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CASE REPORT

ADVANCED

CLINICAL CASE

Noninvasive Stereotactic Radiation for Refractory Ventricular Tachycardia After Failure of Cardiac Sympathetic Denervation

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ABSTRACT

Stereotactic body radiation therapy is a novel treatment option for refractory ventricular tachycardia. We present a case of ventricular tachycardia, with epicardial origin located in large inferior infarct scar, that recurred despite treatment with multiple antiarrhythmic drugs, catheter ablation, and cardiac sympathetic denervation. Stereotactic body radiation therapy safely and effectively terminated the arrhythmia. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:1189–1194) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 75-year-old man presented with palpitations and shortness of breath. He was afebrile, with a pulse of 112 beats/min, blood pressure of 102/56 mm Hg, respiratory rate of 28 breaths/min, and oxygen saturation of 95% on room air. He was alert and responding to questions appropriately. Cardiac examination revealed tachycardia with regular rhythm, and jugular venous distension was present; pulmonary examination revealed bilateral crackles. Electrocardiogram demonstrated wide-complex regular tachycardia (**Figure 1**). He was admitted to the intensive care unit. Home metoprolol and amiodarone were continued; mexiletine was discontinued and lidocaine infusion was started.

LEARNING OBJECTIVES

- To understand different treatment options for refractory ventricular tachycardia.
- To review the role of stereotactic body radiation therapy as a new salvage therapy for refractory ventricular arrythmia.

PAST MEDICAL HISTORY

Medical history includes diabetes, hypertension, coronary artery disease with prior inferior infarct status post-5-vessel coronary artery bypass graft and multiple percutaneous coronary interventions to his right coronary artery, and heart failure with reduced ejection fraction.

Three months before this presentation, the patient experienced multiple episodes of ventricular

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ABBREVIATIONS AND ACRONYMS

4DCT = 4-dimensional computed tomograph

CMR = cardiac magnetic resonance

CSD = cardiac sympathetic denervation

ICD = implantable cardioverter-defibrillator

PTV = planning target volume

SBRT = stereotactic body radiation therapy

VT = ventricular tachycardia

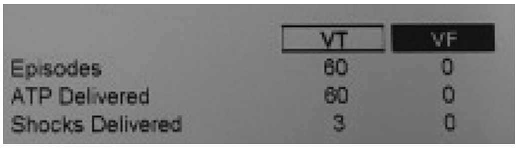
tachycardia (VT) requiring antitachycardia pacing or shock (Figure 2). During a prior admission, coronary catheterization was performed that showed patent grafts not requiring intervention. Cardiac magnetic resonance (CMR) imaging demonstrated a large myocardial scar, consistent with prior infarct, involving the entire basal to apical inferior segments (Figure 3). Electrophysiology study identified a total of 5 separate hemodynamically well-tolerated, slow VTs in different areas of the inferior scar. Four were localized using entrainment activation mapping and successfully ablated (Figure 4). The fifth, with a 500-ms cycle length, initially terminated but later recurred at 560 ms. Given morphology of the QRS complex and inability to ablate from endocardium, this VT was suspected to be epicardial in origin. Epicardial ablation was considered but would require a pericardial window, which was high risk because of prior coronary artery bypass graft and concern for bleeding from grafts caused by adhesions.

The patient underwent stellate ganglion block, which was well tolerated. He then underwent successful robotic sympathectomy of left T2 to T4. Right-sided sympathectomy was not performed because of large pleural plaque. He remained without VT for 72 hours and was discharged home 3 weeks before the current presentation.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for his wide-complex regular tachycardia included VT or supraventricular tachycardia with aberrancy. Given his history and prior electrocardiograms, his presentation was most consistent with VT.

FIGURE 2 Implantable Cardioverter-Defibrillator Interrogation Demonstrating Multiple Episodes of VT Requiring ATP or Shock



ATP = antitachycardia pacing; VF = ventricular fibrillation; VT = ventricular tachycardia.

INVESTIGATIONS

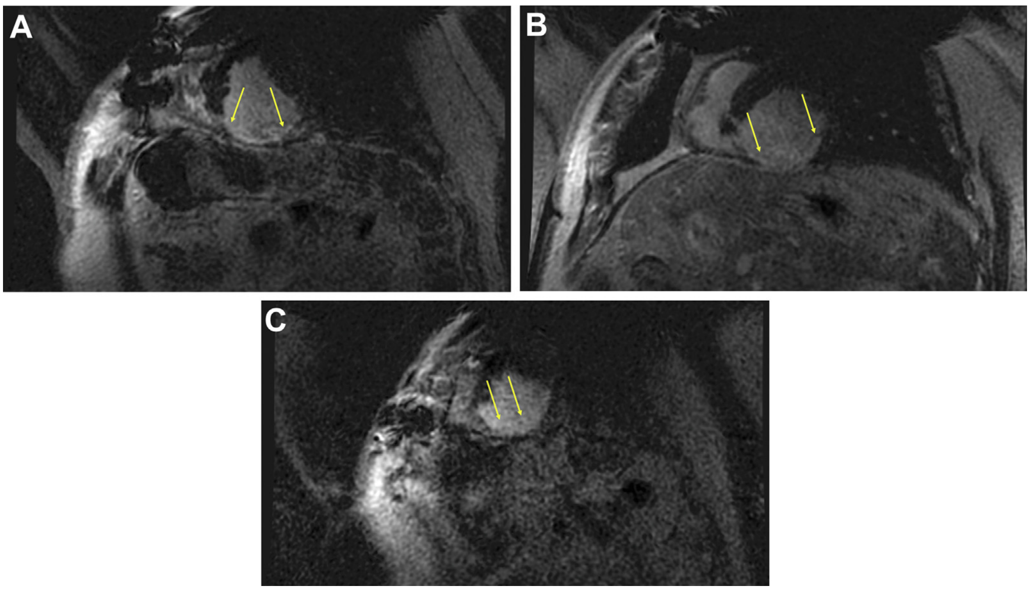
Electrolytes were within normal limits. Transthoracic echocardiography demonstrated stable global hypokinesis and akinesis of the inferior wall, with acute drop in ejection fraction from 35% to 20%.

MANAGEMENT

The patient's implantable cardioverter-defibrillator (ICD) was reprogrammed to have a lower VT detection zone with antitachycardia pacing therapy, which terminated his VT temporarily. Right heart catheterization demonstrated cardiogenic shock, with an index of 1.97 L/min/m^2 (Fick) and elevated filling pressures, which was managed with discontinuation of metoprolol, placement of an intra-aortic balloon

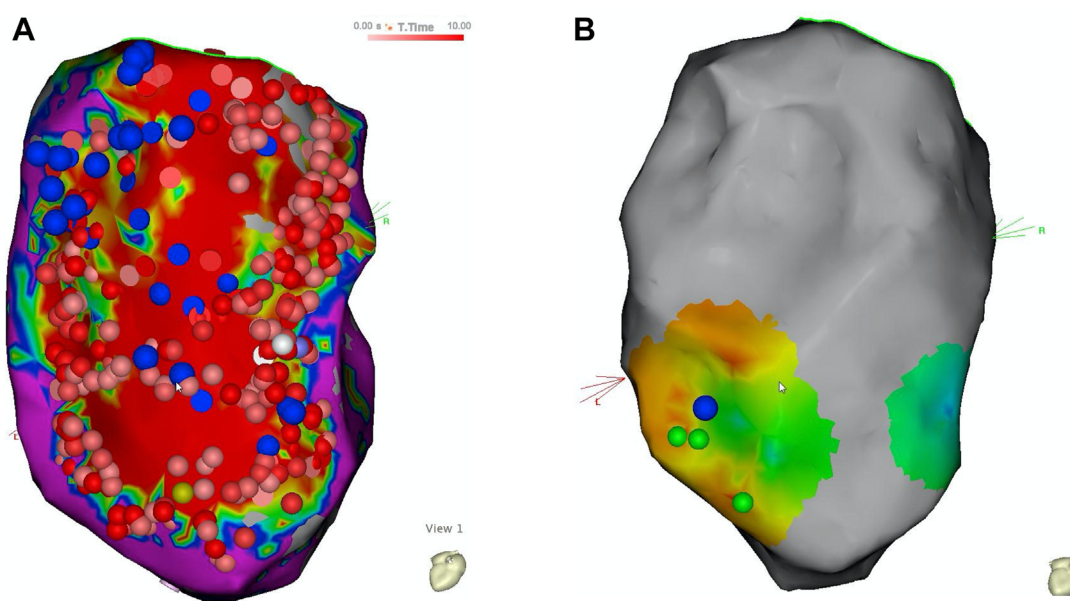
FIGURE 1 Electrocardiogram During Admission With Wide QRS Complex Monomorphic Tachycardia at a Rate of 110 Beats/Min

FIGURE 3 **Late Gadolinium Enhancement Cardiac Magnetic Resonance Demonstrating Large Ischemic Scar With Corresponding Location in 17-Segment American Heart Association Cardiac Model**



(A) Short axis of the mid left ventricle demonstrating ischemic subendocardial scar in segment 10. **(B)** Short axis of the left ventricle base demonstrating ischemic subendocardial scar in segments 3, 4, and 5. **(C)** Short axis of the left ventricle apex demonstrating ischemic subendocardial scar in segment 15. The **yellow arrows** show the ischemic scar.

FIGURE 4 **Voltage Mapping Demonstrating Extensive Area of Scar**



(A) Voltage map demonstrating extensive inferior scar **(red)** and healthy myocardium **(purple)** with adjacent border zones that were extensively ablated **(red tags)**. **Blue tags** indicate areas of interest/fractionation. **(B)** Map of the patient's refractory source of ventricular tachycardia.

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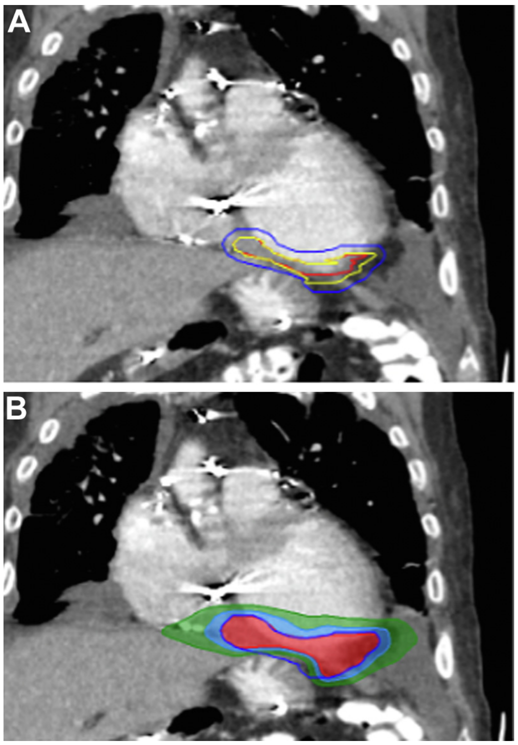
FIGURE 5 4-Dimensional Computed Tomography Imaging Used for Radiation Planning



(A) Coronal view of stereotactic body radiation therapy planning original target volumes **(red)**, internal target volumes incorporating the breathing motion **(yellow)**, and final planning target volumes to account for the image registration and patient setup error **(blue)**. **(B)** The resulting radiation dose cloud with 12 Gy **(green)**, 20 Gy **(blue)**, and 25 Gy **(red)**.

pump, and milrinone infusion. After diuresis, euvolemia was confirmed with repeat right heart catheterization. Telemetry demonstrated several episodes of VT despite multiple antiarrhythmic drug therapies.

The patient was not a transplant candidate because of his age. Because he continued to have intermittent VT despite all available therapeutic options and cardiomyopathy was rapidly progressing, it was decided to attempt stereotactic body radiation therapy (SBRT) for noninvasive cardiac radioablation. The off-label nature of the therapy was discussed and, in conjunction with radiation oncology, the decision was made to proceed. Electroanatomic map images were evaluated with 12-lead electrocardiogram correlation of clinical VT. The source of VT was identified as the mid to apical inferior wall, corresponding to the location of scar on CMR.

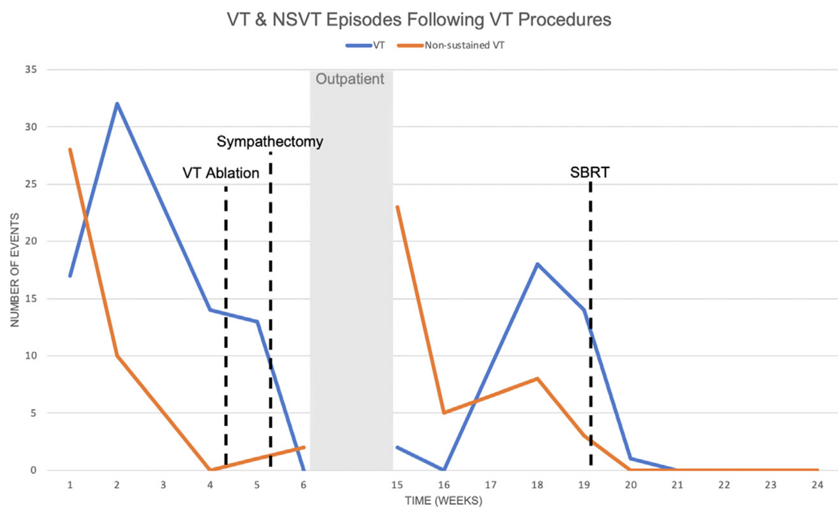
For SBRT simulation, 10-phase respiratory gated 4-dimensional computerized tomography (4DCT) was obtained with abdominal compression to limit respiratory motion. CMR and the average intensity projection from the 4DCT were fused in the treatment planning system using rigid registration, and segments for ablation were identified and contoured. Cardiac motion was assessed using the 10-phase respiratory gated 4DCT to create an internal target volume. An additional 5-mm planning target volume (PTV) margin was added to account for daily setup variability. The original target volume, internal target volume, and PTV resulted in 21.4, 29.9, and 87.9 cm^3, respectively (Figure 5). A total of 25 Gy in a single fraction was prescribed in accordance with prior studies. The SBRT plan was designed using 3 coplanar arcs using 6-MeV flattening free-filter beams using RayStation treatment planning software (RaySearch Laboratories), which resulted in a highly conformal radiation plan with a total delivery time of <4 minutes. Inverse plan optimization was used to reduce the dose to healthy myocardium, stomach, and bowel. The stomach was constrained to a point maximum dose of <15 Gy and <0.3 cm^3 to 12 mL. The bowel was limited to a point maximum dose of <15 Gy and, to meet normal tissue constraints for the adjacent stomach, the PTV coverage was 80%, receiving the prescription dose of 25 Gy, with undercoverage of the portion of the PTV directly abutting the stomach. Abdominal compression was used throughout treatment, and conebeam computed tomography was used for image guidance immediately before treatment. ICD interrogation postprocedure confirmed normal function.

The patient tolerated the procedure without any acute complications. For 3 days, he continued to have nonsustained VT on telemetry. After 4 days, ventricular ectopy burden significantly decreased.

DISCUSSION

Catheter ablation remains the mainstay treatment for drug-refractory ventricular arrhythmias in patients with structural heart disease; however, it is not curative in many patients. Acute failure of VT ablation can be seen in 10% of patients and long-term recurrence in more than 50%, with epicardial origin of VT identified as a major cause of ablation failure.[1] Epicardial ablation, percutaneously or via surgical pericardial window, cannot always be performed in patients with a history of cardiac surgery because of the presence of pericardial adhesions and possible damage to bypass grafts.

FIGURE 6 Graph Displaying the Number of VT and NSVT Events, as Detected by Implantable Cardioverter-Defibrillator, Per Week



NSVT = non-sustained ventricular tachycardia; SBRT = stereotactic body radiation therapy; VT = ventricular tachycardia.

Autonomic modulation is an option for patients with persistent VT for whom pharmacologic and catheter ablation therapies have failed. Sympathectomy involves denervation of postganglionic sympathetic fibers from the stellate and T2 to T4 thoracic ganglia and is an effective treatment for refractory ventricular arrhythmia.[2] Cardiac sympathetic denervation (CSD) is included in the most recent American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines as a reasonable therapy in selected patients with VT storm.[3] Although CSD has been shown to reduce sustained VT and number of ICD shocks in approximately 50% of patients at a follow-up of 10 to 15 months, a cycle length of >400 ms and extensive scarring are associated with minimal response.[2,4]

SBRT, commonly used to treat malignant tumors, uses highly focused radiation therapy and 3-dimensional imaging guidance. Cardiac side effects of radiation therapy have been observed after treatment of thoracic cancers, causing damage to arterial endothelium and premature coronary atherosclerosis, myocardial fibrosis, and conduction disturbances, usually 10 to 15 years after treatment and at doses of >40 Gy.[5] Although myocyte cell death and subsequent fibrosis are expected years after exposure to chest radiation, decrease in VT has been seen nearly immediately after SBRT, suggesting additional mechanisms that are not yet entirely known.[5,6] When used for the treatment of VT, radiation is usually delivered as single-fraction dose of 25 Gy, which is less than the required dosage to induce late-stage cardiac fibrosis.[6] As opposed to conventional catheter thermal ablation, where energy delivery to the epicardium or mid-myocardium may be limited by the depth of penetration, SBRT ablation targets transmural lesions. Histologic examination of explanted hearts of patients treated with SBRT did not demonstrate transmural fibrosis, further supporting the notion that a different mechanism is responsible for the reduction in VT seen at 25 Gy.[6] Up-regulation of connexin 43 and cardiac sodium channel $Na_V1.5$ causing increased conduction velocity and QRS interval shortening have been suggested as the antiarrhythmic mechanism of cardiac SRBT at the treatment dose of 25 Gy.[6]

Noninvasive radioablation has been shown to be an effective and safe treatment for refractory VT, with markedly reduced VT burden in a series of 5 patients and prospective study of 17 patients.[7,8] The effectiveness was noted after the initial blanking period to allow for inflammation from SBRT.[7] This noninvasive procedure has been performed at varying levels of acuity, from the ambulatory setting to acutely ill patients on mechanical circulatory support.[6,9] The most common side effects of SBRT are pericarditis and pneumonitis.[8] The long-term effects are still not known because the first case series was published in 2017.[7]

Current recommendations for intractable ventricular arrhythmias in patients with reduced left ventricular function include consideration for heart transplantation and durable mechanical assist devices or end-of-life conversations.[10] SBRT represents an additional option for patients with refractory VT despite antiarrhythmic medications and who have undergone prior ablations. SBRT may be considered as a salvage therapy in patients with refractory VT; however, prospective trials and longer follow-up are still required. Because of its off-label use, current expert opinion recommends that use be restricted to patients with refractory VT and under the care of highly specialized interdisciplinary teams.[9]

FOLLOW-UP

At the 6-month follow-up, the patient was still free from VT recurrence and was without cardiac-related hospital admissions (**Figure 6**).

CONCLUSIONS

This case highlights the potential of SBRT as a salvage therapy in appropriately selected patients without other treatment options, with the benefit of radiation delivery to transmural lesions. After medical management, catheter ablation, and surgical left-sided CSD failed, focused cardiac radioablation was fast, painless, and effective in controlling VT. Careful long-term follow-up will be conducted.

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