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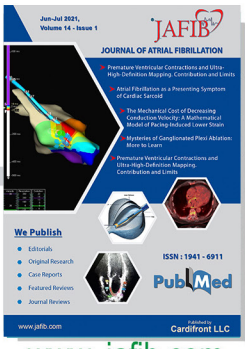

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Premature Ventricular Contractions and Ultra-High-Definition Mapping. Contribution and Limits

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Abstract

Background: The utility of ultra-high definition mapping (UHDM) for ablation of premature ventricular contractions (PVC) remains undetermined. The aim of this study was to investigate UHDM for PVC ablation, and additionally to compare to conventional technique.

Methods: Twenty patients investigated using UHDM were prospectively included and analyzed. Electrophysiological caracteristics and results were compared to 40 patients ablated using fluoroscopy only.

Results: 2541±2033 EGMs and 331±240 PVC beats were recorded for each patient. Surfaces of isochronal activations were 2.3±1.7 and 6.9±6.1 cm2 (first 10 and 20 ms). Local scar was present in 40% and local block in 65%. Areas of pace-mapping > 95, 90 and 85% concordance were 1.5±3.4, 2.1±3.9 and 3.3±5 cm2. Mean distance between the ablation site and the site of best pace-mapping or of earliest activation was 8±8 mm and 5±7 mm. Pre-potential was noted in 17% vs 26% controls (ns). QS pattern was present in 83% vs 83% controls (ns), and earliest activation was - 31±50 vs - 25±14 ms in controls (ns). Procedure (100±36 vs 190±51 min, p< 0.0001) and fluoroscopy duration (15±9 vs 24±9 min, p=0.005) were shorter in controls. Acute success was achieved in 65% patients with UHDM and in 72% controls (p=ns) with lower residual PVC burden in the control group. Over a follow-up of 19±12 months, long-term success was similar between groups (65 vs 68%).

Conclusion: UHDM may reveal poorly recognized activation features and PVC mechanism. In this series, conventional mapping was quicker and did clinically as well as UHDM.

Introduction

Percutaneous catheter ablation has become a therapeutic of choice for patients with premature ventricular contractions (PVC), because of a safe and efficient procedure with good long-term results [1] and because of increasing evidence for the potential deleterious effects of frequent PVCs. Current guidelines favor ablation over antiarrythmic drug therapy for PVC in many situations [2], probably leading to an even more relevant increase in the number of procedures in the future.

The best mapping and ablation technique for PVC remains undetermined. Conventional techniques associate pace-mapping and/or activation mapping based on fluoroscopy only, currently reaching satisfying although imperfect acute and long-term success rates [2-4]. 3D mapping techniques are now largely utilized for many if not most ablation of atrial or ventricular tachyarrhythmias, reducing radiation exposure and allowing more precise mapping, but their true interest for other substrates remains debated. 3D mapping has been occasionally [5-7] or more largely [8-12] used for PVC ablation, but it remains unclear what is the real interest regarding mechanisms and precision in anatomical location of the PVC foci, and which are the benefits in comparison to conventional technique [11].

Ultra-high definition mapping using the Rhythmia ™ system seems to more precisely highlight complex mechanisms [13,14]. This system could be useful for achieving a high level of precision for PVC ablation, while speeding and refining the acquisition process because of the high number of collected EGMs while automatically rejecting interfering nonclinical PVCs. However, it has been rarely reported for PVC ablation so far, with a few case reports [5-7] and descriptive short series [15,16].

The aim of this study was to prospectively investigate the additional capacities of ultra-high definition mapping (UHDM) for PVCs using the Rhythmia ™ system and additionally to compare the characteristics

Key Words

Ablation ; Fluoroscopy ; Mapping ; Premature Ventricular Contraction

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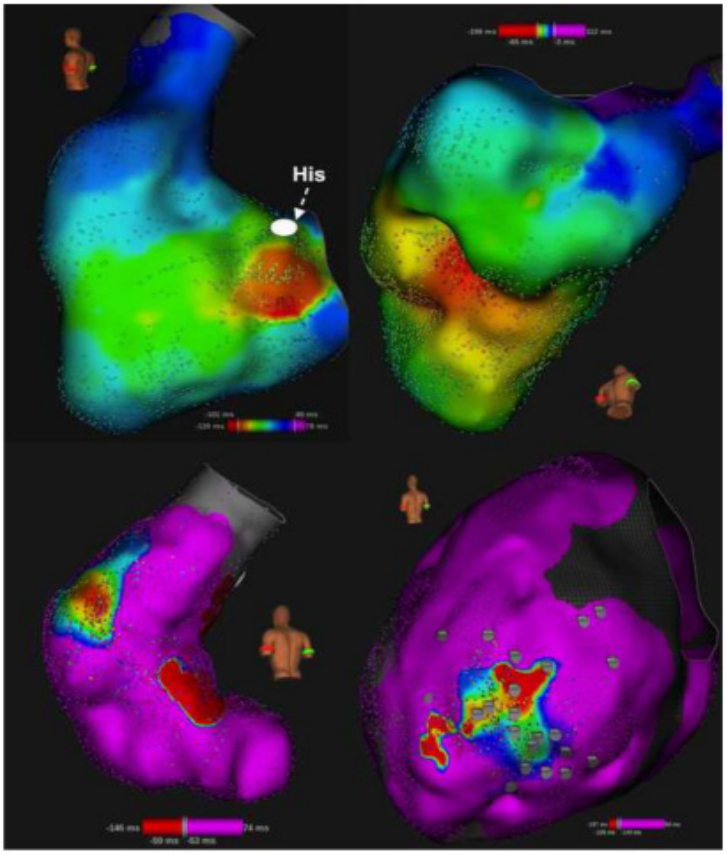

Figure 1: Four exemples of ultra-high definition mapping of various PVCs. Upper left: para-hisian PVC. Upper right: papillary muscle PVC. Lower left: RVOT PVC with dual breakthrough (arisng in fact form the right aortic cusp). Lower right: post-myocardial infarction PVC (grey tags = sites of pace-mapping with % of correlation compared to the QRS template of the PVC as calulated by the Boston Scientific LabSystem™ PRO recording system).

and efficacy of PVC ablation using UHDM compared to conventional technique.

Methods

Twenty consecutive patients referred for ablation of PVCs using the Rhythmia system ™ at our center were prospectively included.

1. Activation mapping :

Activation mapping was performed with the Rhythmia ™ system (Boston Scientific, Inc, Cambridge, MA) in each patient. Briefly, PVC were mapped using the Orion ™ multipolar basket-like catheter (64 electrodes of 0.4 mm2 surface and 2.5 mm interelectrode spacing) with the following operator-defined beat acceptance criteria : respiration gating, stable catheter location, tracking quality and QRS morphology analysis as compared to the template of a reference PVC. Maximal distance of electrodes to anatomical shell was 3 mm. Bipolar electrograms were filtered at 30 and 300 Hz and unipolar electrograms at 1 and 300 Hz, without a notch filter. Local activation time was automatically set to the timing of maximal amplitude of events on bipolar recording.

UHDM was especially performed in the area of earliest activation. Surfaces of isochronal activations –i.e. areas activated over a given range of time – were calculated using system proprietary calipers and serve as a harbinger for local depolarisation velocity. Presence of local block –i.e. some curvature or delay in some direction of the propagating activation wavefront coming from the focal area of origin- was noted.

Presence of a pre-potential (isolated presystolic potential in front of the QRS complexe) was also noted. At the site of interest, precession of the earliest activity on bipolar recordings compared to the QRS onset was measured, as well as the presence of QS pattern on uniporal recordings. Presence of local scar – i.e. < 0.2 mV in bipolar voltage map - [17] before ablation at the area of interest was noted.

The Lumipoint ™ algorithm and especially the « skyline » graph was aslo tested. In addition to usual voltage and activation time annotation, each electrogram was processed to detect all activity even if mutiple during the same cycle, reflecting the presence of deflections for each time point [18]. The "Skyline" graph reflects the surface area associated with active electrograms at each time as a fraction of the total surface area of the map and may therefore be indicative for specific PVC related activation characteristics.

2. Pace-mapping :

Pace-mapping was performed in each patient in the area of interest using the Orion ™ catheter (using the dipoles in closest contact to the endocardial surface) or the ablation catheter, with 10 V output and 1 msec duration. For each site of pace-mapping, the % of correlation compared to the QRS template of the PVC was calulated by the Boston Scientific LabSystem™ PRO recording system [19]. For patients with a sufficiant number of good pacing sites, areas of sites with pace-mapping > 95, 90 and 85% concordance were calculated using the system calipers.

Finally, the distances between the successful ablation site and the sites of best pace-mapping and of earliest activation were measured on the maps.

In a second part of the study, fourty age and gender-matched consecutive unselected patients undergoing conventional fluoroscopic-guided ablation without 3D mapping system during the same period and by the same operators were retrospectively collected and serve as the control group. Ablation was performed in these patients under fluoroscopy only and according to standard techniques, mainly based on activation mapping (earliest activation in bipolar recordings compared to the QRS and QS pattern in unipolar recordings) and limited pace-mapping (analysis based on visual inspection and simply quantified as the proportion of ECG leads where the paced QRS were

Table 1: Clinical characteristics of the population

	Ultra-high density mapping n=20	Conventional mapping n=40	p value
Male gender	13 (65%)	21 (52%)	ns
Age (years)	53±21	60±13	ns
Structral cardiomyopathy	8 (40%)	12 (30%)	ns
PVC induced CM	7 (35%)	16 (40%)	ns
LVEF (%)	46±15	46±15	ns
Anti-arrhythmic drugs or beta-blocker	16 (80%)	32 (80%)	ns
Redo procedure	6 (30%)	2 (5%)	0.007
PVC number/24 hours	12944±9714	18889±12554	ns

Table 2: Location of PVC in each group

	Ultra High density mapping n=20	Conventional mapping n=40	p value
Right/left/PVC ablated from both ventricles	5/14/1	12/22/6	ns
RVOT	5 (25%)	15 (37%)	ns
LVOT/aortic cusp/LV summit/CS/MA cont	8 (40%)	19 (47%)	ns
Papillary muscle	4 (20%)	1 (2.5%)	0.02
Multiple locations	0 (0%)	7 (17%)	0.04

RVOT: right ventricular outflow tract, LVOT: left ventricular outflow tract, LV: left ventricle

visually similar in shape and morphology to the reference PVC, with attemps to achieve matching between paced QRS complex and PVC in ≥11/12 ECG leads) [11, 20, 21]. Mapping in this group was performed using the ablation catheter only.

Ablation was performed with 4 mm tip irrigated catheters (Thermocool Biosense™ or Mifi OI Boston ™) and 30 to 50 W power in both groups, without contact force assessment. Acute success was defined by the complete elimination of PVC at the end of the procedure, with and without isoproterenol infusion. Twenty-four hours ambulatory recording was performed in each patient during the following days and again at least once during the follow-up. Long-term ablation success was defined by a 80% decrease in PVC burden [4, 22] on latest ambulatory recording. Signed informed consent was obtained from each patient. The study was approved by national ethical comity n° RCB 2017-A005777-46 on the 28/04/2017.

Statistics

Continuous variables are reported as mean±SD and compared with unpaired t-test. Categorical variables were compared using Fischer's exact test. Analysis and calculations were performed using StatView ™ program (Abacus Concepts, Inc. Berkeley, CA 1992-1996, version 5.0). A p value < 0.05 was considered statistically significant for each analysis.

Results

Twenty patients were included in the UHDM group and forty in the control group. Clinical characteristics are shown in table I.

Except for more redo procedures in the first group, there was no other difference between patients with UHDM and controls. Underlying structural heart disease associated ischemic cardiomyopathy (n=4), valvular (n=6), congenital (n=2) or dilated cardiomyopathy (n=8) (ns between groups). Fifteen (75%) and 7 (35%) patients from the UHDM group were on beta-blockers or class I or III anti-arrhythmic drugs versus 25 (62%) and 12 (30%) in the control group respectively (p=ns). PVC origin was depicted in table II.

There was no significant différences in PVC origin between groups, except for a higher prevalence of papillary muscle sites in the UHDM group, while more multiple locations were present in the conventional group.

Patients with UHDM:

A mean of 2541±2033 EGMs and 331±240 PVC beats were recorded for each procedure, with a mean duration of mapping of 42±17 minutes.

Surfaces of isochronal activations were 2.3±1.7 cm2 for isochronal 10 ms and 6.9±6.1 cm2 for isochronal 20 ms. Local scar was present in 8 cases (40%) and more frequently in case of cardiomyopathy (p=0.01) but not related to redo cases. Presence of local block or curvature of the wavefront was noted in 11 of the 17 cases (65%) where PVCs were present during mapping, without correlation with local scars or existing cardiomyopathy. Mean number of pace-mapping sites for each patient was 10±5. Best concordance was 89±11%. Areas of pace-mapping > 95, 90 and 85% concordance were 1.5±3.4, 2.1±3.9 and 3.3±5 cm2 respectively.

Mean distance between the final ablation site and the site of best pace-mapping and the site of earliest activation was 8±8 mm and 5±7 mm respectively. The "Skyline" graph, even if interesting, was deceptive due to the lack of available quantitative measurements/datas and this hindered to objectively investigate this algorithm.

Examples of PVC mapped using UHDM are seen in fig 1.

Control group : pace-mapping achieved similar QRS morphology compared to the PVC in a mean of 11.2±1.4 out of 12 ECG leads.

Comparisons with the control group: More patients in the UHDM group displayed bi/trigeminy patterns of PVCs during the procedure (nine in each group, p=0.07). Presence of a pre-potential was noted in 3 of 18 patients (17%) with UHDM and in 8 of 36 controls (25%) (ns). At the site of interest, QS pattern on unipolar recordings was noted in 15/18 (83%) UHDM patients versus 29/35 (83%) controls (ns), and precession of the earliest activity on bipolar recordings compared to the QRS onset was - 31±50 ms and - 25±14 ms in controls (ns).

Number of RF application was 9±5 vs 6±5 for conventional ablation (p=0.08). PVC morphology changed during RF ablation in 7 patients (35%) with UHDM and in four controls (10%) (p=0.02), leading to new targeting and new lesions. Procedure duration was significantly shorter in conventional procedures (107±43 vs 190±51 minutes, p<0.0001), as was fluoroscopy duration (16±11 vs 24±9 minutes, p=0.008).

Acute success was achieved in 13 patients with UHDM (65%) compared to 29 controls (72%) (p=ns), with significant reduction in PVC number on post-ablation ambulatory recording in the whole population (from 15523±11499 to 2791±5603, p<0.0001). PVC number decreased more in the conventional group (12249±92529 PVC less vs 6154±11857, p=0.05) with lower residual PVC burden (4622±8316 vs 1852±3266 in controls, p=0.07) with borderline differences.

No anti-arrhythmic drug was prescribed in 28 patients (47%), while 23 patients were discharged or later treated with beta-blockers and 9 were prescribed class I or class III drugs (ns between groups). Three patients were lost to follow-up. Over a mean follow-up of 19±12 months (ns between groups), long-term success was achieved in

38/57 patients (67%), without difference between groups (65 vs 68%). There was no difference in long-term success when redo procedures or patients with papillary muscle PVCs were excluded.

Discussion

We analyzed in this study the characteristics of PVC ablation using UHDM and further compared with conventional fluoroscopic techniques in another group of patients. Beside obtaining interesting datas on UHDM for PVC, we found that procedures performed using UHDM were longer and led to longer fluoroscopy duration, but did not translate in higher acute or long term success, despite achieving refined location of the focus and obtaining interesting findings.

The best mapping and ablation technique for PVC remains undetermined. Satisfying although imperfect acute and long-term success rates are currently achieved using conventional techniques based on fluoroscopy and combining pace-mapping and/or activation mapping [2-4]. The advent of 3D mapping techniques dramatically changed the paradigm of catheter ablation, so that most atrial or ventricular tachyarrhythmias are currently managed using 3D electroanatomic systems, reducing radiation exposure and allowing more precise mapping. However their true interest and cost-effectiveness for other substrates remains to be proved. 3D mapping has been casually [5-7] or more widely [8-12] used for ablation of PVC, but additional benefits in comparison to conventional technique remain unclear, for example regarding efficacy, mechanisms and precision in anatomical location of the PVC foci. Conventional fluroscopy-based ablation of VT and PVC from the right ventricular outflow tract (RVOT) had been shown to be comparable to first generation-3D mapping systems in terms of acute results, with or without shorter fluroscopy/procedure duration [11, 23], but multipolar catheters were not used at that time. To date, no study has compared UHDM to fluorscopic techniques for PVC ablation, and no data on the PVC characteristics using UHDM is available.

UHDM using the Rhythmia ™ system found a 86% acute and long-term success rate in a short series of 7 cases, emphasizing the automatic ECG template matching algorithm used as a beat selection criteria in this system [15]. Safety and full acute efficiency was recently reported in a series of 17 cases with significant long-term PVC burden reduction [16].

UHDM using the Rhythmia ™ system in our series revealed still unexplored features of myocardial activation during PVCs and of pace-mapping.

1. Local scar was present in 40% of cases, more frequently - but not only - in presence of structural heart disease, together with some local block or curvature of the wavefront in 65%, without correlation with local scars or presence of cardiomyopathy. This may imply some local conduction disturbance and/or fibrosis, even in apparent healthy hearts, and that PVCs may be caused by local reentry in some cases, although local activation during the preceding sinus beat was not studied. Additionally, PVC may arise remote from scar areas in patients with cardiomyopathy.

2. Analysis of isochronal activations shows that a mean of 2.3 cm2 of endocardial surface is activated during the first 10 ms and 6.9 cm2 during the first 20 ms. This means that averaged velocity of activation is around 0.85 m/sec at the breakthrough of activation, then decreases to 0.65 m/sec, possibly due to less recruitment of Purkinje cells or more fibrosis as the activation spreads or because of more tightly coupled cardiomyocytes at the focus location.

3. Areas of good pace-mapping ranged from 1.5 to 3.3 cm2, which were of the same order to the area of 10 ms earliest activation. However, best pace-mapping sites and earliest activation sites located relatively remote to the final ablation site, with a mean distance of 8 mm and 5 mm respectively. This may signify that these refined and detailed patterns using UHDM are in fact not really relevant for locating the effective focus site. When compared to conventional mapping, neither the presence of pre-potential (present in only a minority), nor local precession on bipolar activation or QS pattern in unipolar recordings (present in a majority) benefited from UHDM. This implies that conventional mapping alone is sufficiant to provide these informations.

Beside giving some additional information about the focus location regarding anatomical structures and mechanisms, 3D systems are expected to decrease radiation exposure, although this was not the case in our series. Reasons for this are the more direct targetting of the culprit focus without building unnecessary complete map of the whole ventricle with its associated additional duration and fluoroscopic exposure, even if minimized due to the use of electroanatomical system. Unavoidable shifts and mistrust in the reliability of anatomical reconstruction and catheter location implies also relevant additional durations of fluoroscopy to correct maps and check true catheter location in our experience, while simple fluoroscopic navigation does not suffer from these drawbacks. Moreover, recent progress in fluoroscopic equipments are currently leading to very low irradiation dosings, sometimes close to the level of radiations met in leisure activities (unpublished data). Finally, changes of PVC morphology during ablation was more frequent using UHDM, possibly because of incomplete initial ablations changing the PVC exit, needing new targeting and new lesions and thus increasing the duration of the procedure and fluoroscopy. This was also reflected by the larger number of RF application needed in UHDM patients.

Acute and long-term success were similar using conventional or UHDM techniques in this series, recognizing that the UHDM group included more redo procedures and more papillary muscle, which may have selected more challenging cases, but less multiple foci and more bigeminy/trigeminy which may render procedures more easy. Even if these differences may favor one technique or another, they probably do not have true relevance in interpretating the results. Moreover, there was no difference in acute and long-term success when patients with papillary muscle PVCs or redo procedures were excluded. Thus, PVC ablation may not beneficiate from UHDM techniques in trained hands, because achieving higher anatomical precision in activation or pace-mapping does not translate into a better result, or because of the lack of true enhanced precision provided by 3D systems.

No such comparison seemed to have been performed using UHDM before. There is probably no reason to achieve more reliable activation mapping using UHDM. In fact unipolar QS patterns or earliest bipolar activation did not differ compared to fluoroscopic mapping in our study. Visual analysis of EGMs are probably at least

as good as automated annotations by the 3D system, because some early activations are difficult to correctly annotate, while being highly suggestive at visual inspection, and because detection of QS pattern in unipolar recordings cannot be currently automatized.

Studies investigating automated versus visual analysis of pace-mapping are scarce : using a software available within the Boston Scientific EP system (LabSystem™ PRO) there was a significant correlation between automated template-matching and visually judged pace-map scores [24]. However, the template matching score reached a larger area under the ROC curve than the pace-map score for successful ablation sites, meaning that automated template matching was a better discriminator than the visual judgment by experienced electro-physiologists [24].

Automated template matching of the Rhythmia™ system has been demonstrated in-vivo to have high specificity and sensitivity, with a pace-mapping spatial resolution of 2 mm [25]. The automated pace mapping system software (PaSo ™ module, CARTO XP v9, Biosense/Webster) allows direct comparisons between paced ECGs and the PVC [12,26]. Impressive results have been described using PaSo ™ module and contact force catheter in a retrospective study [12], which are not consistant with results from most other groups. Interestingly, local precocity of the signal during PVC was not correlated to pace-mapping in this study, and additional RF were needed in surrounding areas in patients with ineffective RF applications based on the PaSo ™ module [12]. Pace-mapping alone using the PaSo ™ module was associated to a more usual 76% long-term success in another study [9].

Other template-matching techniques has been proposed such as manual scoring (similar R/S ratio and fine notching in each lead, maximal 24 points) [27] or using diverse sophisticated mathematical calculations by custom written softwares [21, 28] such as correlation coefficient (from - 1 for completely opposite waveform to + 1 for identical waveforms) and mean absolute deviation (from 0% for two identical waveforms to 100% for completely different waveforms, tending to be more sensitive to differences in waveform amplitude) [28] or others [28,29].

Using these techniques in patients with PVC from RVOT, pace maps with good correlation coefficient were confined to an area of 1.8 cm2 while the area of the first 10-ms isochrone measured 1.2 cm2, and pace-mapping was unreliable in identifying the site of origin in a fifth of patients [21]. However to the best of our knowledge, no comparison with visual analysis using simple scoring on the 12 ECG leads has been made.

In conclusion, conventional mapping techniques do as well as UHDM for PVC ablation, probably needing more experience than physicians dependent on 3D mapping, while achieving comparable acute and long-term success. UHDM however may reveal still unrecognized activation features and PVC mechanism the conventional techniques cannot do, whose clinical interest could only be demonstrated by additional works.

Limitations

Intra-cardiac echocardiography was not used in this study. Although potentially useful, especially for PVC from the papillary muscles, it requires additional costs and learning curve and is not widely utilized in France to date.

Non invasive ECG imaging (30) was not used here. Even if potentially interesting in planing ablation procedure and technique, it remains to be proved that this technique achieves better results compared to UHDM or conventional mapping for PVC ablation.

Although we tested the Lumipoint ™ algorithm, the lack of available quantitative data avoided any objective investigation. Additional improvements of the algorithms are needed before exploring its capacities in PVC mapping.

Finally, unexplained catheter displacements using 3D system have recently been demonsrated for PVC mapping and considered as an issue [31]. This is said to be possible using the Rythmia ™ system also [31] and may explain some discrepancies between catheter locations between sinus beats and PVC. This does not happen of course with conventional mapping.

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