Surgical ablation after stereotactic body radiation therapy for ventricular arrhythmias

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Introduction
Catheter ablation remains the principal intervention to target scar-based, macroreentrant ventricular arrhythmias. However, the use of stereotactic body radiation therapy (SBRT) for recurrent ventricular arrhythmias is becoming increasingly common, with initial case reports and case series describing promising early results, particularly in patients who are poor candidates for, or have failed, catheter ablation procedures. Nonetheless, many questions remain as to the mechanism of action, safety, and long-term efficacy. In this report, we expand upon a case that has been briefly described previously that provides important insights into the limitations of SBRT in a patient who required open chest surgical ablation after failing SBRT.

Case report
The patient was a 78-year-old man with ischemic cardiomyopathy with left ventricular ejection fraction 10%–15% with prior left ventricular apical aneurysm who underwent endocardial parachute device implantation 7 years previously at an outside institution. His case has been briefly described previously, highlighting the unforeseen downstream complexities of the parachute device implantation. He suffered from recurrent monomorphic ventricular tachycardia (VT) and had undergone multiple procedures, including 4 prior endocardial ablation attempts and an unsuccessful percutaneous epicardial ablation attempt, during which epicardial access could not be obtained owing to dense pericardial adhesions, all at outside institutions. A minimally invasive surgical access hybrid ablation procedure was performed via anterolateral thoracotomy, with successful termination of VT during cryoablation; however, VT recurred 2 months later, this time with a more inferior exit site (Figure 1). Of note, the inferior aspect of his epicardium could not be accessed during the thoracotomy owing to dense pericardial adhesions. He was then referred and underwent bilateral surgical stellate ganglionectomy, but he continued to have intermittent slow VT requiring antiarrhythmic pacing (ATP) therapies via his implantable cardioverter-defibrillator for termination, despite amiodarone therapy. He was subsequently referred for SBRT. He was felt to be a good candidate for this owing to the inaccessibility of the substrate region, and the presence of the left ventricular parachute device could aid in targeting the treatment planning. He underwent 25 Gy radiation delivery in a single fraction (Figure 2) with a Novalis Tx Medical Linear Accelerator (Brainlab, Inc, Westchester, IL) via previously reported methods. Unfortunately, 3 months later he developed VT storm, and during hospitalization he was diagnosed with amiodarone lung toxicity. He continued to have VT with superior axis, suggesting inferior apical exit site. He was evaluated for advanced heart failure therapies, but was felt to be a poor candidate owing to his comorbidities. He received steroids and supportive care, and gradually improved, to be safely discharged on prednisone and mexiletine. During follow-up, he continued to experience slow VT requiring ATP therapies with an average of 86.2 ATPs delivered per month over a 5-month period. He was admitted to an outside facility for incessant slow VT and subsequently transferred to our institution for definitive management.

He was reevaluated for advanced heart failure therapy options, as he had improvement in his comorbid conditions, including his pulmonary disease; however, the patient declined those options. He was then evaluated for a hybrid surgical ablation procedure in conjunction with the cardiothoracic surgical team, with plan for median sternotomy for optimal access to the target region. This would also allow for upgrade of his dual-chamber device with placement of an epicardial left ventricular lead, as he had baseline left bundle branch block with QRS duration >150 ms. The patient agreed to proceed.

Keywords
Catheter ablation; Cryoablation; Stereotactic body radiation therapy; Surgical ablation; Ventricular tachycardia

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Following induction of general anesthesia, noninvasive programmed stimulation was unable to induce his VT. Median sternotomy was performed, and owing to the dense pericardial adhesions, cardiopulmonary bypass was initiated in order to safely mobilize the heart. Full exposure of the entire left ventricular surface was then obtained (Figure 3).

During epicardial mapping in sinus rhythm using a LiveWire 2-2-2 duodecapolar catheter (Abbott, Chicago, IL), extensive local abnormal ventricular activities and late potentials were encountered in the border zone regions of the left ventricular aneurysm. Generally, these extended radially from the central aneurysm (Figure 3). These were targeted for cryoablation using the CryoIce probe (Atricure, Mason, OH) and eliminated on postablation mapping. The patient was monitored in the surgical intensive care unit postoperatively. During the postoperative period, he experienced atrial tachycardia, for which he was initiated on sotalol 80 mg orally 2 times a day, but he otherwise recovered well and was discharged. He has had monthly follow-up, with no episodes of VT on implantable cardioverter-defibrillator interrogation at 6 months.

**Discussion**

The application of SBRT for ventricular arrhythmias is increasing in usage, with multiple initial promising case reports and series. However, there are many important questions as to the long-term efficacy and safety, as well as the mechanism of action, optimal targeting and delivery strategy, and proper dose selection. In a case series of 5 patients by Gianni and colleagues, 3 patients underwent mapping and ablation procedures after receiving SBRT, and all were found to have low-amplitude, fractionated electrograms in the regions targeted by SBRT. Kiani and colleagues performed histopathologic analysis after cardiac transplantation in 4 explanted hearts that had previously received SBRT. In their study, they found extensive damage to intercellular junctions and other findings of acute injury; however, fibrosis was variable. Such findings cast uncertainty as to whether scar homogenization is the principal mechanism of action for SBRT effect, or at least not in the same manner as what is achieved with catheter ablation.

It is important to consider the reasons SBRT did not eliminate VT in our patient. By all means, our patient had multiple ablation procedures, multiple imaging modalities, and
Figure 2  Stereotactic body radiation therapy treatment planning. A–C: Four-chamber (A), short-axis (B), and anteroposterior (C) computed tomography views for treatment planning. Cyan contour line indicates gross target volume, pink contour indicates planning target volume, and multicolor shades indicate isodose regions. D: Cardiac magnetic resonance image demonstrating extensive late gadolinium enhancement and thinning of the left ventricular apex.

Figure 3  Open chest surgical ablation. A: Intraoperative photograph following median sternotomy and cardiopulmonary bypass cannulation. Large apical left ventricular aneurysm is shown (hatched outline with yellow shading). A Livewire 2-2-2 duodecapolar catheter (Abbott, Chicago, IL) was utilized for intraoperative high-density mapping. B: Epicardial electroanatomic voltage map (EnSite; Abbott, Chicago, IL) at standard scar settings (0.5–1.5 mV) from a left posterior oblique view. The duodecapolar catheter was placed with proximal end within the aneurysm, with distal end extending radially outward from the aneurysm. Various positions illustrated in (1) apical anterolateral, (2) apical inferolateral, and (3) apical inferior orientations showing late potentials and fractionated electrograms in the border zone regions.
a parachute device in the left ventricle to aid in radiation treatment planning, which should have theoretically all been factors in his favor to achieve success. There are a number of considerations that may have impacted the unsuccessful outcome of SBRT. First, by design, there is a fall-off in SBRT dose delivery between the targeted area and adjacent tissues. As indicated by isodose lines during treatment planning, the dose delivered gradually decreases further away from the central target region. Interestingly, in our patient, the border zone regions were the areas that presented extensive local abnormal ventricular activities, which could conceivably promote reentrant arrhythmias. These areas likely fell within the lower range of the isodose lines from SBRT. Second, as discussed above, scar homogenization via fibrosis may not be the mechanism of action for SBRT efficacy. Indeed, this cannot be the case if SBRT does in fact provide near-immediate effect, as has been reported in multiple case series.2,6,7 This highlights our limited understanding of SBRT. Third, uncertainties in targeting or radiation delivery cannot be ruled out. However, given all the factors previously mentioned, which should have been in the favor of our patient, this seems less likely.

Conclusion

This patient represents a unique opportunity to observe the effects of SBRT with follow-up intraprocedural electroanatomic mapping. To our knowledge, this is the first report of open surgical ablation in a patient who had previously undergone cardiac SBRT. The parachute device served as an optimal target for SBRT delivery. On post-SBRT open chest surgical mapping, extensive areas of abnormal electrograms were observed in the border zone regions of the aneurysm, which could support reentrant arrhythmia mechanisms. While the impact of sotalol and biventricular pacing may have also contributed to the improvement in this patient, following ablation he has done well, with no arrhythmia recurrence.

References

1. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2018; 15:e190–e252.
2. Cuculich PS, Schill MR, Kashani R, et al. Noninvasive cardiac radiation for ablation of ventricular tachycardia. N Engl J Med 2017;377:2325–2336.
3. Chin R, Hayase J, Hu P, et al. Non-invasive stereotactic body radiation therapy for refractory ventricular arrhythmias: an institutional experience. J Interv Card Electrophysiol 2021;61:535–543.
4. Cuculich P. Longer term results from the ENCORE-VT study. Heart Rhythm Scientific Sessions (virtual); 2020.
5. Diamantakos E, Harvey R, Shivkumar K, Bradfield JS. Structural interventions and potential unforeseen limits on access to ventricular tachycardia substrates. JACC Clin Electrophysiol 2019;5:996–997.
6. Neuwirth R, Cvek J, Knybel L, et al. Stereotactic radiosurgery for ablation of ventricular tachycardia. Europace 2019;21:1088–1095.
7. Robinson CG, Samson PP, Moore KMS, et al. Phase I/II trial of electrophysiology-guided noninvasive cardiac radioablation for ventricular tachycardia. Circulation 2019;139:313–321.
8. Lloyd MS, Wight J, Schneider F, et al. Clinical experience of stereotactic body radiation for refractory ventricular tachycardia in advanced heart failure patients. Heart Rhythm 2020;17:415–422.
9. Gianni C, Rivera D, Burkhardt JD, et al. Stereotactic arrhythmia radioablation for refractory scar-related ventricular tachycardia. Heart Rhythm 2020;17:1241–1248.
10. Kiani S, Kutoh L, Schneider F, Higgins KA, Lloyd MS. Histopathologic and ultrastructural findings in human myocardium after stereotactic body radiation therapy for recalcitrant ventricular tachycardia. Circ Arrhythm Electrophysiol 2020; 13:e008753.