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Original Article

Safety and Efficacy of Stereotactic Cardiac Radio-Ablation for Ventricular Tachycardia in Patients at High Risk of Mortality

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ABSTRACT

Background: Patients who have recurrent ventricular tachycardia (VT) despite receiving antiarrhythmic drugs (AADs), implantable cardioverter defibrillator placement, and catheter ablation (CA) are at significant risk of morbidity and mortality.

Methods: We offered completely noninvasive cardiac radio-ablation (CRA) on a "compassionate use" basis for patients who were unable or unwilling to undergo CA for recurrent VT despite their having received treatment with AADs and placement of an implantable cardioverter defibrillator. All patients who were referred to the CRA program were entered into a prospective registry and followed indefinitely thereafter.

Results: A total of 20 patients were referred for CRA, and 10 elected to undergo the treatment as outpatients. Ten patients declined CRA therapy, owing to fear of complications and/or logistic concerns relating to attending multiple hospital visits; they received escalated drug therapy. All patients who were referred to and were agreeable to CRA received CRA. No patients were excluded or were denied CRA by clinicians for any reason, and all patients were followed clinically. The VT burden decreased significantly, by $>$ 90% (both anti-tachycardia pacing and shocks), and 1 patient died of a cardiovascular cause at 1 year following a single CRA treatment of 25 Gy. One patient experienced steroid-responsive pneumonitis as an adverse event post-CRA

RÉSUMÉ

Contexte : Les patients atteints de tachycardie ventriculaire (TV) récurrente malgré la prise d'antiarythmiques, l'insertion d'un défibrillateur cardioverteur implantable et l'ablation par cathéter sont exposés à un risque important de morbidité et de mortalité.

Méthodologie : Nous avons offert à des patients qui ne pouvaient ou ne voulaient pas se prêter à une ablation par cathéter pour une TV récurrente malgré la prise d'antiarythmiques et l'insertion d'un défibrillateur cardioverteur implantable la possibilité de subir une ablation par radiofréquence, une intervention totalement non invasive, « à titre humanitaire ». Tous les patients orientés vers le programme d'ablation par radiofréquence ont participé à un registre prospectif et ont été suivis indéfiniment par la suite.

Résultats : Au total, 20 patients se sont vu proposer de subir une ablation par radiofréquence et 10 d'entre eux ont décidé de se prêter à l'intervention, pratiquée en clinique de jour. Dix patients ont décliné l'offre, par crainte des complications et (ou) pour des raisons logistiques liées à la nécessité d'effectuer de multiples visites à l'hôpital; ils ont reçu un traitement médicamenteux dont la dose a été graduellement augmentée. Tous les patients à qui l'ablation par radiofréquence a été proposée et qui ont accepté l'offre ont subi l'intervention. Aucun patient n'a été exclu ou ne s'est vu refuser l'ablation par radiofréquence par les cliniciens pour un motif quelconque. Tous les pa-

In patients who already have been treated with antiarrhythmic drugs (AADs) and Implantable cardioverter-defibrillators (ICDs), recurrent ventricular tachycardia (VT) results in painful shocks, reduced quality of life, deteriorating ventricular function, and death.[1] Canadian Cardiovascular Society guidelines suggest referral for catheter ablation (CA) as the gold-standard treatment for VT.[2] CA often is limited by

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(common terminology criteria for adverse events [CTCAE] grade 2). For the 10 patients who declined CRA, no appreciable reduction in VT occurred, despite their receipt of increasing dosages of AADs, and 5 patients died of cardiovascular causes within 1 year.

Conclusions: Noninvasive stereotactic CRA is well tolerated with good short-term efficacy for recurrent VT on a "compassionate use" basis. Prospective randomized controlled trials to determine the relative efficacy of CA vs CRA for VT are urgently required.

tients ont fait l'objet d'un suivi clinique. Le fardeau associé à la TV a considérablement diminué, de plus de 90 % (stimulation antitachycardie et chocs); un patient est décédé d'une cause cardiovasculaire 1 an après avoir subi un seul traitement d'ablation par radiofréquence de 25 Gy. Un patient a présenté une pneumonite corticosensible après avoir subi une ablation par radiofréquence (critères terminologiques standard pour les effets indésirables [CTCAE; *common terminology criteria for adverse events*] du National Cancer Institute, grade 2). Chez les 10 patients qui ont refusé de se prêter à une ablation par radiofréquence, aucune réduction appréciable de la TV n'a été observée malgré l'administration de doses plus fortes d'antiarythmiques, et cinq patients sont décédés de causes cardiovasculaires en l'espace de 1 an.

Conclusions : L'ablation par radiofréquence stéréotaxique non invasive est bien tolérée et offre une bonne efficacité à court terme lorsqu'utilisée « à titre humanitaire » en cas de TV récurrente. Il est impératif de réaliser des études prospectives comparatives à répartition aléatoire pour déterminer l'efficacité relative de l'ablation par cathéter comparativement à l'ablation par radiofréquence dans le traitement de la TV.

complex logistics, complications, and recurrent VT, especially in patients with significant comorbidities or nonischemic cardiomyopathy.[3-7] Stereotactic radio-ablation recently has shown promising results in patients who suffer recurrent VT despite undergoing CA.[8]

Stereotactic cardiac radio-ablation (CRA) attempts to compensate for the limitations of conventional invasive mapping and ablation by delivering a single dose of noninvasive radiotherapy guided by electrocardiographic and/or electroanatomic mapping in combination with multimodality imaging.[8] This approach significantly reduces the probability of adverse events occurring in the short term while permitting targeting of the entire endocardial and epicardial arrhythmia substrates, apparently with few limitations.[9-11] Although initial reports describe a high level of VT suppression with a minimal number of adverse events in the short term, a variety of methodologies have been described, and clinical success is not universal.[12,13] We describe our initial results of a "compassionate use" CRA program, with follow-up censored at 1 year.

Materials and Methods

All patients were treated under a "compassionate use" protocol following approval of the University of Ottawa Heart Institute Research Ethics Committee. Indications for referral to the program were symptomatic VT resulting in ICD shocks, despite amiodarone therapy, in patients who were medically unable to undergo CA, termed "unable", or who had undergone prior CA and declined a repeat procedure, termed "unwilling." No formal exclusion criteria were used for our CRA program. All patients were followed up clinically as part of routine ICD care in our cardiac device clinic. Patients who declined CRA received escalated AAD therapy in accordance with Canadian Cardiovascular Society guidelines.[2] All patients receiving CRA were treated on an outpatient basis. Clinical follow-up care was a hybrid of cardiology assessment, primarily via the cardiac implantable electronic devices clinic at the University of Ottawa Heart Institute and, for those receiving CRA, radiation oncology follow-up care via the Ottawa Hospital Cancer Centre. Device clinic appointments with ICD interrogation were scheduled at 1, 3, 6, and 12 months for all patients, and an echocardiogram was scheduled for 3 to 6 months post-CRA. In the event of an ICD shock, patients were reassessed within 24 hours at the University of Ottawa Heart Institute. If patients were VT-free at the 3- and 6-month visits, then reduction or withdrawal of AADs was offered. Radiation oncology clinic appointments routinely were scheduled at 30 days and at 1 year, with additional appointments made as necessary if adverse events were suspected.

Arrhythmia substrate identification: overview

Patients wishing to receive CRA (n = 10) underwent the following protocolized set of multimodality imaging: late iodine enhancement (LIE) and 4-dimensional (D) computed tomography (CT) scanning with abdominal compression; static and free breathe perfusion positron emission tomography (PET) scanning; and a modified noninvasive electrophysiology (EP) study (noninvasive programmed stimulation [NIPS]) study with noninvasive electrocardiographic (ECGi) mapping. Following this process, a team comprising cardiac electrophysiologists, imaging cardiologists, radiation oncologists and medical physicists identified the arrhythmia substrate for radio-ablation, and then, following visual consensus, translated these targets, by hand, into stereotactic radiation treatment planning.

CT scar imaging with LIE. Cardiac images were acquired on a dual-source cardiac-enabled CT scanner (Somatom Definition, Siemens Medical Solutions, Munich, Germany). An arterial phase data set was acquired using full retrospective electrocardiogram (ECG) gating from the aortic arch to the diaphragm (100-120 kVp, depending on patient size, 370 mAs). LIE images were acquired in a single end-systolic phase (370 mAs, a dual energy 100/140 kVp protocol). Images were

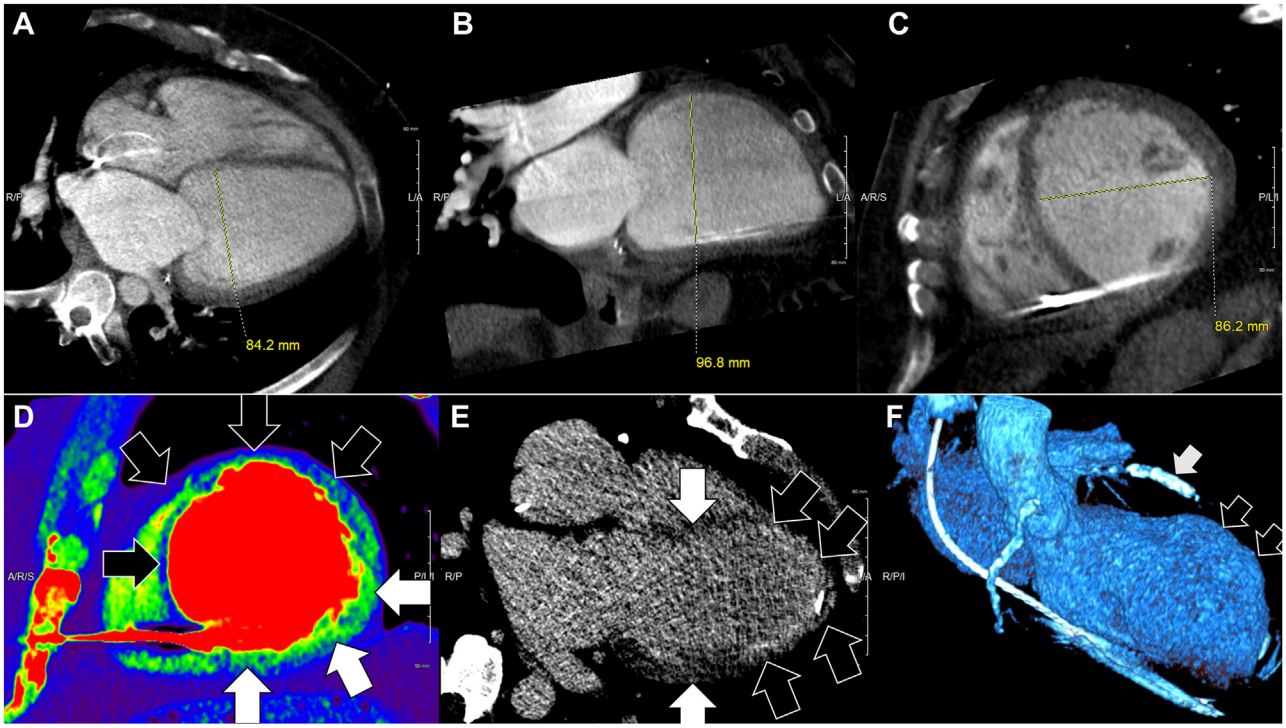

Figure 1. Role of scar imaging computed tomography (CT) late iodine enhancement (LIE). (**A**–**C**) Patient 1, contrast-enhanced multiplanar reformat CT images with nonischemic cardiomyopathy. Here, the role of CT imaging is limited to anatomic delineation of the ventricular size and function. Scar tissue is extremely difficult to reveal by CT in patients with nonischemic dilated cardiomyopathy, as it often is diffuse, and was not visible in this examination (images not shown). (**D**–**F**) Patient 2, different CT approaches to revealing scar tissue in a patient with ischemic cardiomyopathy. (**D**) Arterial phase short-axis reconstruction of the left ventricle using a colour look-up table designed to enhance the contrast differences between well-perfused and hypo-perfused myocardium. The inferolateral wall is not infarcted and remains relatively well perfused (**in green**; **white arrows**), whereas the anterior wall, anterior septum, and anterolateral wall are severely hypoperfused (**in blue; black arrows**), indicating the presence of ischemic scar tissue. (**E**) LIE image acquired 5 minutes after contrast injection depicts a 4-chamber slice of the heart in which both infarcted (**black arrows**) and noninfarcted (**white arrows**) myocardium are present. The contrast difference between normal and abnormal areas is less striking than it is with magnetic resonance imaging late gadolinium enhancement, but with experience, ischemic scar tissue usually is readily detectable. (**F**) An alternative approach to scar tissue identification is to use 3D volume rendered images; an example is shown here in end systole. Not only is the stented and occluded left anterior descending artery shown (**white arrow**), but a focal aneurysmal expansion (indicating transmural scar tissue) also is readily identified (**black arrows**).

acquired with the patient in quiet respiration. A compression board was applied to the patient's abdomen to reduce respiratory motion, or during interrupted inspiration. Two-D (D), 3D, and 4D multiplanar reformats were created offline on a dedicated workstation (Siemens Syngo.via) and reviewed for evidence of systolic wall thickening, fatty metaplasia, and the presence of myocardial enhancement suggestive of scar (Fig. 1).

Cardiac PET. All patients underwent resting myocardial perfusion assessment with ^{82}rubidium or ^{13}N-ammonia PET imaging on a Discovery 690 scanner (GE Healthcare, Waukesha, WI). Patients with ischemic cardiomyopathy (N = 9) also underwent viability imaging following administration of 3 MBq/kg of ^{18}fluorodeoxyglucose (FDG) according to our standard protocol.[14] FDG and perfusion images were processed using FlowQuant v2.5 software (FlowQuant, Ottawa, Canada) to create polar-maps identifying regions of matched defects (fibrotic scar) and mismatched regions of FDG excess (hibernation; Fig. 2).

Noninvasive electrocardiographic mapping (NIPS)

First, a 12-lead ECG, if available, was analyzed to determine the site of origin and then was projected on the American Heart Association (AHA) 17 segment model.[15] ICD interrogation and electrogram analysis was performed to identify VT initiation, tachycardia cycle length, and response to right ventricular apical pacing (anti-tachycardia pacing [ATP]). A noninvasive EP study (NIPS) was performed with the patient under intravenous sedation, using the ECGi CardioInsight system (Medtronic, Minneapolis, MN; Fig. 3). A modified Wellens protocol was used to induce VT via the RV ICD lead in all patients.

Stepwise approach to targeting

Step 1: arrhythmia substrate delineation. Site(s) of origin from a12-lead ECG were compared to areas of slow conduction during sinus rhythm and the site of earliest epicardial activation during VT identified during NIPS. We employed the AHA 17-segment left ventricular (LV) anatomy model to

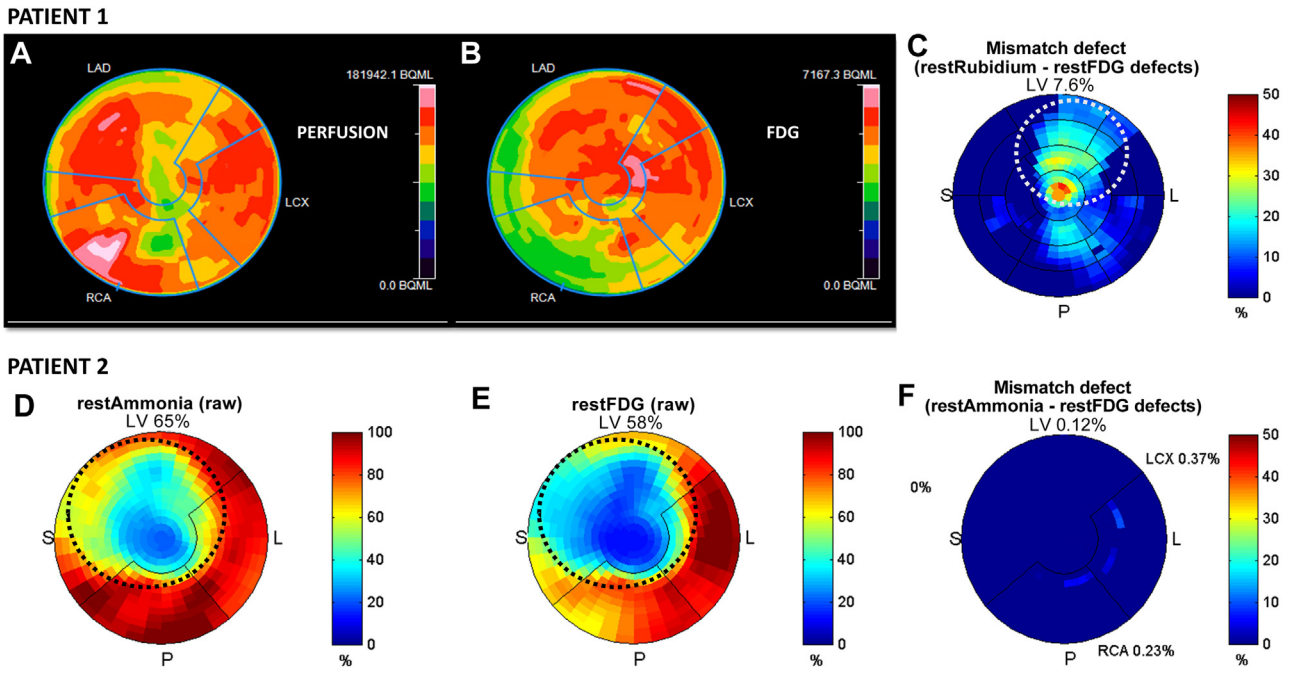

Figure 2. Role of positron emission tomography (PET) imaging: PET viability imaging was used to try to identify areas of intermingled viable and nonviable myocardium. This technique utilizes measurement of both resting perfusion and metabolic cell activity to characterize myocardium as being either normal, scarred, or downregulated but potentially recoverable ('hibernating'). Given that ventricular tachycardia (VT) is conducted through channels of viable myocardium in proximity to scar tissue, identification of hibernating regions likely indicates a zone of mixed viability and/or nonviability to target with stereotactic ablative radiotherapy. Patient 1 demonstrates (**A**) a mild reduction in perfusion in the anterior wall, although the same area exhibits (**B**) preserved ^{18}fluorodeoxyglucose (FDG) metabolism, indicating viability; this (**C**) so-called "mismatch" between perfusion and metabolism is frequently co-localized with the area of VT emergence on electroanatomic mapping. Patient 2 represents the converse situation in which both (**D**) perfusion and (**E**) metabolism are reduced severely in the same myocardial segments (**dotted circles**)—referred to as a "matched" defect (**F**). Given that most of this region is dense scar tissue, it is unlikely to provide exit points for VT. The margins of the scar (where there is intersection with viable myocardium) are often of greater electrophysiological importance. L, lateral; LAD, left anterior descending; LCX, left circumflex; LV, left ventricle; P, posterior; RCA, right coronary artery; S, septal.

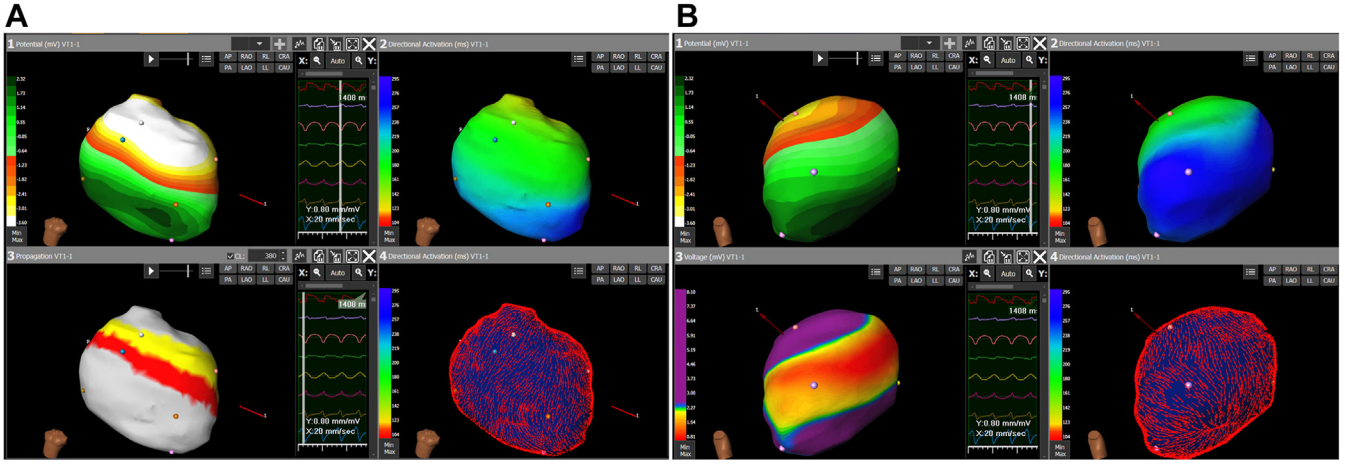

Figure 3. Noninvasive electrocardiographic (ECGi) images of patient 1 during ventricular tachycardia (VT): (**A**) left anterior oblique (LAO) cranial views, and (**B**) left caudolateral views. CardioInsight system (Medtronic, Minneapolis, MN) projections of VT indicating earliest epicardial activation (VT exit), (**A**) conducting in a "clockwise" direction around (**B**) an area of low voltage. ECGi Video 1, (view videos online) of VT propagation are available in Supplemental Appendix S1.

Table 1. Patient characteristics

Parameter	All patients (n = 20)	Declined CRA (n = 10)	Treated with CRA (n = 10)	Declined vs treated *P*
Age, y	70 ± 8	73 ± 6	66 ± 9	< 0.05
LVEF, %	31 ± 13	36 ± 12	25 ± 12	0.058
Charlson Comorbidity Index	7 (5, 8.8)	6.5 (5.8, 8.3)	7 (5, 9)	ns
eGFR (CKD-EPI), mL/min	64 ± 21	61 ± 21	67 ± 22	ns
BMI, kg/m^2	31 ± 7.6	32 ± 8	31 ± 8	ns
PAINESD score	20 (17, 23)	17 (13, 22)	23 (17, 26)	< 0.05
ATP pre-referral, n	38 (15, 58)	37 (12, 62)	39 (19, 61)	ns
ICD shocks pre-referral, n	4 (2, 6)	2 (1, 7)	5 (3, 7)	ns

Values are mean ± standard deviation, or median (interquartile range), unless otherwise indicated.

ATP, anti-tachycardia pacing; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CRA, cardiac radio-ablation; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; ns, nonsignificant; PAINESD, Risk of Acute Haemodynamic Decompensation during Catheter Ablation of VT; VT, ventricular tachycardia.

ensure all areas of disease were included in the radiotherapy target.[15,16] To ensure high-fidelity target identification, the cardiologist, the radiologist, and the radiation oncologist met to delineate a consensus target in the cardinal planes on planning CT.

Step 2: multimodality imaging review. Images were acquired by PET and CT LIE as described above and processed in both orthogonal and cardiac planes (Hermes workstation, Hermes Medical Solutions, Montreal, Canada) and displayed offline (Invia Corridor 4DM, INVIA Medical Imaging Solutions, Ann Arbor, MI). Reconstructed images were displayed side-by-side in both multiplanar reformats and 17-segment model bullseye plots of thickening, perfusion, LIE, viability, and mismatch. From this display, a single reader attempted to classify each segment into 1 of 3 categories, as follows: (i) transmural scar tissue; (ii) no scar tissue at all; or (iii) partial scar tissue. This "substrate" for ablation was then cross-correlated with the EP opinion until agreement between the 2 readers could be established and a maximum of 4 segments of myocardium were selected as the target. Once identified, the target was then manually transferred to the radiotherapy ungated CT through visual slice-by-slice comparison, using anatomic landmarks to ensure that the same slice was being identified on both CT data sets. The target was delineated in dedicated radiotherapy planning software by the clinical oncologist on the team.

Step 3: interdisciplinary targeting of radiotherapy treatment. Cardiac stereotactic body radiotherapy represents a unique challenge in radiotherapy delivery, requiring careful consideration of target motion within the cardiac cycle, and within the respiratory cycle. To restrict target motion, the patient setup included abdominal compression. Further, to account for target motion, target delineation was completed on multiple treatment-planning sequences, including respiratory-correlated 4D CT scans. We estimated the uncertainty of targeting and treatment delivery to be $\leq$ 5 mm, similar to the size of a standard radiofrequency ablation catheter tip. The confluence of the target volumes on each sequence was combined to create an internal Gross Target Volume (iGTV) ("ITV"). A planning target volume was determined by creating a 5-mm isotropic expansion on the iGTV ("ITV") to account for intrafraction variability.

Organs at risk (OARs), including the stomach, small bowel, large bowel, esophagus, and proximal bronchial tree were contoured. This procedure is especially important for the stomach and any other viscous structures near the target, owing to the risk of perforation or gastropericardial fistula, as documented in the Electrophysiology-Guided Noninvasive Cardiac Radioablation for Ventricular Tachycardia (ENCORE-VT) phase I/II trial.[8]

With target and OAR contours complete, a radiation treatment plan was generated to deliver a prescription of 25 Gy to the target in a single fraction. Each plan was carefully reviewed, with attention paid to target coverage (to ensure efficacy) and OAR and/or planning organ-at-risk volume (PRV) dose constraints (to ensure safety). When necessary, coverage was compromised to ensure that OAR dose constraints were met.

Treatment comprised a single outpatient session of 25 Gy, with an on-beam time of approximately 15 minutes targeting the VT exit site and with adjacent myocardial scar constrained to $\leq$ 4 segments of the AHA model. All patients had ICD tachytherapies temporarily discontinued during CRA and ICD interrogation post-treatment. All patients received oral anticoagulation with new oral anticoagulants for 30 days post CRA to prevent LV thrombus formation.

Continuous variables with normal distribution are presented as mean (standard deviation) with non-normally distributed variables reported as median (interquartile range [IQR]). In sample sizes of $\leq$ 10 per group, nonparametric tests, such as the Mann−Whitney *U* test and the Wilcoxon signed-rank test, were used. Statistical testing was performed using GraphPad Prism (version 10) statistical software (GraphPad, La Jolla, CA). The threshold for statistical significance was set at $P < 0.05$.

Results

Between August 2019 and June 2023, a total of 30 patients were referred to the compassionate use CRA program, and to date, 20 patients have received CRA. We describe the outcomes of the first 20 patients referred to the program who have completed 1 year of follow-up care—10 patients who received CRA and 10 patients who declined CRA.

All patients had symptomatic VT and received appropriate shock therapy within 30 days of referral to the program. The vast majority (90%) were taking amiodarone at the time of VT; the remaining 2 patients had been diagnosed previously as being amiodarone-intolerant. All patients were considered for CA therapy but were deemed to be high risk, using the

Table 2. Radiotherapy target volumes

Gross tumour volume, cc	Internal target volume, cc	Planning target volume, cc
52.6 (18.9−86.4)	57 (29.6−109.2)	110 (54.2−204.3)

Values are median (range).

PAINESD score (Risk of Acute Haemodynamic Decompensation during Catheter Ablation of VT).[6] Ten patients had previously undergone a total of 16 CA procedures, prior to their referral. The most common reason for being "unable" to have CA was persistent LV thrombus (7 patients), and the most often−cited reason for declining CA (ie, being "unwilling") was complications from prior and/or repeat CA (4 patients). Of the 10 patients who declined CRA, escalating AAD therapy consisted of increasing the dose of amiodarone in 9 patients (90%), with the addition of mexiletine in 2 patients (20%).

The mean age of all 20 patients was 70 ± 8 years (90% male), and in 19 patients (95%), the etiology was ischemic cardiomyopathy resulting in a severely reduced ejection fraction and frequent ICD therapies (Table 1). Patients who were referred to the program had significant noncardiac comorbidities, which contributed to their having a perceived high risk of adverse outcomes from CA (Table 1). The median time from referral to NIPS was 13 days (IQR: 8, 32), and the median time from referral to CRA was 69 days (IQR: 38, 80). For all patients, heart failure medications were optimized. In 2 patients, the "time to treatment" was in excess of 100 days, owing to their having a prolonged hospitalization with decompensated heart failure during workup for CRA. No patients received shocks for VT while awaiting CRA.

NIPS results

Clinical localization of the VT site of origin from a 12-lead ECG was available for 3 patients (30%). All 10 patients had inducible VT when they underwent NIPS. The 12-lead ECG of VT in the EP lab matched the clinical ECG in 2 patients (67%). The first and/or dominant VT elicited by NIPS was within 20 ms of the detected ICD electrogram tachycardia cycle length (TCL) in 9 patients (90%). Multiple VT morphologies were observed in 5 patients (50%), and 18 VT circuits were mapped in total. The median VT-TCL was 400 ms (IQR: 320, 490). Surface ECG localization of VT elicited by NIPS was projected to colocalize within 1 segment, by ECGi in 9 patients (90%), and in 15 of 18 VT circuits (83%). The majority of inducible VTs were pace terminable (86%), but internal ICD rescue shock for failed ATP was required in 4 patients. Cardiac implantable electronic devices tachytherapy settings were not altered following NIPS or CRA. The median duration of NIPS was 62 minutes (IQR: 52, 85), with no clinically apparent complications, and all patients had same-day discharge without sequelae.

ECGi mapping was performed in all 18 VT circuits in the 10 treated patients, and on each occasion co-located with an area of scar and/or intermediate viability contemporaneously identified on PET and/or CT scanning (100%). In 2 of the 3 patients who had previously undergone CA, the ECG of VT elicited during NIPS was similar (≥ 11 of 12 leads) to that induced during prior CA, and the exit site identified by ECGi was collocated in both with prior ablation targets.

Medical physics and radiotherapy results

In 2 patients, the target had to be revised to provide enhanced safety to OARs. On both occasions, the target was apical VT, and the revision was made to reduce risk of injury to the stomach. The aggregate volume data are presented in Table 2; the mean on-table treatment time was 12 minutes, 12 seconds (± 5 minutes, 10 seconds).

Safety and efficacy of CRA

Of the 10 patients who underwent CRA, 1 patient (10%) experienced pneumonitis responsive to steroids within 2 weeks of receiving RA (common terminology criteria for adverse events [CTCAE] grade 2—no hospitalization or additional oxygen therapy required). The LV ejection fraction was assessed via echocardiogram 3-6 months following radio-ablation in all patients and was found to have increased from 25% ± 12% to 31% ± 10% (n = 10, paired *t*-test $P = 0.027$). No other complication attributed to radio-ablation was observed.

Total cumulative VT therapies 1 year pre- and post-CRA were reduced by 93% (712 ATP therapies and 62 ICD shocks pre-CRA, vs 49 ATP and 5 shocks post-CRA; $P < 0.05$ Wilcoxon signed-rank test; Fig. 4). Seven patients (70%) were completely free of symptomatic VT for 1 year (Figs. 5 and 6). Three patients (100%) were able to discontinue mexiletine, and 7 (70%) were taking a reduced dose or had discontinued amiodarone at 1 year post−radio-ablation treatment.

Three patients (30%) suffered a total of 5 ICD shocks, and another 3 patients had ≤ 2 episodes of asymptomatic ATP during 1 year of follow-up care (Fig. 6). One patient suffered recurrent VT and ICD shocks and was considered to have treatment failure, as suggested by early recurrence (at < 1 month) with similar morphology TCL, and localization of VT as compared to VT induced during NIPS. Two other patients had recurrence at 4 and 10 months post-CRA, respectively, with markedly different QRS morphology on 12-lead ECG, an 80-120 ms increase in TCL, and localization to nonadjacent segments of the AHA model, suggestive of new VT circuits.

One patient with recurrent admissions for heart failure prior to CRA died of heart failure at 11 months post-CRA, following 10 months of being free from symptomatic VT with no appreciable change in systolic function. Two patients died at 1 year of confirmed noncardiac causes and were arrhythmia-free on postmortem ICD interrogation. No ICD malfunctions post-CRA were observed in any patient.

By contrast, patients who declined CRA had a poor prognosis, despite receiving escalated AAD therapy. The arrhythmia burden was similar during 1 year of follow-up (467 ATP therapies and 42 ICD shocks prior to referral, and 342 ATP therapies and 29 shocks during follow-up care, P = nonsignificant; Figs. 4 and 6). Death and/or recurrent ICD shocks occurred in 8 patients (80%) within 1 year, of whom 5 patients (63%) died from cardiovascular causes

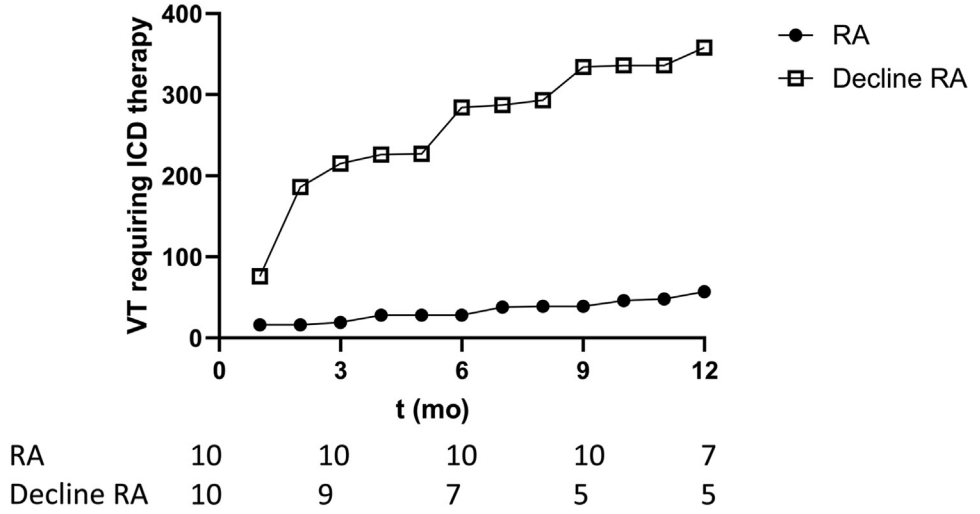

Figure 4. Cumulative ventricular tachycardia (VT) events follow-up evaluation at 1 year. ICD, implantable cardioverter defibrillator; RA, radio-ablation; t, time.

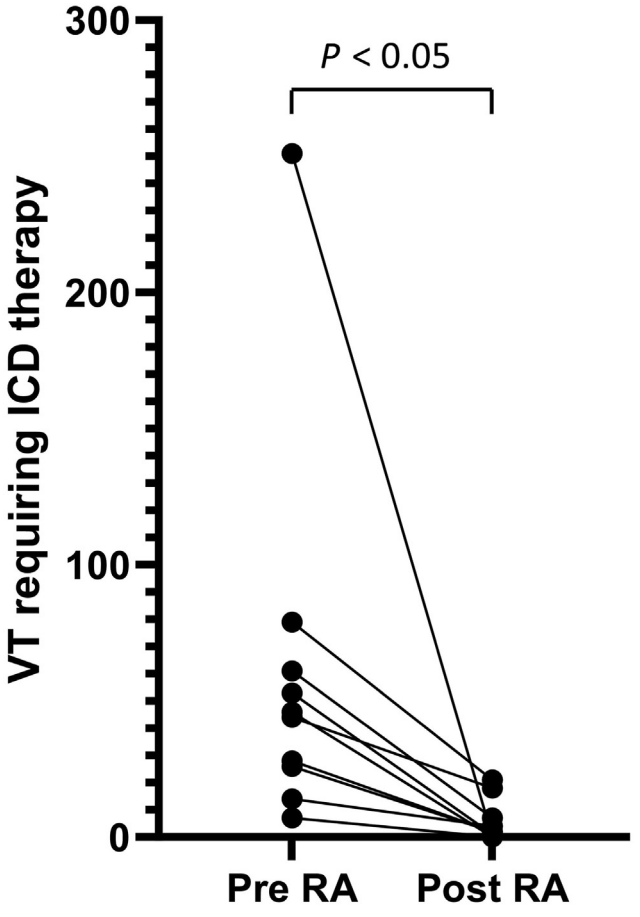

Figure 5. Ventricular tachycardia (VT) burden pre and post radio-ablation (RA), showing VT reduction post-RA. ICD, implantable cardioverter defibrillator.

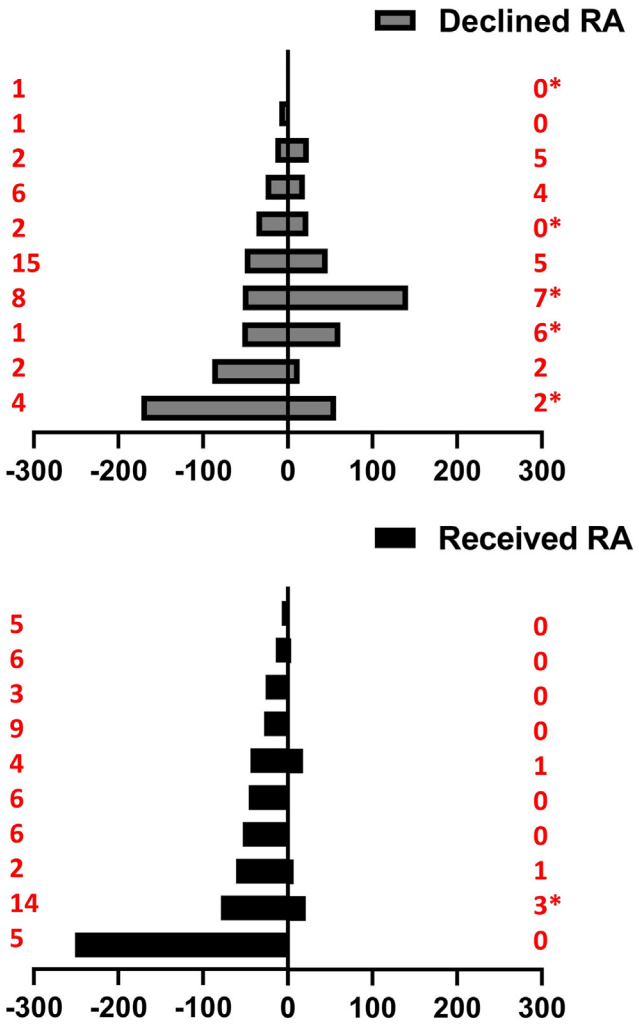

Figure 6. Cumulative implantable cardioverter defibrillator therapy (number of shocks) / ventricular tachycardia burden, per patient at 1-year follow-up. RA, radio-ablation. *Cardiovascular death.

(Fig. 7). Only 1 patient (10%) was free from VT and alive at 1 year of follow-up care (Figs. 6 and 7). Compared to those patients receiving CRA, those who had escalating drug therapy had significant increased cardiovascular mortality at 1 year ($P = 0.038$).

Limitations

This is a small, single-centre, nonrandomized study of a "compassionate use" program of CRA. Although multiple sources of bias are likely present, no patients who were referred were declined or excluded from this analysis. Those who declined CRA serve less as a control group, but rather their results can be used to approximate the natural history of recurrent VT in this high-risk population.

Although the antiarrhythmic mechanism(s) of radiobiology and the long-term effects of CRA are unknown, we believe these results demonstrate the benefits of CRA in those patients who are unwilling or unable to undergo conventional CA.

Our population, almost universally (90%), had ischemic cardiomyopathy. How well our imaging and ECGi tools would have performed with nonischemic patients is unclear, and we cannot extrapolate the success of CRA to a nonischemic population. Doing so requires larger studies or use of registry data.

All patients were stabilized with escalating doses of AADs during workup for CRA. All patients were well enough to undergo outpatient treatment. We did not perform rescue procedures in those who remained in a state of electrical storm despite receiving AADs and propofol sedation, or in those who had an LV assist device *in situ*. Other alternative treatment modalities are available for those patients who have recurrent VT despite CA, such as sympathectomy and/or alcohol ablation, but these options were not available in our institution.

Discussion and Conclusions

In this study, we describe highly effective VT suppression at 1 year (> 90%) following a single CRA treatment of 25 Gy, which has been associated with improved quality of life, prevention of hospital admissions, and increased incidence of survival.[17,18] Of the patients accepting CRA, 70% were alive

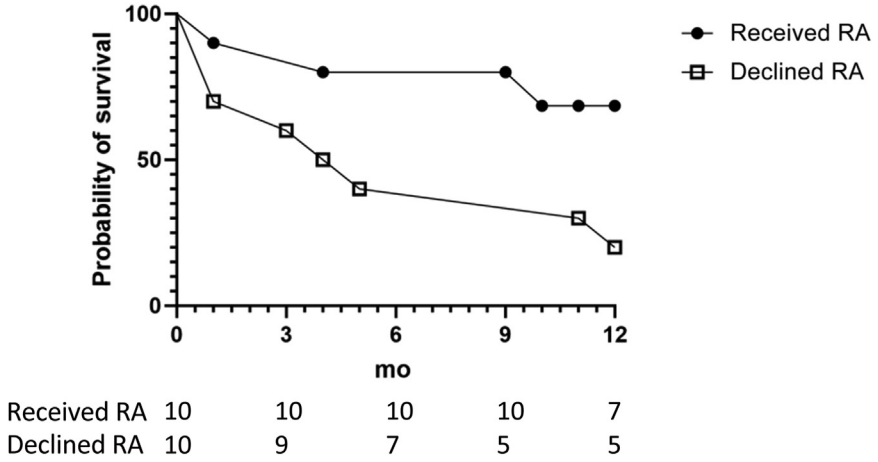

Figure 7. Freedom from implantable cardioverter defibrillator shock or CV death at 1 year. RA, radio-ablation.

and free from shocks at 1 year; only 1 (10%) declined CRA. Although they do not constitute a randomized comparator group, those who declined CRA and received usual clinical care experienced a high frequency of recurrent symptomatic VT and death.

Our results, in terms of both safety and efficacy, are comparable to data published by groups using similar methodologies.[8,9,19,20] Although the mechanism is unknown, CRA appears to have a consistent, immediate antiarrhythmic effect.[21,22]

Safety data published to date appear to confirm that, at least in the short term, CRA is well tolerated, and has relatively few side effects.[9,11] However, methodologies vary widely in arrhythmia mapping, substrate targeting, and CRA delivery; thus, the fact that outcomes are highly variable should not be surprising.[11-13,23] This disparity in outcomes obligates the standardization of operating procedures performed as part of a randomized controlled trial, such as Catheter Ablation Versus Radio-Ablation for Ventricular Tachycardia: a Randomized Controlled Trial (CARA-VT [NCT05047198]).

We chose to use CT and PET as our imaging approaches to define scar tissue. This approach may seem counterintuitive, given the recognized superiority of using cardiac magnetic resonance (CMR) imaging for tissue characterization. However, the use of CMR in this population has several limitations. First, although CMR examination with magnetic resonance—conditional devices can be achieved safely using specialized protocols, the presence of both the pulse generator and the leads inevitably compromises image quality and sometimes obscures a significant portion of the left ventricle. Second, standard CMR late gadolinium enhancement (LGE) protocols routinely acquire 2D slices of nonisotropic image data; this approach eliminates any possibility of subsequent creation of a 3D shell without causing severe pixelation. Although isotropic whole-heart methods exist, they are currently both cumbersome and time-consuming.

CT LIE is a relatively new technique that allows for the delineation of scar tissue according to delayed retention of iodine (as occurs with gadolinium in LGE imaging). However, unlike in LGE imaging, nulling the signal from unscarred myocardium is not possible, and therefore, the image contrast between normal and abnormal tissue is reduced for CT LIE, compared to that with CMR LGE. However, identification of scarred myocardium is possible from a combination of increased myocardial intensity and reduced systolic contractility, especially in the 4D reconstructed images.

We decided to additionally include PET because of prior work suggesting that border zones of intermediate viability are usually involved in the VT circuit. We employed a common clinical protocol that compares perfusion with residual metabolic activity and thus is able to identify areas of hibernating myocardium through perfusion and/or metabolism mismatch. This technique is also relatively isotropic and allows for the creation of 3D shells, facilitating comparison to the LIE and ECGi data. In this predominantly ischemic cohort, we found consistent colocalization of ECGi site of origin within areas of PET "mismatch."[24]

Completely noninvasive CRA on an outpatient basis offers the opportunity to treat frail or multimorbid patients with VT, once they are temporized in specialized centres. CRA delivered by linear accelerators has the potential to be more convenient for patients who live far from the small number of specialized cardiac centres where CA can be performed in Canada. These data require replication in a multicentre RCT, prior to their generalization.

Ethics Statement

The research reported herein adhered to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) and was subject to review by the Human Research Ethics Board.

Patient Consent

The authors confirm that patient consent is not applicable to this article, as this is a retrospective case report using de-identified data; therefore, the institutional review board did not require consent from the patients.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit CJC Open at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2025.01.015.