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CLINICAL RESEARCH
Ventricular tachycardia: mapping and ablation

Bipolar ablation of therapy-refractory ventricular arrhythmias: application of a dedicated approach

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Aims Bipolar radiofrequency ablation (B-RFA) has been reported as a bail-out strategy for the treatment of therapy refractory ventricular arrhythmias (VA). Currently, existing setups have not been standardized for B-RFA, while the impact of conventional B-RFA approaches on lesion formation remains unclear.

Methods and results (i) In a multicentre observational study, patients undergoing B-RFA for previously therapy-refractory VA using a dedicated B-RFA setup were retrospectively analysed. (ii) Additionally, in an *ex vivo* model lesion formation during B-RFA was evaluated using porcine hearts. In a total of 26 procedures (24 patients), acute success was achieved in all 14 ventricular tachycardia (VT) procedures and 7/12 procedures with premature ventricular contractions (PVC), with major complications occurring in 1 procedure (atrioventricular block). During a median follow-up of 211 days in 21 patients, 6/11 patients (VT) and 5/10 patients (PVC) remained arrhythmia-free. Lesion formation in the *ex vivo* model during energy titration from 30 to 50 W led to similar lesion volumes compared with initial high-power 50 W B-RFA. Lesion size significantly increased when combining sequential unipolar and B-RFA (1429 mm^3 vs. titration 501 mm^3 vs. B-RFA 50 W 423 mm^3, $P < 0.001$), an approach used in overall 58% of procedures and more frequently applied in procedures without VA recurrence (92% vs. 36%, $P = 0.009$). Adipose tissue severely limited lesion formation during B-RFA.

Conclusion Using a dedicated device for B-RFA for therapy-refractory VA appears feasible and safe. While some patients need repeat ablation, success rates were encouraging. Sequential unipolar and B-RFA may be favourable for lesion formation.

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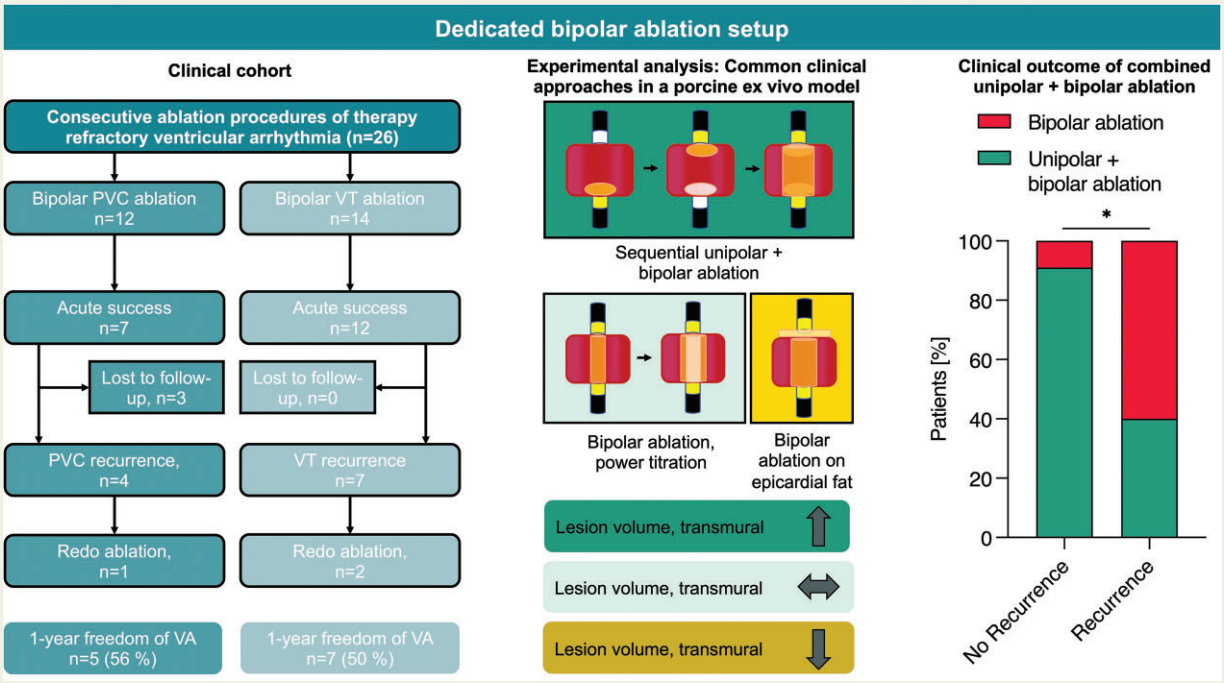
Graphical Abstract



Keywords Bipolar ablation • Ventricular tachycardia • Ventricular arrhythmias • Premature ventricular contractions • Radiofrequency generator

What's new?

- This case series reports the experience of the first dedicated approach using a radiofrequency generator for bipolar ablation.
- In patients with otherwise therapy refractory ventricular arrhythmias, bipolar ablation was associated with a freedom from arrhythmia in 52% of patients in a follow-up of up to 2 years.
- The combination of unipolar ablation followed by bipolar radiofrequency ablation led to enhanced lesion formation in a porcine *ex vivo* model and the clinical cohort, whereas epicardial adipose tissue significantly reduces bipolar ablation efficacy *ex vivo*.

Introduction

Catheter ablation is increasingly used to treat ventricular arrhythmias (VA) refractory to medical therapy. However, arrhythmias of deep intramural origin may not be accessible through unipolar ablation, as often encountered at the interventricular septum or the left ventricular summit.[1,2] Bipolar radiofrequency ablation (B-RFA) is described as a bail-out method in such a scenario.[3] However, clinical setups for B-RFA often employ custom solutions with cable connectors using a single generator.[4] The 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of VA emphasizes the concern over present custom-made approaches particularly due to the lack of temperature monitoring for both catheter tips.[5] In 2017, the first dedicated device for B-RFA received its CE mark (HAT500, Osypka AG, Rheinfelden, Germany). This device allows for a standardized dedicated approach with two ablation catheters and separate irrigation pumps. Clinical approaches often employ prior unipolar ablation before B-RFA or titration of power from lower to higher levels. The rationale behind these strategies is a supposed reduction in risk for adverse events, whereas optimal B-RFA approaches remain unclear. Data supporting specific approaches are limited especially when joined by additional challenges such as the presence of significant epicardial adipose tissue (EA).[2]

This study reports (i) the first multicentre experience of B-RFA using a dedicated single ablation generator in patients presenting with VA refractory to conventional therapy and (ii) assessment of common clinically used B-RFA approaches in an *ex vivo* model.

Methods

Clinical cohort

Consecutive patients that underwent B-RFA for VA were retrospectively studied at participating tertiary care centres from July 2017 until July

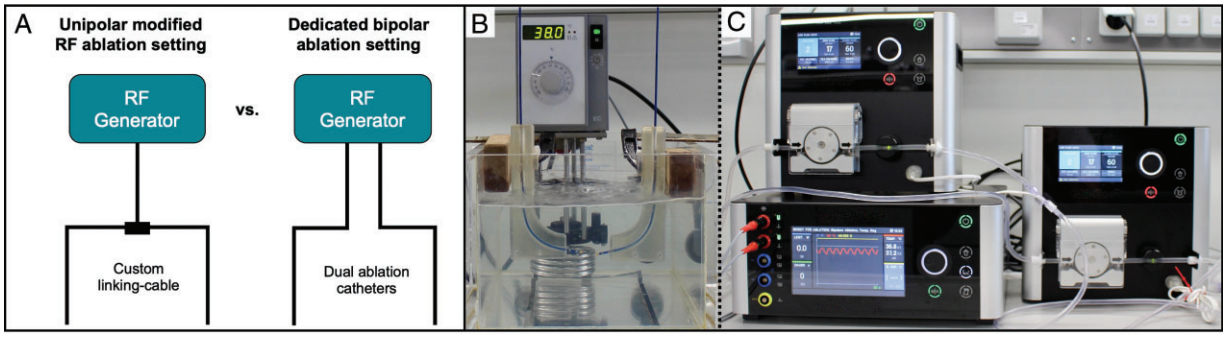


Figure 1 Clinical and *ex vivo* bipolar ablation setup. (*A*) Schematic overview on custom-made solutions and presented approach using a dedicated radiofrequency (RF) generator setup for bipolar ablation. (*B*) Experimental setup of custom catheter guiding blocks in a temperature-controlled saline bath with two irrigated 3.5 mm ablation catheters on either side. (*C*) Catheters are connected to a single ablation generator with two separate irrigation pumps.

2020. Inclusion criteria were defined as therapy refractory VA with a history of previous unsuccessful antiarrhythmic medication and/or unipolar RF ablation. Moreover, patients with suspected deep intramural VA origin were included based on previous 12-channel ECG and pre-procedural cardiac imaging including transthoracic/transesophageal echocardiography, cardiac computed tomography or cardiac magnetic resonance imaging. Patients with idiopathic VA or known structural heart disease were included. Exclusion criteria were current critical illness, severe acute liver or kidney dysfunction, acute hyperthyroidism, age <18 years and patients with insufficient procedural data. Baseline patient characteristics and history were evaluated via a standardized questionnaire sent to the treating electrophysiologist at the respective centres [University Medical Center Hamburg-Eppendorf, University Hospital Düsseldorf, EVK Düsseldorf, Karlsruhe Hospital, Heart Center Bad-Neustadt, German Heart Center Munich (all Germany) and Grochowski Hospital Warsaw, Poland]. Data collection and analysis were performed with approval of the institutional ethics committee. All patients gave written informed consent.

Electrophysiological study setup

The procedures were carried out in accordance to existing consensus statements as well as previously published protocols.[6] Patients underwent the procedure in a fasting state under conscious sedation using propofol or midazolam and fentanyl. General anaesthesia was applied, if deemed necessary by the respective centres. Access to the ventricles was gained anterograde via the femoral vein or transseptal access and retrograde via the femoral artery.

In short, the diagnostic setup included catheters placed in the coronary sinus and the right ventricular apex. Substrate mapping was conducted during sinus rhythm in the right (RV) and/or left ventricle (LV) using the Smarttouch Thermocool single-tip catheter, the 20-pole Pentaray catheter (Biosense Webster, Diamond Bar, CA, USA) or the 64-pole Orion catheter (Boston Scientific, Marlborough, MA, USA). Maps were created with the Carto® 3 (Biosense Webster) or Rhythmia™ mapping system (Boston Scientific) and left at the treating physicians discretion. For VT induction, programmed ventricular stimulation was conducted with two different baseline cycle lengths and up to three extra stimuli with a minimal coupling interval of 180 ms. Additional incremental atrial and ventricular pacing was performed following programmed stimulation. The induced VT was regarded as the clinical VT when cycle length and morphology conformed with previous recording.[6] Activation mapping was performed whenever VT was haemodynamically tolerated, with additional entrainment or pace mapping conducted at the operator's discretion. In case of non-inducibility, additional intravenous orciprenaline or isoproterenol administration was performed.

Procedural workflow and bipolar ablation

A schematic ablation generator setup is shown in *Figure 1A*. The HAT500 single ablation generator (OSYPKA AG, Rheinfelden, Germany) enables usage of two ablation catheters with individual irrigation pumps. This allows for separate monitoring of power levels, temperature and either separate unipolar or bipolar impedance for both catheters individually. Furthermore, it is possible to switch between unipolar and B-RFA without changing cable connections. The general unipolar ablation setting has been described before.[7] For B-RFA, two open-irrigated 3.5 or 4 mm tip ablation catheters were used, with one catheter being placed at the endocardial site in the RV/LV and the other at the opposing epicardial or septal site or within the coronary sinus/great cardiac vein. In either system, one ablation catheter is declared as a diagnostic catheter and disappears during energy application. Additional coronary angiography and intracardiac echocardiography were performed before energy application in selected cases if the suspected critical VA site was in close proximity to the coronary vessels or for better visualization of catheter positioning.

Ablation points were chosen based on the earliest activation site and/or best pace map. Unipolar RF energy current was first applied to the suspected critical isthmus site followed by B-RFA with a maximum power of 50 W. Immediate B-RFA without prior unipolar ablation was conducted in selected cases with ≥2 prior ablation procedures and/or at sites of high myocardial tissue thickness such as the aorto-mitral continuity or left/right ventricular outflow tract.

Follow-up

Acute procedural success was defined as non-inducibility of the clinical VT for VT ablation and complete cessation or PVC burden reduction >90% after 30 min waiting time and subsequent isoproterenol/orciprenaline provocation testing during PVC ablation. Antiarrhythmic treatment was continued at the operator's discretion. Patients were asked to visit the outpatient clinic every 3–6 months after the initial catheter ablation at respective centre site. A 12-lead ECG or 24-h Holter ECG monitoring was performed at every visit and whenever patients complained about symptoms. Device interrogation for VA detection was additionally conducted whenever applicable. Long-term recurrence of VT was defined as sustained VT or appropriate ICD therapy and PVC recurrence as a PVC

Table 1 Baseline characteristics

Parameter	All patients $n = 24$	Idiopathic $n = 12$	SHD $n = 12$	Idiopathic vs. SHD, *P*-value
Age (years)	57 ± 15	55 ± 17	61 ± 13	0.29
Female sex, *n* (%)	5 (21)	3 (25)	2 (17)	>0.99
Body mass index (kg/m^2)	28 ± 4.9	26 ± 3	29 ± 6	0.31
CHA_2DS_2VASc score, *n* (inter-quartile range)	3 (0–3)	1 (0–3)	3 (3–4)	0.01
HAS-BLED score, *n* (inter-quartile range)	1 (0–2)	0 (0–1)	1 (0–2)	0.12
LVEF, % (total range)	47 ± 15 (23–74)	61 ± 8 (47–74)	36 ± 9 (23–50)	<0.001
ICD present, *n* (%)	12 (50)	0 0	12	<0.001
Antiarrhythmic medication, *n* (%)				
Ajmalin	1 (4)	0 0	1 (8)	>0.99
Flecainid	1 (4)	1 (8)	0 0	>0.99
Propafenone	0 0	0 0	0 0	>0.99
Amiodaron	7 (29)	1 (8)	6 (50)	0.07
Sotalol	0 0	0 0	0 0	>0.99
Mexilitine	2 (8)	0 0	2 (17)	0.48
Quinidine	1 (4)	0 0	1 (8)	>0.99
Underlying condition, *n* (%)				
Post-myocarditis	3 (13)	0 0	3 (25)	0.22
Dilated cardiomyopathy	6 (25)	0 0	6 (50)	0.01
Ischaemic cardiomyopathy	2 (8)	0 0	2 (17)	0.48
Idiopathic	12 (50)	12 (50)	0 0	<0.001
Sarcoidosis	1 (4)	0 0	1 (8)	>0.99
Procedure indication, *n* (%)				
Recurrent PVC	12/26 (46)	9/12 (75)	3/14 (21)	0.02
Recurrent VT	12/26 (38)	2/12 (17)	10/14 (71)	0.008
VT storm	2/26 (8)	1/12 (8)	1/14 (7)	>0.99
Previous VA Ablation, *n* (%)	22/26 (85)	9/12 (75)	13/14 (93)	0.31
No. of previous ablation, median (inter-quartile range)	2 (1–2)	1 (0–2)	2 (1–3)	0.01

Variables are expressed as absolute values, mean ± standard deviation, or median with inter-quartile ranges.
ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; PVC, premature ventricular contraction; SHD, structural heart disease; VA, ventricular arrhythmia; VT, ventricular tachycardia.

burden reduction ≤90% during 24-h Holter ECG monitoring after a blanking period >3 months.

Ex vivo model setup

An experimental setup overview is displayed in *Figure 1B and C*. For evaluation of lesion formation during different clinical approaches, ablation was conducted in freshly explanted swine hearts using the HAT500 generator and two irrigated 3.5 mm ablation catheters (Cerablade cool, Osypka AG, Rheinfelden, Germany). Left ventricular and septal myocardium was dissected in regions with a myocardial thickness ≥15 mm. Extracted tissue was positioned in a temperature-controlled saline bath at 37°C with active and ground ablation catheter positioned orthogonally to each side of the myocardium applying a constant force of ∼10 g for 60 s with an irrigation rate of 30 mL/min. Each investigated ablation approach was conducted for 60 s, with 30 s resting period separating sequences within each group: (i) 30 W B-RFA followed by 50 W B-RFA (titration group); (ii) 30 W sequential unipolar ablation (SUA) followed by 50 W B-RFA (SUA+B-RFA group); (iii) 50 W B-RFA in areas of significant epicardial adipose (EA) tissue (EA group); (iv) sole B-RFA using 30/40/50 W (B-RFA group); (v) sole 30 W SUA (SUA group). Baseline generator impedance and maximum generator impedance drop were assessed. Only lesions without occurrence of steam pops were considered for analysis. The following lesion parameters were macroscopically analysed using a digital caliper for estimation of the intramural lesion volume[8]: maximal lesion depth (*A*), maximal intramural diameter (*B*), depth at maximum diameter (*C*), and lesion surface diameter (*D*).

$$V_{\text{Non-transmural}} = \left[0.75\pi\left(\tfrac{B}{2}\right)^2(A–C)\right]–\left[0.25\pi\left(\tfrac{D}{2}\right)^2(A–2C)\right]$$
$$V_{\text{Transmural}} = \left[\pi\left(\left(\tfrac{B}{2}+\tfrac{D}{2}\right)/2\right)^2 A\right]$$

In non-transmural B-RFA lesions, the maximal lesion depth was determined based on the deepest lesion from either active or returning ablation catheter, whereas in transmural lesions it was calculated by halving the measured total myocardial thickness. Furthermore, a combined lesion depth of both endocardial and epicardial lesions as well as the ratio of the combined lesion depth to the myocardial tissue thickness was calculated accordingly. Transmurality was defined as a macroscopically visible continuous lesion between both catheters reviewed by two independent

Table 2 Procedural data

Electroanatomic mapping system, *n* (%)	
Carto	23 (88)
Rhythmia	3 (12)
Pre- or periprocedural imaging, *n* (%)	
Intracardiac echocardiography	4/26 (15)
Magnetic resonance imaging	4/26 (15)
Computed tomography	1/26 (4)
Clinical VT inducible, *n* (%)	24 (92)
Number of inducible VT, *n* (inter-quartile range)	1 (1–1)
Clinical VT cycle length (ms)	385 (343–428)
Haemodynamic support, *n* (%)	
General anaesthesia	1 (4)
Impella	1 (4)
Procedure duration (min)	196.5 ± 55.8
Fluoroscopy time (min)	19.5 ± 9.4
Fluoroscopy dose (cGy·cm^2)	3847 ± 5613
Coronary angiography before energy application, *n* (%)	12 (46)
Unipolar ablation in same procedure, *n* (%)	15 (58)
Mean maximum applied energy during B-RFA (W) (total range)	37.5 ± 8.9 (24–50)
Acute success, *n* (%)	
PVC, suppression	7/12 (58)
Clinical VT, non-inducibility	14/14 (100)
Overall VT, non-inducibility	12/14 (86)
Periprocedural complications, *n* (%)	
Overall	3 (12)
Groin complications	2 (8)
Atrioventricular block with pre-existing ICD	1 (4)
Follow-up (*n* = 23 patients)	
Median follow-up duration, days (inter-quartile range)	139 (75–245)
Freedom of arrhythmia, *n* (%)	
PVC	5/9 (56)
VT	7/14 (50)
Re-do ablation, *n* (%)	
PVC	1/9 (11)
VT	2/14 (14)

Variables expressed as *n* (%) or *n* ± standard deviation.
B-RFA, bipolar radiofrequency ablation; ICD, implantable cardioverter-defibrillator; PVC, premature ventricular contraction; VA, ventricular arrhythmia; VT, ventricular tachycardia.

investigators (F.-A.A. and K.S.). The transmurality rate was calculated as the percentage of transmural lesions within all set lesions of the respective approach.

Statistical analysis

All continuous variables were tested for normal distribution using the Shapiro–Wilk test. Parametric data are expressed as mean ± standard deviation, whereas results of non-parametric data are provided as medians with inter-quartile ranges. If applicable, minimum and maximum values are also indicated. Analysis was performed using Graphpad Prism 9® (Graphpad Inc., La Jolla, CA, USA) and Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). For calculation of differences of continuous data, either Student's *t*-test or ordinary one-way ANOVA tests were conducted for parametric data. For non-parametric data, either the Mann–Whitney *U* test or Kruskal–Wallis test were applied. Differences of categorical variables were determined using a χ^2 test. A *P*-value <0.05 was considered statistically significant.

Results

Patients and baseline characteristics

Baseline characteristics are shown in *Table 1*. A total of 26 procedures in 24 patients were investigated (VT *n* = 13/PVC *n* = 11). Underlying structural heart diseases included ischaemic cardiomyopathy (*n* = 4), dilatative cardiomyopathy (*n* = 6), previous myocarditis (*n* = 3) and cardiac sarcoidosis (*n* = 1), whereas the majority of patients presented with idiopathic VA (*n* = 12). Recurrent VT (14/26) or a relevant PVC burden (12/26) was targeted. Patients without structural heart disease presented more often for PVC ablation and less often for VT ablation compared with patients with structural heart disease (PVC *P* = 0.02; VT *P* = 0.008). A median of 1 previous ablation (range 0–5) of various approaches had been performed before inclusion, with *n* = 2 patients presenting for initial VA ablation (all PVC).

Procedural data

Procedural data are listed in *Table 2*. High-density mapping was employed in 10 out of 26 procedures. In 92% of the cases, the clinical arrhythmia was inducible or occurred spontaneously. In one procedure, prophylactic mechanical circulatory support via Impella™ (Abiomed Europe, Aachen, Germany) was established to prevent cardiogenic shock during the procedure. Coronary angiography was performed before energy application in 12 procedures (*Table 3*). Unipolar ablation was carried out in 15 out of 26 procedures before switching to B-RFA. Maximum applied energy ranged between 20 and 50 W with an average of 37.5 ± 8.9 W.

Target location and mid-term outcome

The placement of both active and grounding catheter as well as detailed procedure characteristics are presented in *Table 3*. Main target sites were located at the right/left ventricular outflow tract (11/26) with *n* = 2 involving either the left coronary or pulmonary cusp, interventricular septum (8/26), left ventricular anterior/septal/posterior wall (*n* = 5) and aorto-mitral continuity (2/26). Clinical PVC morphologies included left bundle branch block morphology in 10/12 cases (83%), while in two procedures of the same patient a right bundle branch block morphology was present with subsequent B-RFA between the right ventricular outflow tract and the left coronary cusp/coronary sinus. A median of 1 VT per procedure with a median cycle length of 385 ms was induced, with the clinical VT morphologies being left bundle branch block in 8/14 procedures (57%) and right bundle branch block in the remaining 6/14 cases (43%). The VA origin in the *n* = 2 patients with VT storm were the aorto-mitral continuity (LBBB morphology) and the interventricular septum (RBBB morphology).

Acute success with non-inducibility of the clinical VT was achieved in all 14 VT cases. In 7/12 patients undergoing ablation of PVCs, PVCs were successfully suppressed. Minor groin complications without need for surgical intervention were observed in two procedures. In

Table 3 Detailed procedure characteristics

Case no.	Cardiomyopathy	Procedure	Maximum energy (W)	Unipolar ablation in same procedure	Coronary angiography conducted	Position catheter 1	Size (mm)	Position catheter 2	Size (mm)	Target region
1	Post myocarditis	VT	45	No	Yes	Anteroseptal left	3.5	Epicardial	4	IVS
2	Post myocarditis	VT	50	No	No	Septal LV	3.5	Septal RV	4	IVS
3	Post myocarditis	VT	42	No	No	Septal LV	3.5	Septal RV	3.5	IVS
4	Post myocarditis	VT	45	No	Yes	Septal LV	3.5	Epicardial LV	3.5	Septal LV
5	DCM	VT	35	Yes	No	Septal LV	3.5	Septal RV	4	IVS
6	DCM	VT	40	Yes	No	RVOT	3.5	CS	4	RVOT
7	DCM	VT	50	Yes	No	Septal LV	3.5	Septal RV	3.5	IVS
8	DCM	VT	50	Yes	No	Septal LV	3.5	Septal RV	3.5	IVS
9	DCM	PVC	36	Yes	No	LV antero-basal	3.5	CS	3.5	Anterobasal LV
10	DCM	PVC	36	Yes	Yes	LVOT	3.5	RVOT	3.5	LCC/RVOT
11	DCM	PVC	29	Yes	Yes	RVOT	3.5	CS	4	RVOT
12	ICM	VT	45	Yes	No	Septal LV	3.5	Septal RV	4	IVS
13	ICM	VT	30	No	Yes	Posterior wall LV epicardial	3.5	LV posterior wall	3.5	LV posterior wall
14	Idiopathic	VT	41	Yes	No	Septal LV	4	Septal RV	3.5	IVS
15	Idiopathic	PVC	30	No	No	RVOT	3.5	CS	3.5	RVOT
16	Idiopathic	VT	24	No	No	LVOT	3.5	CS	3.5	LVOT
17	Idiopathic	PVC	50	Yes	Yes	RVOT	3.5	CS	3.5	RVOT/CS
18	Idiopathic	PVC	50	Yes	Yes	AMC	3.5	CS	3.5	AMC
19	Idiopathic	VT	40	Yes	Yes	AMC	3.5	CS	3.5	AMC
20	Idiopathic	PVC	25	No	No	LVOT	3.5	CS/GCV	3.5	LVOT/CS
21	Idiopathic	PVC	30	Yes	Yes	LVOT	3.5	Pulmonary cusp	3.5	LVOT
22	Idiopathic	PVC	20	Yes	Yes	RVOT/LVOT	3.5	CS/GCV	3.5	RVOT
23	Idiopathic	PVC	35	Yes	Yes	LVOT	3.5	CS	3.5	LVOT
24	Idiopathic	PVC	32	No	Yes	RVOT	3.5	CS	3.5	RVOT
25	Idiopathic	PVC	30	No	No	Septal LV	3.5	CS/GCV	3.5	Septal LV
26	Sarcoidosis	VT	35	Yes	No	Epicardial left	3.5	Septal left	3.5	Septal LV

B-RFA, bipolar radiofrequency ablation; CS, coronary sinus; DCM, dilatative cardiomyopathy; GCV, great cardiac vein; ICM, ischaemic cardiomyopathy; IVS, interventricular septum; LCC, left coronary cusp; LV, left ventricle; LVOT, left ventricular outflow tract; MVA, mitral valve annulus; RF, radiofrequency energy; RVOT, right ventricular outflow tract.

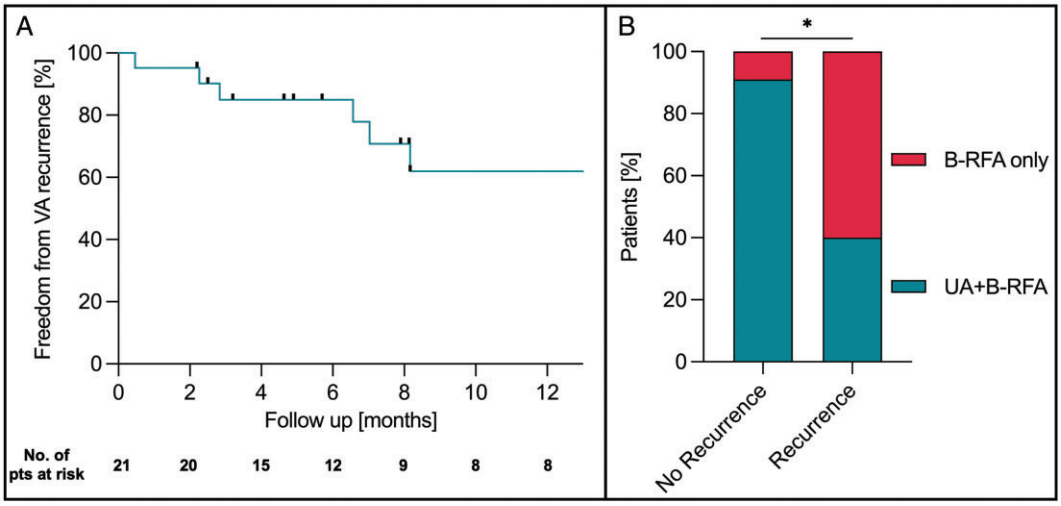


Figure 2 Mid-term follow-up after bipolar ablation. (A) Freedom of ventricular arrhythmia (VA) was observed in 59% of patients within 12 months after initial B-RFA. (*B*) Lower VA recurrence rates were observed in patients with unipolar ablation followed by bipolar ablation (UA+B-RFA) compared with B-RFA alone. B-RFA, bipolar radiofrequency ablation; UA, unipolar ablation; VA, ventricular arrhythmia.

Table 4 Lesion characteristics during *ex vivo* ablation

	B-RFA 30 W	B-RFA 40 W	B-RFA 50 W	SUA 30 W	EA 50 W	Titration (B-RFA 30 + 50 W)	SUA 30 W + B-RFA 50 W	*P*-value All groups
Number of lesions, *n*	15	9	15	11	15	12	11	
Myocardial tissue thickness (mm)	19.4 ± 2.2	18.8 ± 1.8	19.0 ± 1.8	18.0 ± 2.1	18.7 ± 1.7	18.2 ± 1.9	18.4 ± 2.1	0.59
Transmural lesions without steam pop, *n* (%)	0 0	0 0	1 (7)	1 (9)	1 (7)	5 (42)	8 (73)*,†	<0.001
Steam pops, *n* (%)	0 0	0 0	2 (13)	2 (18)	4 (27)	2 (17)	3 (27)	0.29
Lesion volume (mm^3)	231* (97–382)	224 (163–452)	307 (261–561)	463 (303–1405)	95* (41–313)	421 (259–683)	1386*,† (1303–1647)	<0.001
Lesion surface diameter endocardial (mm)	3.9 (2.5–5.9)	4.0 (3.2–5.3)	4.5 (3.8–5.2)	5.5 (4.5–6.4)	4.2† (0–4.7)	4.3† (3.2–4.9)	7.1*,† (6.1–8.6)	0.001
Lesion surface diameter epicardial (mm)	1.4*,† (0–3.2)	3.7 (2.8–5.4)	3.8 (3.1–4.6)	3.9 (3.2–6.7)	2.1 (0–5.4)	3.4 (2.8–4.4)	8.3*,† (7.8–10.0)	<0.001
Maximum lesion depth (mm)	4.8 (3.0–6.9)	4.8 (4.0–6.0)	5.9 (4.0–8.9)	8.1 (5.2–8.7)	4.1 (3.8–5.9)	8.1 (5.2–8.7)	9.3*,† (8.9–10.5)	<0.001
Combined endo- + epicardial lesion depth (mm)	7.5*,† (5.7–9.5)	11.0 (8.9–12.4)	11.7 (10.4–14.2)	11.4 (10.4–14.0)	8.7* (3.8–11.8)	13.5 (11.1–16.9)	18.7*,† (17.6–21.0)	<0.001
Combined lesion depth/tissue thickness ratio (%)	37*,† (28–56)	58 (47–68)	63 (55–76)	65 (53–77)	48*,† (20–61)	68 (61–100)	100*,† (100–100)	<0.001
Maximum intramural lesion diameter (mm)	9.3 ± 3.7	9.5 ± 1.5	10.1 ± 1.4	12.1 ± 2.5	8.3 ± 3.7†	10.5 ± 2.2	12.0 ± 0.9*	0.018
Depth at maximum diameter (mm)	2.3 (1.1–2.6)	2.3 (2.0–2.8)	2.2 (1.8–2.6)	2.4 (2.1–2.8)	2.5 (2.2–3.3)	2.5 (2.0–3.7)	3.8* (2.5–4.6)	0.023

Values are reported as mean ± standard deviation or absolute numbers and percentages. In case of non-parametric data, results were provided as medians with inter-quartile ranges.
*$P < 0.05$ vs. B-RFA 50 W.
†$P < 0.05$ vs. SUA 30 W.
B-RFA, bipolar radiofrequency ablation; EA, epicardial adipose tissue; SUA, sequential unipolar ablation.

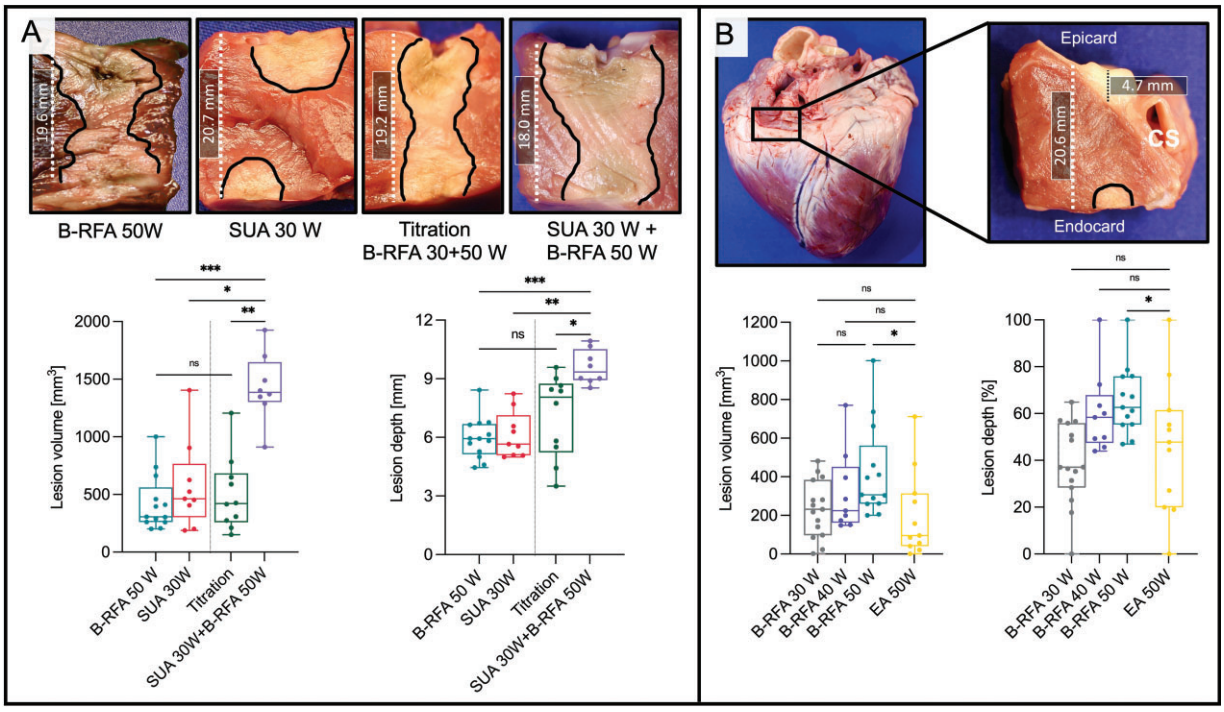


Figure 3 Lesion formation during common clinical bipolar ablation approaches. (A) Lesion volume and depth significantly increased after combination of sequential unipolar (SUA) and bipolar ablation (B-RFA), whereas energy titration did not significantly alter macroscopic lesion characteristics. (*B*) B-RFA with 50 W in regions of significant epicardial adipose tissue (EA) close to the coronary sinus (CS) significantly reduced lesion volume and depth compared with B-RFA at regions without EA. Commonly, no lesion was visible at the epicardial site (upper right image). B-RFA, bipolar radiofrequency ablation; EA, epicardial adipose tissue; SUA, sequential unipolar ablation.

one patient with an existing implantable cardioverter-defibrillator, a permanent atrioventricular block III° occurred after B-RFA at the high interventricular septum.

A median follow-up of 211 days (inter-quartile range: 116–453 days) was obtained in 21 patients (*Figure 2*), with three patients lost to follow-up ($n = 2$ VT/$n = 1$ PVC). Freedom from any VT was found in 6/11 patients undergoing VT ablation. One patient presented with recurrence of electrical storm and underwent additional B-RFA VT ablation 50 days after the initial B-RFA procedure.

Successful PVC ablation was observed in 5/10 patients. One patient received repeat B-RFA PVC ablation 69 days after the initial procedure with success during 66 days follow-up. In the remaining four patients, burden reduction varied between 55% and 75%, with one patient showing no PVC burden decrease. No difference in VA recurrence was observed between patients with or without structural heart disease (57% vs. 33%, $P = 0.40$).

Ex vivo ablation

A total of 88 ablation lesions (LV free wall $n = 67$, interventricular septum $n = 21$) were analysed. A detailed overview about lesion characteristics is given in *Table 4*. The mean myocardial tissue thickness was 19 ± 2 mm (range 15–23 mm). Audible and macroscopic steam pops were registered in 13 lesions (range 0–27%) without significant differences between groups ($P = 0.29$). The maximum bipolar impedance drop was not associated with steam pop occurrence [no steam pop: median—31 (inter-quartile range 24–49) vs. steam pop—38 (30–59) Ω, $P = 0.24$] and did not differ between all groups ($P = 0.08$).

Influence of bipolar energy titration on lesion formation

Energy titration resulted in similar mean lesion volume compared with direct B-RFA using 50 W ($P = 0.52$) and a trend towards higher transmurality rates without reaching statistical significance ($P = 0.052$). Steam pop rates were similar between both groups, ranging between 0% and 27% ($P > 0.99$). Titration did not influence the endo-/epicardial lesion surface diameter ($P = 0.44$; $P = 0.33$), maximum lesion depth ($P = 0.10$), maximum intramural diameter ($P = 0.61$), or depth at the maximum intramural diameter ($P = 0.10$).

Combined sequential unipolar and bipolar ablation increases lesion volume and transmurality rates

Combined unipolar and B-RFA was a common approach in our cohort used in 58% of cases. *Figure 3A* displays lesion characteristics of energy titration and combined SUA+B-RFA approaches in comparison to B-RFA 50 W and SUA 30 W controls. B-RFA with 50 W resulted in increased lesion volume but not depth in comparison to

SUA 30 W (lesion volume: $P = 0.05$; lesion depth $P = 0.31$). Combined SUA+B-RFA resulted in an increased transmurality rate compared with the titration, B-RFA 50 W and SUA 30 W control group ($P < 0.001$). Furthermore, the lesion volume increased in comparison to all three groups ($P < 0.001$) and displayed the highest combined endo- and epicardial lesion depth ($P < 0.001$). The epicardial lesion surface diameter was also increased compared with all three groups ($P < 0.001$), whereas the endocardial lesion surface diameter appeared larger compared with titration as well as B-RFA 50 W group only. In the clinical cohort, this approach was more frequently observed in patients with arrhythmia freedom during follow-up compared with patients with VA recurrence irrespective of underlying myocardial substrate and applied maximum power (92% vs. 36%, $P = 0.009$).

Epicardial adipose tissue impacts lesion formation

In our clinical cohort, B-RFA was conducted in 81% of procedures at sites where high EA thickness can be expected (outflow tract, aorto-mitral continuity, left ventricular summit, epicardial LV). *Figure 3B* displays lesion characteristics during B-RFA in EA. Lesion transmurality was similar between EA and B-RFA 30–50 W control groups (range 0–7%, $P = 0.55$). The total lesion volume as well as the combined endo- and epicardial lesion depth were lower in the EA group compared with the B-RFA 50 W group (endocardial $P = 0.03$; epicardial $P = 0.018$). No epicardial lesion was detected in 36% of lesions in the EA group, significantly less compared with the B-RFA 50 W group ($P = 0.03$). The maximum intramural diameter, depth at the maximum diameter, endocardial and epicardial lesion surface diameter were similar between EA and B-RFA 30–50 W groups.

Discussion

To our knowledge, this study provides the first multicentre experience of patients with therapy-refractory ventricular arrhythmias undergoing B-RFA using a dedicated setup. The major findings are as follows: (i) B-RFA using a dedicated RF generator appears feasible and safe, with a high acute success rate and minor adverse events without need for surgical intervention or prolonged hospital stay. During a follow-up of up to 2 years, 52% of patients remained arrhythmia-free after one B-RFA procedure, a high success rate in view of the unsuccessful prior procedures in all patients. (ii) The combination of unipolar ablation followed by B-RFA might enhance lesion formation.

Challenges of bipolar radiofrequency ablation

The 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement addresses current challenges of B-RFA VA catheter ablation, which was not recommended routinely because of the lack of standardized settings.[5] Previous studies using different custom built setups for B-RFA did not address the limitation of lacking temperature and/or impedance monitoring for both catheters.[9,10] With power settings ranging between 25 and 50 W, reported complication rates varied overall.[9,11,12] In our multicentre cohort, B-RFA using a dedicated setup was performed safely at an average maximum power of 40 W (range 20–50 W). One non-randomized study comparing unipolar to B-RFA using a custom setup in VA was recently suspended because of higher adverse events in the bipolar group (NCT02374476). The dedicated B-RFA setup appears to be safe in this report. Unlike other systems, it addresses the need for simultaneous monitoring of temperature, impedance and irrigation of both catheters as well as changing between unipolar and B-RFA without significant setup changes needed during the procedure.

An overview on published clinical B-RFA studies in patients with VA can be found in the supplementary material. Long-term outcome after B-RFA remains challenging: Two B-RFA multicentre series reported acutely reduced VA burden, but relevant VT recurrence rates in ~50% and 67% of patients.[9,12] This is in line with our observed acute and mid-term outcome. However, in mentioned studies only patients with structural heart disease were included for B-RFA, whereas our collective consisted of 50% of patients without detectable structural heart disease. As deep intramural foci are a relevant cause for unipolar ablation failure,[13] they are common not only in patients with structural heart diseases: Approximately >10% of idiopathic septal VA and 20% of idiopathic LVOT VA have been described to be of intramural origin.[14,15] In our cohort, 83% of patients without structural heart disease presented VA originating in the left/right ventricular outflow tract or aorto-mitral continuity. Therefore, B-RFA displays a valuable therapeutic option in patients with idiopathic VA.

Nevertheless, when considering the bail-out situations in which B-RFA is mostly employed often with several unsuccessful previous ablation attempts, we believe that this partial success is promising. Della Bella *et al.*[12] recently published a case series using a dedicated 3-D software for B-RFA enabling visualization of both catheters during ablation. Although not described so far in detail, this might be additionally helpful in combination with presented dedicated B-RFA setup as a next step to improve B-RFA applications and procedural workflow.

Impact of commonly used clinical approaches during bipolar ablation

The effect of B-RFA on lesion depth and transmurality rates may be limited in myocardial tissue exceeding 15 mm thickness resulting in similar lesion volumes compared with unipolar ablation.[16] *Ex vivo* power titration during sole B-RFA resulted in similar lesion volume levels and steam pop rates compared with immediate higher power B-RFA, while being associated with a trend towards increased transmurality rates. Furthermore, combining unipolar with consecutive B-RFA was conducted in approximately two-thirds of presented cases, which significantly increased lesion volume and transmurality rates without increasing steam pop rates in our *ex vivo* model. Interestingly, patients without VA recurrence underwent combined unipolar and B-RFA significantly more frequently than patients with recurrence in our clinical cohort. Therefore, this may be a valuable B-RFA approach for therapy-refractory VA in the clinical setting. How a systematic application of these specific approaches may influence lesion formation *in vivo* needs further investigation.

Importance of epicardial adipose tissue assessment

Areas of thickest EA are commonly found along the basal perivascular segments, reaching >5 mm in 60% of wall segments during systole.[17] Of interest, our data on ablation in areas with significant EA confirmed recent *ex vivo* study results[18]: EA has lower electrical conductivity compared with pericardial fluid, leading to RF current preferably flowing through surrounding fluid instead of EA and underlying myocardial tissue.[2] Accordingly, epicardial sites did not show any significant lesion formation in one-third of lesions in our *ex vivo* model. Whether emerging catheter systems such as RF needle catheters, pulsed-field or high intensity ultrasound ablation may be able to overcome limited lesion formation at EA sites needs further investigation.[19–21]

Limitations

This study has several limitations. Being a retrospective multicentre study, ablation protocols and settings differed between centres with possible selection bias. As we report the so far largest clinical cohort with a dedicated B-RFA setup, the total number of procedures remains small with no matched control group which has to be considered during interpretation of presented safety data. Furthermore, an exact validation of the distance between active and return catheter and their respective position was not possible. Limitations of our *ex vivo* model include presence of ischaemic myocardium due to non-perfusion as well as altered cellular and inflammatory reaction to RF ablation compared with *in vivo* models. The used model did not allow to investigate lesion formation in areas of myocardial scar. Immediate translation of presented *ex vivo* data into our clinical cohort remains challenging, as there are no histological data displaying the relationship between lesions and ablation targets. Passive catheter cooling characteristics may also differ compared with epicardial catheter positioning/positioning in the coronary sinus.

Conclusion

Bipolar catheter ablation using a dedicated approach is feasible and safe for the treatment of VA. Using this standardized setting, acute efficacy is high with low complication rates. Overall follow-up is encouraging as more than half of the patients remain arrhythmia-free within 12 months. Combined SUA and B-RFA may enhance ablation efficacy.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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Oesophagopericardial fistula as a late complication of stereotactic radiotherapy for recurrent ventricular tachycardia

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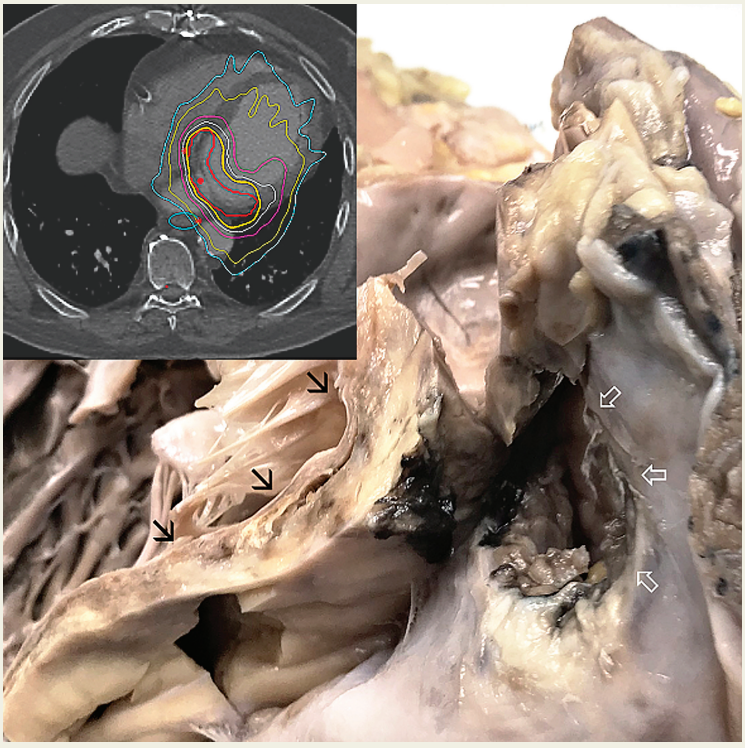
Severe adverse effects of stereotactic body radiotherapy (SBRT) for recurrent ventricular tachycardias (VTs) have not been reported. We describe the late complication of SBRT (25 Gy, CyberKnife, Accuray) in a 67-year-old patient with previous arterial coronary revascularization, including gastroepiploic artery, and subsequent recurrent VTs despite catheter ablation. He developed radiation oesophagitis 18 days after SBRT, which resolved on antiulcer therapy, and 6 months later was admitted for severe symptomatic ulcer. Despite intensive treatment, he died because of bleeding oesophagopericardial fistula. Post-mortem macroscopic picture shows the myocardial substrate in the inferior wall (black arrows) and adjacent oesophagopericardial fistula through the parietal pericardium (open arrows). Inset depicts radiosurgical treatment plan with coloured isodose lines.



Our case illustrates that SBRT may be complicated even in a long-term course, and oesophagopericardial fistula could be one of the potential complications. Therefore, the risk/benefit of SBRT for VT should be always carefully considered, and long-term follow-up is advisable.

The full-length version of this report can be viewed at: https://www.escardio.org/Education/E-Learning/Clinical-cases/Electrophysiology.