

Teaching Case

Stereotactic Arrhythmia Radioablation for Ventricular Tachycardia: Single Center First Experiences



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Received November 9, 2020; revised March 14, 2021; accepted March 31, 2021

Introduction

Ventricular tachycardia (VT) is a potentially life-threatening arrhythmia characterized by electrical re-entry within patches of heterogeneous myocardial fibrosis leading to sustained consecutive ventricular beats at a rate >100/min.¹ In patients with monomorphic VT, implantable cardioverter-defibrillators (ICD) have become the cornerstone of therapy in decreasing mortality through the prevention of sudden death.² However, ICDs have no effect on the arrhythmogenic substrate and address symptom-control only. Patients often receive recurrent and debilitating shocks associated with an increase in mortality.³ Currently, catheter ablation (CA) for VT is used as an adjunctive therapy for those refractory to medical therapy.⁴ A recent systematic review and meta-analysis shows that CA is superior to medical therapy for scar-related VT with

respect to VT recurrence and life-threatening VT storm.² Despite this, there is still a high incidence of VT recurrence in both medically treated (48%) and ablation-treated (39%) patients suggesting the current treatment paradigm is suboptimal.

In 2015, Loo et al⁵ were the first to use stereotactic ablative radiation therapy (StAR) for VT in humans. In 2017, Cuculich et al⁶ built on this technique, identifying arrhythmogenic scar regions by noninvasive cardiac mapping. More recently, Robinson et al⁷ demonstrated positive results in the Electrophysiology-Guided Noninvasive Cardiac Radioablation for Ventricular Tachycardia (ENCORE-VT) trial using a similar StAR technique for refractory VT. These works report a marked reduction in VT burden,^{6,7} a decrease in antiarrhythmic drug use,⁷ and improvement in quality of life.⁷ Since then, several centers have reported their early experience with this technique⁸ with both positive⁹⁻¹¹ and negative¹² results. In this report, we add to the limited evidence detailing our experience with 2 patients for StAR for VT at the McGill University Health Centre. Written informed consent for StAR-VT and publication of the treatment process was obtained from both patients. All images are published under agreement of the patients with anonymity.

In addition, we add to the very limited data on cardiac substructure countouring and complementary dose volume histograms (DVH; Table 1).

Sources of support: The authors received no financial support for the research, authorship, or publication of this article.

Disclosures: The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or nonfinancial interest in the subject matter or materials discussed in this manuscript.

All data requests should be submitted to the corresponding author for consideration. Access to anonymized data may be granted after review.

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<https://doi.org/10.1016/j.adro.2021.100702>

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Table 1 Mean and max radiation dose to cardiac structures

Structure	Case 1		Case 2		Knutson et al ¹⁴
	D _{Max} (Gy)	D _{Median} (Gy)	D _{Max} (Gy)	D _{Median} (Gy)	D _{Median} (Gy)
Heart (total)	33.8	5.9	32.8	2.5	Not reported
Right atrium	14.1	4.3	3.4	1.8	2.9
Right ventricle	14.1	4.9	32.8	4.8	8.3
Left atrium	31.5	4.6	3.3	1.3	3.6
Left ventricle	33.8	9.1	32.5	5.1	11.3
Left coronary artery	1.0	0.9	0.4	0.3	1.3
Right coronary artery	28.6	6.4	Not visualized	Not visualized	3.2
Left anterior descending	10.2	0.9	31.0	25.6	10.1
Circumflex artery	31.3	21.6	3.6	2.5	9.2
Pulmonary artery	0.7	0.4	17.0	0.3	0.66
Aorta	26.5	0.5	5.1	0.2	1.6
Superior vena cava	0.4	0.3	1.9	0.1	0.9
Inferior vena cava	11.7	5.8	2.6	1.8	2.7
Interventricular septum	11.2	4.8	30.5	6.5	Not reported
Aortic valve	Not visualized	Not visualized	5.0	3.0	3.5
Pulmonic valve	Not visualized	Not visualized	1.3	0.6	1.8
Mitral valve	Not visualized	Not visualized	2.9	1.7	Not reported
Tricuspid valve	Not visualized	Not visualized	3.6	2.5	Not reported

Case Descriptions

Case 1

A 65-year-old man known with recurrent VT secondary to ischemic cardiomyopathy presenting to the emergency department (ED) in VT storm requiring multiple ICD shocks. Reversible precipitating factors including ischemia, electrolyte imbalances, and drug interactions were ruled out in the ED. The patient had a significantly reduced left ventricular ejection fraction 30%, and multiple comorbidities, including coronary artery disease, type 2 diabetes mellitus, and chronic kidney disease. The patient underwent quintuple coronary artery bypass graft surgery (in 2004) after a myocardial infarction, and in 2013, a prophylactic ICD was placed. The patient was on maximum tolerable amiodarone (400 mg daily). Ablation was attempted in 2017 targeting a scar on the lateral wall of the LV. Reviewing the ICD suggested multiple VT circuits and cycle lengths consistent with the previous electrophysiologists (EP) study. The likelihood of clinical success with a repeat CA was deemed low given the large number of morphologies and complex substrate underlying the arrhythmias.

Case 2

A 65-year-old man with recurrent VT secondary to myocardial infarction (in 2002) presented to the ED in VT storm requiring multiple ICD shocks. Reversible

precipitating factors including ischemia, electrolyte imbalances, and drug interactions were ruled out in the ED. The patient's left ventricular ejection fraction was 35%, and he had an apical aneurysm containing a chronic, prominent LV thrombus, making him ineligible for CA.¹³ An ICD was placed for sudden cardiac death prophylaxis in 2019 after an out of hospital infarct, otherwise the patient's past medical history is unremarkable. He was on maximum dose amiodarone (400 mg daily).

After detailed consultation, the decision to perform StAR was reached. Both patients were considered for the experimental treatment as they had no further options for either medical or surgical treatment. They were treated on a compassionate basis after multiple conversations about the risks with both the cardiology and radiation oncology teams.

Treatment

For treatment planning, 4-dimensional computed tomography (4D-CT), cardiac mapping (case 1), cardiac ultrasound, electrocardiogram (ECG), and technetium-99m perfusion scan (case 1) were acquired for target localization.

Cardiac mapping was performed using the Carto system and merged with intracardiac ECG. A single transseptal approach was used for voltage mapping. A window of 0.5 to 1.5 mV was used to differentiate between scar and healthy tissue. More than 7 different VT morphologies were induced, all poorly tolerated hemodynamically, making the mapping procedure extremely challenging. Enough information was obtained to delineate the area of scar and

get tracings of VT morphologies to localize the exit sites of the circuits. In case 2, owing to the chronic and prominent LV thrombus, the patient was considered unsafe for electrophysiology study.¹³

Target delineation is done through an iterative process with medical physicists, EP, and radiation oncologists (RO). The patient's clinical information and imaging is reviewed. The EP translates mapping/scar location to the tomographic equivalent of the heart using the 17-section cardiac model.¹⁴ The RO contours these segments with real-time feedback from the EP. The internal target volume (ITV) contains components of the respiratory and cardiac motion and are not decoupled. The ITV was created by contouring the clinical target volume (CTV) on all respiratory phases of the 4D-CT. Finally, an isotropic margin of 3 mm was added to create the planning target volume (PTV).

Before creating a radiation treatment plan, organs-at-risk, including the spinal cord, stomach, liver, lungs, esophagus, and heart substructures were contoured. Normal cardiac structure and substructures were contoured based on the atlas by Duane et al¹⁵ by the RO and reviewed by the EP (Table 1). The PTVs were prescribed 25 Gy in 1 fraction with the plan normalized so that 95% of the PTV was covered by the 25 Gy isodose. Pretreatment quality assurance plan review was performed according to internal department guidelines for stereotactic body radiation therapy. Radiation was delivered with a TrueBeam STx Linear Accelerator (Varian Medical Systems) using a 6-MV flattening-filter-free beam and a volumetric modulated arc therapy technique. The treatments were delivered with 3 coplanar partial arcs. Although the heart can be considered central, in both cases, the target's centroid was near the middle of the left lung. Angles were chosen to avoid unnecessary irradiation of the right lung. The use of abdominal compression was evaluated, but it did not provide ITV margin reductions, brought the stomach closer to the PTV, and thus was not used. Respiratory gating was not performed to minimize treatment time and complexity because it had minimal ITV margin gains. Pretreatment position was verified with kV-kV x-rays and cone beam CT. Treatment was delivered under cardiac monitoring, with the ICD in service-mode, as per recommendation by the cardiology team, and emergency team stand-by.

Case 1

CT-imaging was performed without contrast as the patient's creatinine was $>300 \mu\text{mol/L}$ (estimated glomerular filtration rate = 41) and was unwilling to consider dialysis as part of the therapy. Treatment planning imaging and EP mapping demonstrated a targetable substrate localized to the lateral and inferior walls of the LV. Owing to the proximity of the esophagus to the target, 4 mL of the

substrate directly adjacent to this organ was not included in the PTV to prioritize safety over target coverage.

Case 2

A targetable substrate in the apical aneurysm was localized through contrast-enhanced 4D-CT, echocardiogram, and ECG.

Results

Dose quality information as per The International Commission on Radiation Units and Measurements report 91,¹⁶ and single-fraction stereotactic body radiation therapy dose constraints^{17,18} are summarized in Table 2 for both cases. In case 1, the only unmet organ-at-risk constraint was D_{max} of the stomach (21.3 Gy). All recommended dose constraints were met in case 2. For both cases, the ICDs received <0.1 Gy.

Figures 1 and 2 summarize the treatment volumes, DVH and treatment arcs for case 1 and case 2, respectively. D_{Max} and D_{Median} to the different cardiac substructures is summarized in Table 1. Figure 3 highlights an illustrative case of the cardiac contours and associated DVH for case 1.

Neither patient has experienced any lasting radiation-related side effects. Both patients demonstrated an initial decrease in both VT burden and ICD shocks. Figure 4 highlight the incidence of VT events and ICD shocks before and after treatment for both patients. Both patients have routine follow-up in cardiology and radiation oncology for toxicity surveillance. The complete follow-up schedule is included as supplemental material.

Case 1

After treatment, this patient experienced mild esophagitis, which was treated with pantoprazole and was self-limited. Two days after treatment the patient had 3 episodes of asymptomatic VT with additional intermittent asymptomatic episodes until 7 months posttreatment when an ICD shock was delivered. Ten months after treatment, the patient had VT storm and was admitted to the hospital for an acute pneumonia which was successfully treated. There has been one recorded VT event since and no other ICD shocks. He remains on the same dose of amiodarone.

Case 2

After treatment, this patient experienced mild self-limited presyncopal symptoms for 1 hour and has no documented episodes of VT since treatment. His amiodarone is currently weaned to 100-mg/d.

Table 2 Treatment plan quality information

	Case 1	Case 2
Dose quality information		
No. of arcs (angle coverage)	3 (330-180)	3 (315-145)
Treatment time	24 min (8 min, 0 seconds beam-on)	20 min (7 min 20 seconds beam-on)
CTV (mL)	41.9	17.4
PTV (mL)	102.9	66.4
Target covered, %	95 by Rx dose (25 Gy)	95 by Rx dose (25 Gy)
Prescription isodose volume/tumor volume (CI)	1.03	0.95
Max dose/prescribed dose (HI)	1.35	1.31
PTV		
D98%	24.2 Gy	24.5 Gy
D50%	28.3 Gy	28.0 Gy
D2%	32.2 Gy	30.1 Gy
Dmean	28.3 Gy	27.7 Gy
V20 Gy (%) $\geq 95\%$	V20 Gy (%) = 99.5%	V20 Gy (%) = 100%
V19 Gy (%) $\geq 99\%$	V19 Gy (%) = 99.6%	V19 Gy (%) = 100%
Esophagus		
Esophagus V11.9 Gy (mL) <5 mL	V11.9 Gy (mL) = 0.3 mL	V11.9 Gy (mL) = 0.0 mL
Esophagus D0.035 mL (Gy) <16 Gy	D0.035 mL (Gy) = 11.7 Gy	D0.035 mL (Gy) = 1.4 Gy
Esophagus Dmax <19 Gy	Dmax = 16.3 Gy	Dmax = 1.7 Gy
Stomach		
Stomach V13 Gy (mL) <10 mL	V13 Gy (mL) = 4.3 mL	V13 Gy (mL) = 0.08 mL
Stomach D0.035 mL (Gy) <16 Gy	D0.035 mL (Gy) = 19.8 Gy	D0.035 mL (Gy) = 13.6 Gy
Stomach Dmax <16 Gy	Dmax = 21.3 Gy	Dmax = 15.2 Gy
Lungs		
V7 Gy (mL) <1,500 mL (L)	V7 Gy (mL) = 376 mL	V7 Gy (mL) = 182 mL
V7 Gy (mL) <1,500 mL (R)	V7 Gy (mL) = 0.1 mL	V7 Gy (mL) = 3.2 mL

Abbreviations: CI = confidence interval; CTV = clinical target volume; HI = homogeneity index; PTV = planning target volume; Rx = prescription.

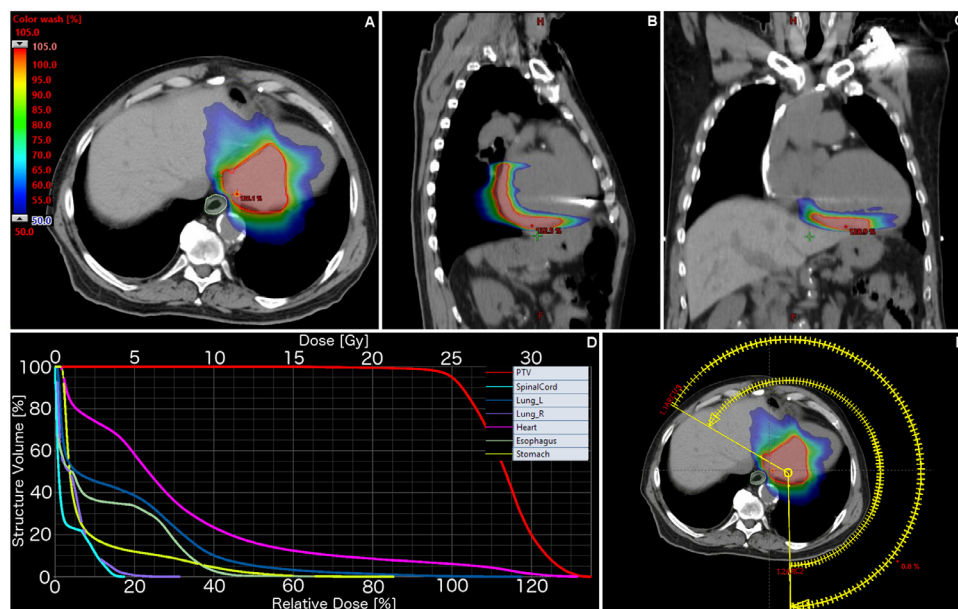


Figure 1 Case 1: Planning computed tomography with overlaid dose distribution in axial (A), sagittal (B), and coronal (C) planes. Dose volume histograms of the treatment plan with relevant organs-at-risk (D). Treatment arcs (E). PTV = planning target volume.

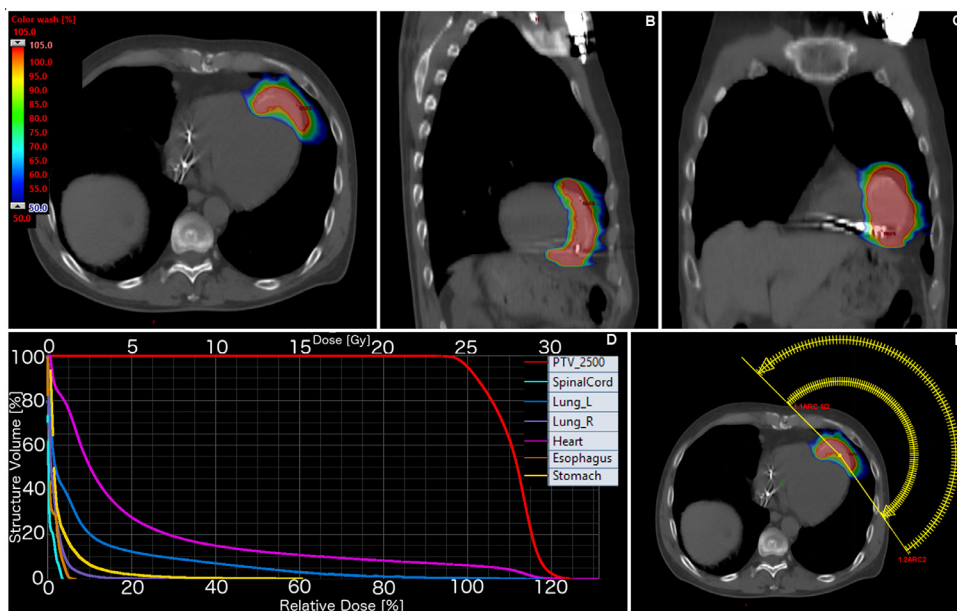


Figure 2 Case 2: Planning computed tomography with overlaid dose distributions in axial (A), sagittal (B), and coronal (C) planes. Dose volume histograms of the treatment plan with relevant organs-at-risk (D). Treatment arcs (E). PTV = planning target volume.

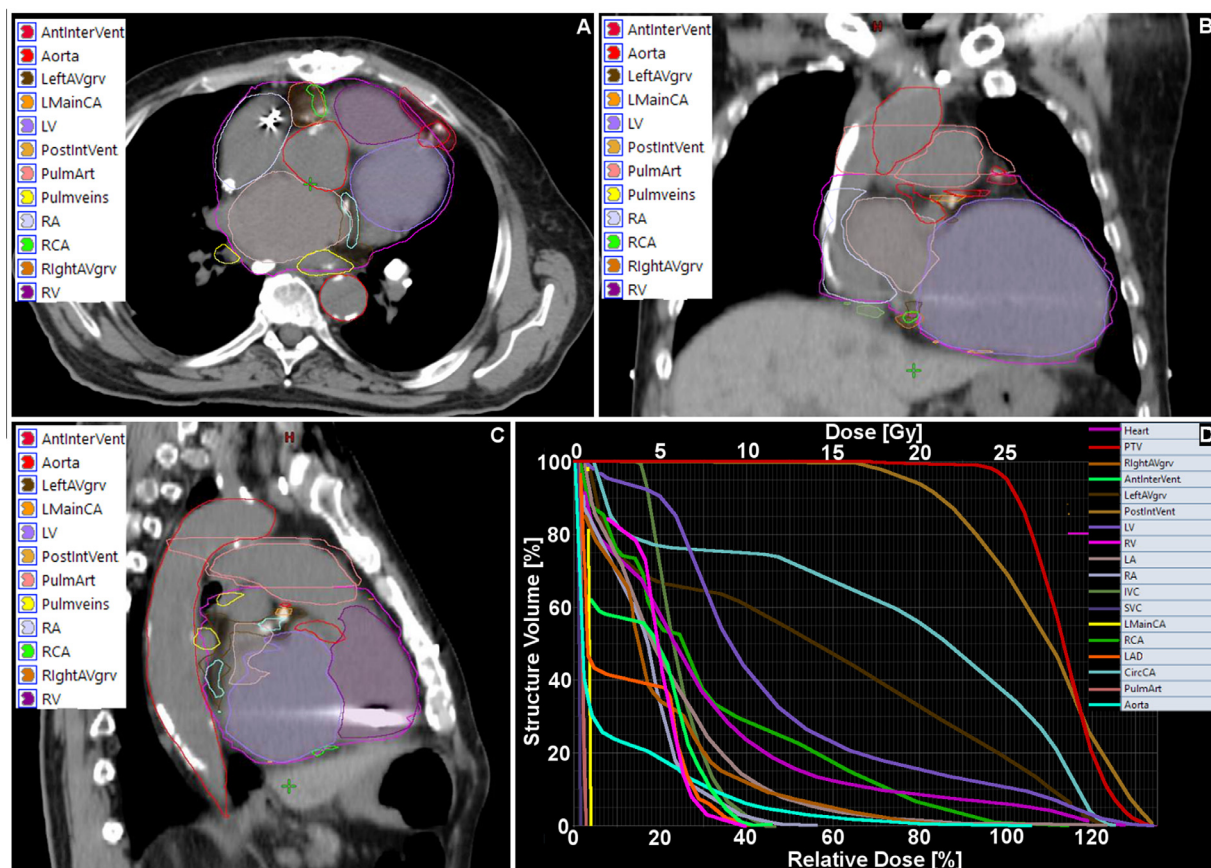


Figure 3 Contoured cardiac substructures in the axial (A), coronal (B), and sagittal (C) planes, and dose volume histograms (D). CA = coronary artery; IVC = inferior vena cava; LA = left atrium; LV = left ventricle; RA = right atrium; RCA = right coronary artery; RV = right ventricle; SVC = superior vena cava.

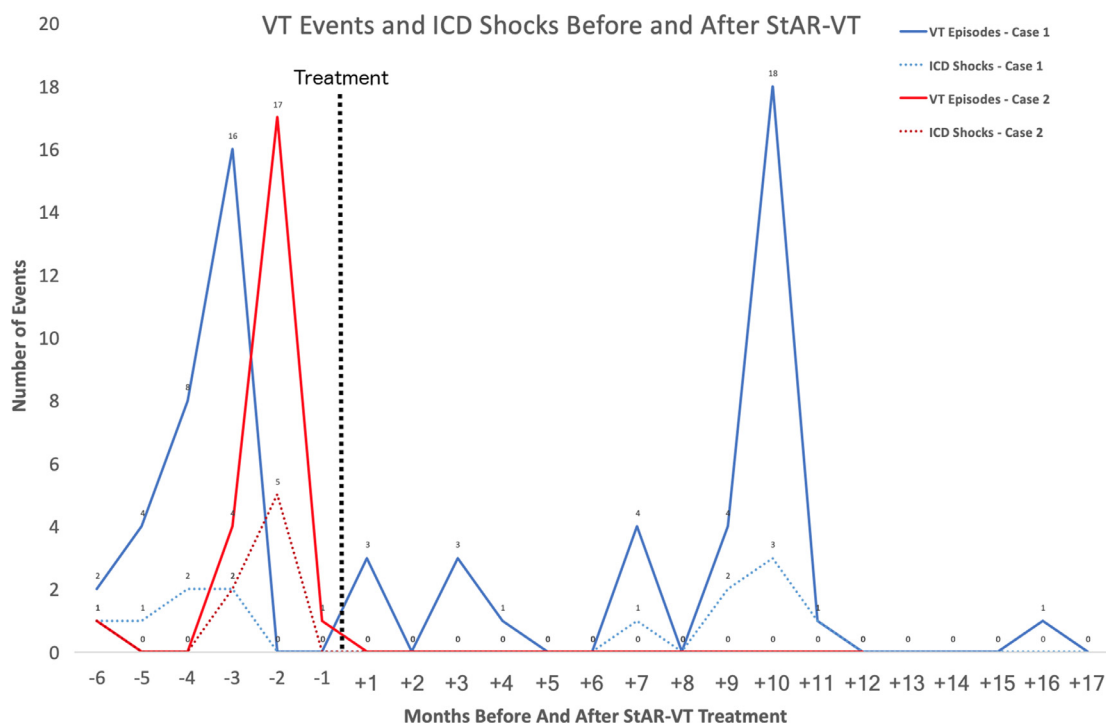


Figure 4 Ventricular tachycardia events for 6 months before treatment and up to 15 months after. Abbreviation: ICD = implantable cardioverter-defibrillator; StAR-VT = stereotactic arrhythmia radioablation for ventricular tachycardia; VT = ventricular tachycardia.

Discussion

We present our experiences with 2 patients treated with StAR-VT at the McGill University Health Centre. Cases 1 and 2 have been followed-up for 17 months and 12 months, respectively since treatment.

Case 2 remains VT free and has been weaned to 100 mg/d of amiodarone. Case 1 had a relapsing event 10-months after treatment thought to be provoked by an acute pneumonia. In case 1, part of the relevant substrate was not irradiated. Given the large PTV and esophagus safety concerns, the relapsing event could be related to a “geographic miss” of this region. The consequence of suboptimal coverage and subsequent relapse has also been reported by Gianni et al¹² in 2 out of 5 patients treated. Despite suboptimal coverage with the prescription dose the minimum threshold dose for response has not been established, and positive results have been reported with lower doses than what was prescribed here.⁸ Neither patient has exhibited any significant acute or late radiation-related side effects.

Conclusions

The effects of extensive radiation to cardiac substructures is not well understood, and there are no well-established constraints for most. In our present experience, we

have yet to encounter any radiation-related side effects to these substructures; however, it is early, with only 12-month follow-up to make any strong conclusions about this.

Despite increasing experience in the literature, there are no established criteria to predict success for this treatment, making it difficult to identify optimal selection criteria for StAR-VT, a treatment that can only be delivered once. The mechanism of action for success remains unclear as the marked clinical improvement seems to occur before the formation of new fibrotic tissue in the area of irradiation.¹⁹ The present limited evidence suggests that StAR-VT is effective for treatment-resistant VT and often provides an immediate reduction in disease burden. Safety remains a prominent question despite mild adverse events and rare severe (gastropericardial fistula, bleeding) adverse events^{8,20} (10.5% rate of severe events including pericardial effusion and CHF exacerbations¹⁹). Owing to the stochastic nature of radiation-induced damage, and limited safety and efficacy data, it is not possible to assume StAR-VT is completely safe and it should not be performed outside of tailored clinical studies for treatment-resistant disease.

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