, Irvine, CA, USA). Finally, the earliest activation sites were identified using activation mapping. During this mapping, lead I was selected as the reference for the mapping.

2.3. Study population and assessment of the accuracy of the contraction mapping

Twenty-two consecutive patients whohad undergone radiofrequency catheter ablation of PVCs at Saitama Red Cross Hospital were enrolled. In four of the enrolled patients, the performance of contraction mapping and activation mapping was impossible because not enough spontaneous PVCs appeared to measure the QRS-c-time and local activation time during the procedures. The remaining 18 patients (10 males and eight females, 63 ± 12 years)

with 18 idiopathic PVCs were included in this study. Their baseline characteristics, including the data from Holter monitoring and ultrasound, serum brain natriuretic peptide (BNP) level, and origin of the PVCs, were studied. The correlations between the QRS-c-time and local activation time of each of the 104 mapped points in the 18 patients were determined. All patients provided their written informed consent, and the ethics committee of Saitama Red Cross Hospital approved the study protocol.

2.4. Statistics

Continuous data are presented as mean $\pm$ standard deviation if normally distributed or as the median with an interquartile range if not normally distributed. The categorical data are presented as the count and percent. The continuous data were compared using a Student's t test when normally distributed orusing a Mann-Whitney U test when not normally distributed. The categorical data were compared usingchi-squared testacross the groups. A mixed effects model was used to study the relationship between the local activation time and QRS-c-timeto assess the accuracy of the contraction mapping. All tests were two-sided, and a p value of < 0.05 was considered statistically significant. The analyses were performed using JMP 8.0.1 software (SAS Institute Inc., Cary, NC, USA).

3. Results

Patient baseline characteristics, clinical data, and origins of the PVCs are shown in Table 1. No patients with bundle branch block or intraventricular conduction delays were included in this study, and the average QRS width during sinus rhythm was 105 ± 13 ms. The number of PVCs per day was a median of 23,902 beats (interquartile;10,210-31,979). All patients were diagnosed with idiopathic PVCs, and patients 5 and 12, who demonstrated left ventricular (LV) dysfunction and mild dilatation of the left ventricle, were suspected of having arrhythmia-induced cardiomyopathy. The average plasma BNP level was 54.5 pg/ml (38.7–82.5 pg/ml). The earliest activation sites of the PVCs were located equally on the walls of both ventricles. No complications, including cardiac tamponade, bleeding, or embolisms, occurred after the contraction mapping.
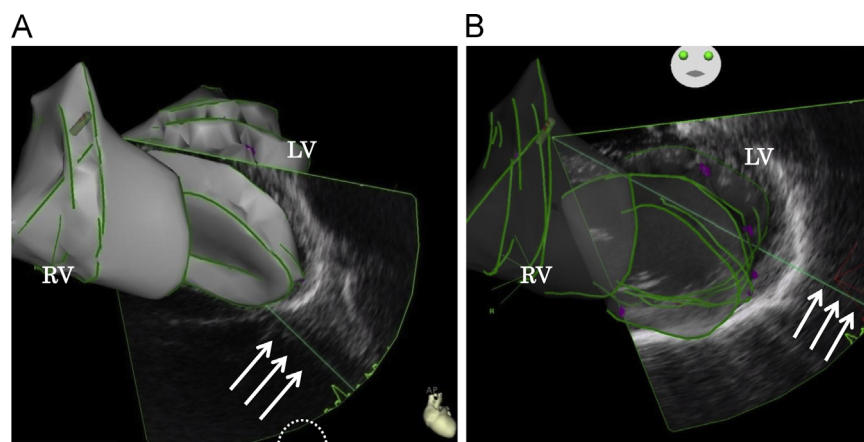
Fig. 1. A. The shell of the ventricle is constructed using an ICE probe positioned in the right ventricle. B. The M-mode interrogation line is available using two-dimensional echocardiography. Arrow; M-mode interrogation line. LV; left ventricle, RV; right ventricle.
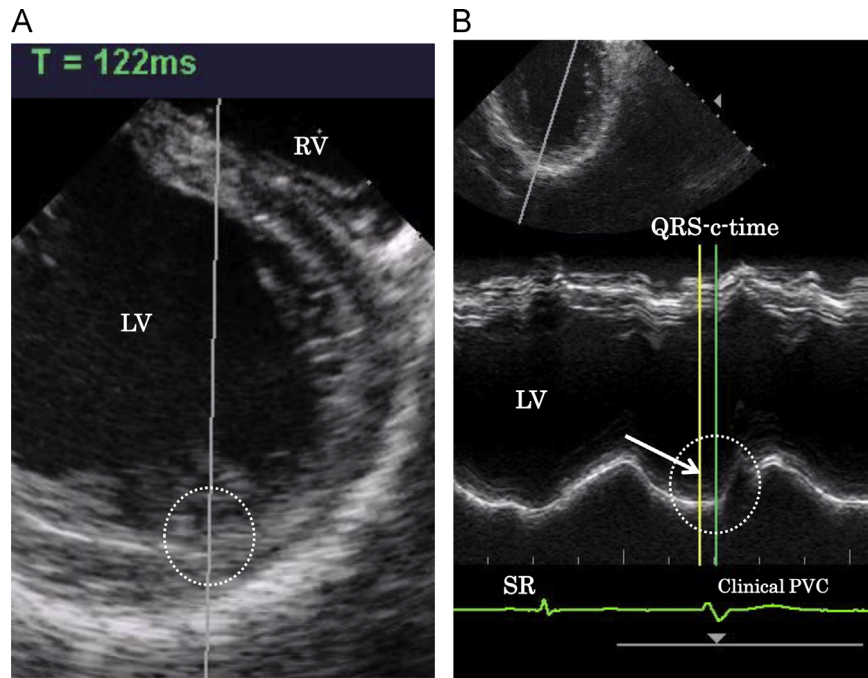
Fig. 2. A. The M-mode beam is swept to the mapped point. B. M-mode echocardiography at the mapped point is shown, and the electrocardiogram is recorded below the ultrasound image. The QRS-c-time was measured using this image. Circle; mapped point, Arrow; onset of the contraction, SR; sinus rhythm, PVC; premature ventricular contraction, other abbreviations as Fig. 1.

Table 1
Baseline characteristics.

	Age	Sex	Wt	HT	QRS in SR	Axis in SR	Number of PVCs	Total beats	PVCs width	EF	LVDd	BNP	Outcome of ablation	Origin of PVCs
Patient 1	29	0	46	168	87	74	10000	94317	150	59	43	11.3	Success	RVOT
Patient 2	79	0	46	152	91	40	32189	98429	160	65	44	41.4	Success	RVOT
Patient 3	67	1	78	162	106	-17	14500	99228	190	44	55	31.4	Success	LV inf
Patient 4	46	0	62	166	101	66	24317	111898	160	55	50	16.8	Success	RVOT
Patient 5	63	1	60	170	139	0	1389	104430	170	34	55	56.7	Recurrence	LV inf
Patient 6	74	1	72	168	113	-35	23486	96032	170	65	48	52.1	Success	LVOT
Patient 7	65	0	41	154	104	-44	37138	107260	190	71	46	38.8	Success	LCC
Patient 8	75	1	55	160	103	47	31735	95013	150	56	50	126	Success	RVOT
Patient 9	62	0	49	154	96	-13	29424	106534	160	58	42	41.8	Recurrence	APM
Patient 10	66	1	74	160	110	51	10242	111249	160	56	45	40.3	Success	MA inf
Patient 11	76	0	47	143	106	83	10113	109205	170	69	49	81.6	Success	LV ant
Patient 12	61	1	78	168	106	59	37967	119542	170	30	53	224	success	MA ant
Patient 13	67	1	66	170	93	30	47093	122164	160	54	44	75.8	Success	MA inf
Patient 14	65	1	##	170	110	29	1581	97796	160	50	63	262	Success	APM
Patient 15	53	0	50	150	89	26	31909	111561	140	71	56	38.2	Success	RV sep
Patient 16	60	1	68	180	124	90	10251	104120	200	43	51	59.8	Success	MA ant
Patient 17	61	0	72	161	107	11	25107	108000	170	59	38	76.4	Success	LVOT
Patient 18	62	1	50	158	104	30	18332	101044	170	46	48	85	Success	RVOT

Wt; body weight, HT; body height, SR; sinus rhythm, PVCs; premature ventricular complexes, EF; left ventricular ejection fraction, LVDd; left ventricular diastolic diameter, BNP; brain natriuretic peptide, RVOT; right ventricular outflow tract, LVOT; left ventricular outflow tract, LSV; left aortic sinus of Valsalva, APM; anterior papillary muscle, MA; mitral annulus.

3.1. Patient examples

3.1.1. Example patient 1

Example patient 1 was a 61-year-old male with a frequent PVC burden of over 40%. The twelve-lead electrocardiograms of the PVC, activation map, and contraction map are shown in Fig. 3A, B, and C, respectively. To present a 3D image of the contraction mapping, all labeled points on the contraction map were annotated manually as the QRS-c-time in the activation mapping mode. Early contractions are represented in red and later contractions in yellow, green, blue, and purple,in line with the activation mapping of CARTO in this representative case. The earliest activation site was the lateral mitral annulus as shown in Fig. 3, on the left.

Contraction mapping could accurately estimate the earliest activation site in this case.

3.1.2. Example patient 2

Example patient 2 was a 67-year-old male who presented with frequent PVCs that originated from the inferior left ventricle (Fig. 4A). His PVC burden was determined to be 36% of the total heartbeats in a previous instance of Holter monitoring, and his LV function and size were within normal limits. Contraction mapping estimated the earliest activation site as similar to that in example patient 1 (Fig. 4B and C). In this case, the shortest QRS-c-time was 50 ms at the earliest activation site, in which the local activation time was 22 ms before the onset of the QRS (Fig. 5).
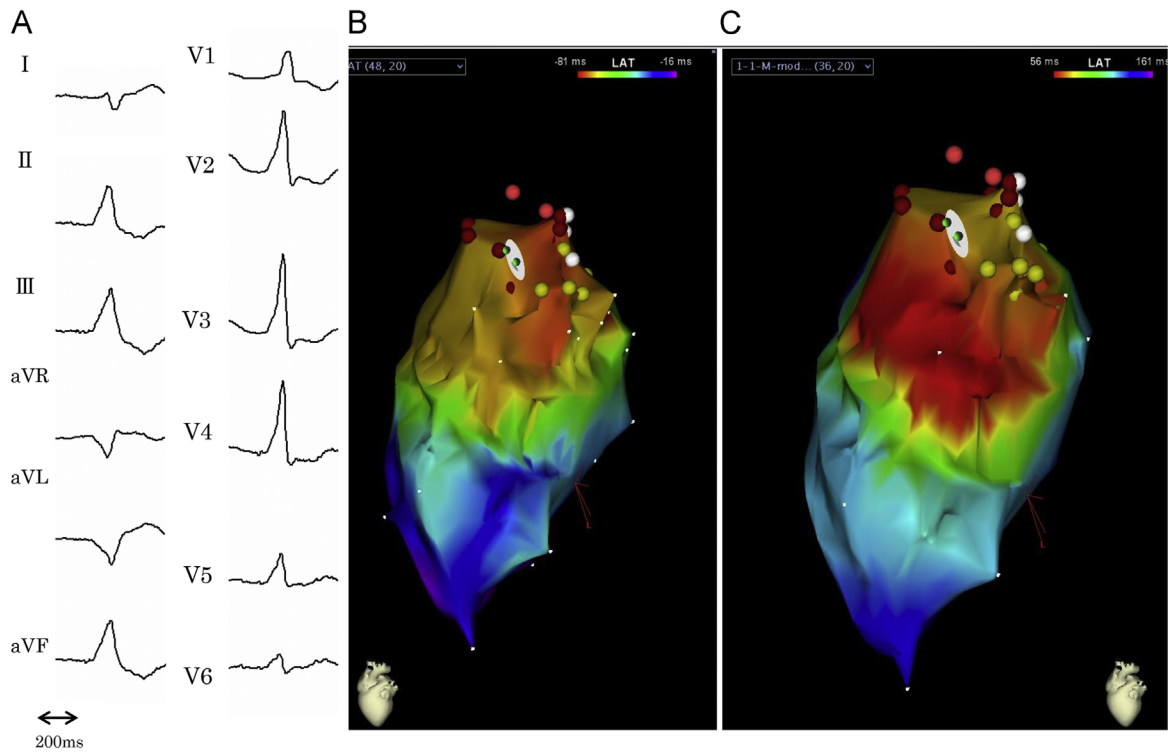
Fig. 3. A. The twelve-lead electrocardiogram of the PVCs is shown. B, C. Activation map (B) and contraction map (C) of a representative patient. The earliest site of the PVCs was the anterior MA. In the contraction mapping, all labeled points were annotated manually as in the QRS-c-time using the activation mapping mode. The contraction mapping determined a similar site as the activation mapping.
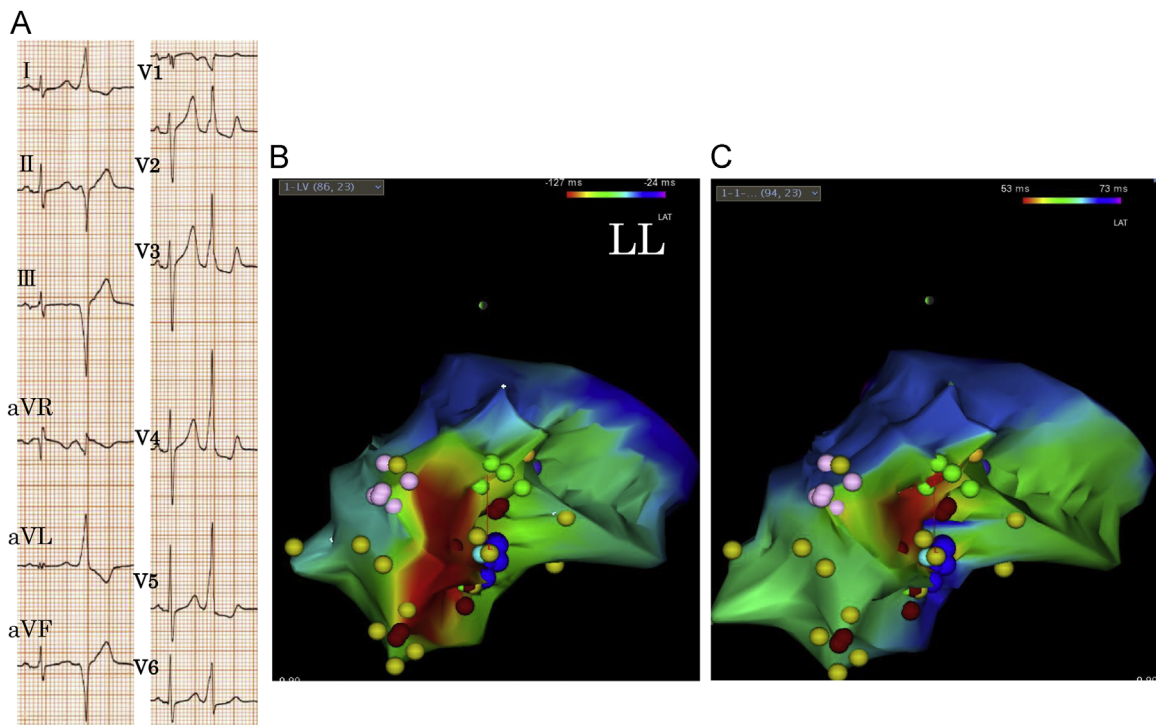

Fig. 4. An example of an electrocardiogram of the PVCs (A), activation map (B), and contraction map (C) in Patient 2 are shown.

3.2. Accuracy of the contraction mapping

The QRS-c-time and local activation time were studied at 104 points in the 18 patients for an assessment of the accuracy of the contraction mapping. There was a significant co-relation between the QRS-c-time and local activation time (activation time $= -66.8 + 0.882$ * QRS-c-time, $R2 = 0.794$, $p < 0.0001$, 95% CI $= 0.663$, 0.928, respectively) (Fig. 6). Contraction mapping in
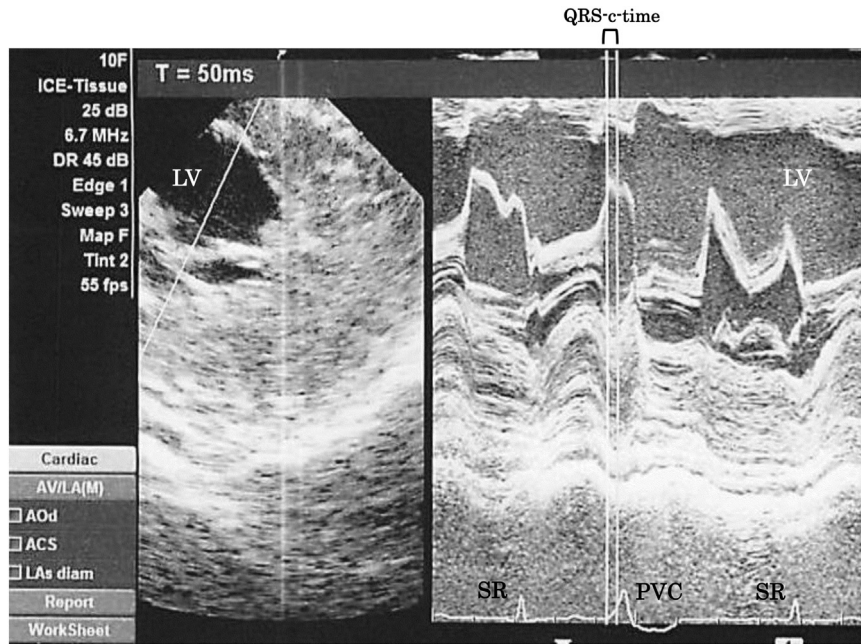
Fig. 5. The M-mode swept to the inferior LV revealed that the QRS-c-time was 50 ms. The local activation time at that site was 22 ms before the onset of the QRS. SR; sinus rhythm, PVC; premature ventricular complex, LV; left ventricle.
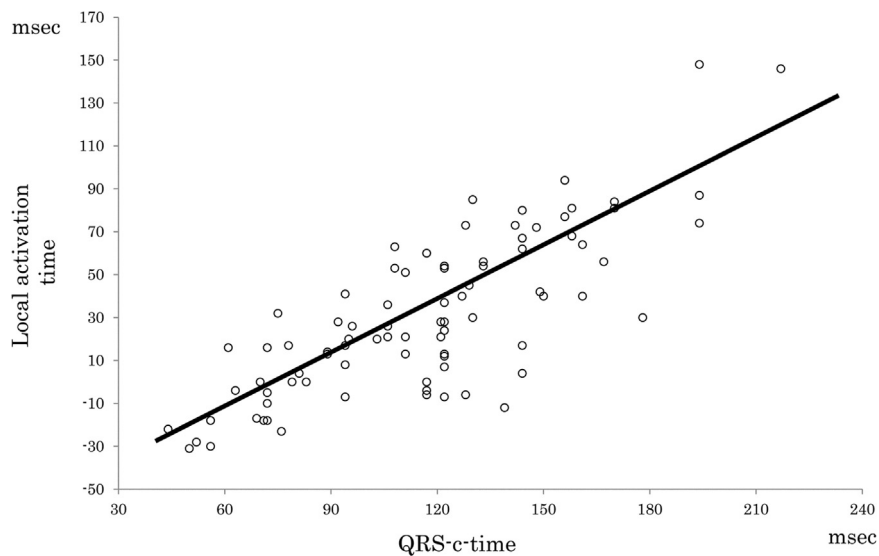
Fig. 6. There was a significantly strong correlation between the local activation time and QRS-c-time.

four patients in this assessment revealed that at six points, the local activation time was earlier than 20 ms before the onset of the QRS, with QRS-c-time ranging from 43 to 58 ms. The origins in those four patients were the anterior papillary muscle, anterior mitral annulus, inferior left ventricle, and right ventricular septum, respectively.

4. Discussion

A number of reports have previously described the estimation of PVC origins or exit sites via electrocardiogram (ECG) algorithms [14–21]. Since the ECG is easily available and repeatable and non-invasive, these criteria are important and essential for the catheter ablation of PVCs. The contraction mapping described in the present study is a supplemental method for PVC mapping for both ECG estimation and conventional mapping methods. Contraction mapping has two advantages. One is that it allows an estimation of both the earlier sites, which is necessary for detailed mapping, and the delayed sites, which has little value for treatment, using only an ICE probe located in the right heart without the need for an catheter to be delivered to the mapped sites. This mapping method could work well, especially if the mapped PVCs originated from the left side, because the local activation time of the left ventricle is predictable without a transseptal or arterial puncture. Similarly, in theory, contraction mapping may estimate the exit sites located on either the endocardium or epicardium. Unfortunately, PVCs that originated from the epicardium were not included in this study; therefore, we could not assess the predictive power of contraction mapping for PVCs that originated from the

epicardium. The other advantage was that a co-operator could manipulate the ICE probe and perform this mapping, while the main operator handled the ablation catheter to create the activation or pace map. Because the contraction mapping is concurrently available, this method might allow for a reduced time of mapping.

Local activation mapping may be indispensable for PVC ablation to detect the optimal ablation site. However, this study never assessed a comparison between contraction mapping and the conventional method. We considered that contraction mapping would be able to take on a supplemental role with activation mapping for these reasons.A similar approach using ultrasound for PVC ablation has been reported. Tada et al. described the efficacy of tissue tracking imaging to estimate the foci before the ablation procedure [22] Our approach differed from this one in that our study used 3D electroanatomical mapping and the M-mode, which are simple and easily available techniques. One of the characteristics of the M-mode is its high resolution time, which can discriminate distance in 1 ms. This high resolution time allows the contraction mapping to accurately estimate the local activation time.

Another aspect of this study was that a correlation between the QRS-c-time and local activation time was revealed. From our results, the contractile motion of the local myocardium started about 70 ms after the onset of the local electrical activation in patients without conduction abnormalities. Estimating from our result, it would take some amount of time before an action potential could make the sarcoplasmic reticulum release calcium, causing the excitation-contraction coupling to be triggered. Additionally, to detect contraction movement by M-mode, it might be necessary for a certain amount of muscle cells to contract simultaneously. We considered that the sum of these intervals was about a 70-ms delay from local activation time to QRS-c-time.

To the best of our knowledge, the present study is the first to describe a prediction formula for activation time from the time of contraction. This data may be applicable to other modalities, which could detect the contraction tile such as cine-magnetic resonance imaging for estimating exit sites including PVCs from the epicardium. Contraction mapping should have the potential to become a useful and helpful modality for catheter ablation of PVCs. Further development of experience and software will be necessary for the operation and commoditization of contraction mapping.

4.1. Limitations of the study

Contraction mapping may have several limitations. First, this method employs contraction movement assessed using M-mode, so it is not suitable for mapping areas with a poor or zero contraction, such as the outflow tracts, coronary cusps, pulmonary artery, and scar lesions. This limitation should be mentioned at first because the frequency of appearance of PVCs from outflow tracts and cusps would be relatively high. Second, the mechanism as to how the electrical-mechanical delay occurs in a structurally normal heart is still unclear. Third, the QRS-c-time could not estimate the pre-potential or preferential conduction in this study and instead only reflected exits of PVCs;thus, this method cannot replace conventional activation mapping or pace mapping.

There were several limitations to the present study as well. First, this study included a small number of idiopathic and drug-discontinued patients in a single center. It was unclear whether the method could be applied to non-idiopathic patients, patients with conduction abnormalities, or those taking anti-arrhythmic medications. Second, this study did not assess the clinical outcomes of PVC ablation after contraction mapping and only determined whether contraction mapping could estimate the local activation time.

5. Conclusions

A new mapping method, called contraction mapping, could estimate the local activation time and identify the optimal ablation sites or areas in which the use of an activation map would be unnecessary, without the need for the delivery of catheters to the various mapping points during the PVC ablation.

Conflict of interest

All authors declare no conflict of interest related to this study. No financial support was received for this study.

Acknowledgements

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