A case report of successful elimination of recurrent ventricular tachycardia by repeated stereotactic radiotherapy: the importance of accurate target volume delineation

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Background	Stereotactic body radiotherapy (SBRT) has emerged recently as a novel therapeutic alternative for patients with ventricular tachycardias (VTs) resistant to convetional treatment. Nevertheless, many aspects related to SBRT are currently unknown.
Case summary	A 66-year-old man with ischaemic heart disease, a history of coronary artery bypass graft surgery and left ventricular dysfunction was referred for recurrent symptomatic episodes of slow VT (108 b.p.m.). The arrhythmia was resistant to antiarrhythmic drug therapy with amiodarone and repeated catheter ablation. The patient was scheduled to SBRT, however, the first session failed to suppress VT recurrences. After 20 months, the patient underwent re-do ablation procedure that revealed a newly developed scar with its core adjacent to the presumed critical part of the VT substrate. Catheter ablation again failed to eliminate VT and the second session of SBRT was scheduled. To improve targeting of the VT substrate for SBRT, we applied our recently developed original method for integration of data from the electroanatomical mapping system with computer tomography images. The second session of SBRT with precise targeting using the novel strategy led within 3 months to the successful elimination of VT.
Discussion	This case report describes a patient in whom the recurrent VT was abolished only by properly targeted SBRT. Above all, the case highlights the importance of precise identification and targeting for SBRT. Our case also documents *in vivo*, by electroanatomical voltage mapping, the development of SBRT-related myocardial lesion. This represents an important mechanistic proof of the concept of SBRT.

Learning points

- Stereotactic radiotherapy is effective for the elimination of ventricular tachycardia not accessible by conventional therapeutic approaches.
- Precise determination of target volume is required to improve efficacy and reduce the risk of potential complications.
- Electroanatomical voltage mapping may be used for evaluation of lesions created by stereotactic radiotherapy.

Introduction

Catheter ablation is an effective method for the treatment of ventricular tachycardias (VTs).[1] However, in some patients, ablation may be ineffective as the critical part of the substrate cannot be reached from the endocardial or epicardial surface. Recently, stereotactic body radiotherapy (SBRT) has emerged as a promising bailout therapy for patients that failed catheter ablation.[2–5] Although reduction in VT burden with acceptable safety was reported for SBRT, the published data are limited to small case series and case reports and many aspects related to this therapy are not known.

This case report describes a patient in whom the recurrent VT was abolished only after two sessions of SBRT, of which the second was performed using our method of accurate targeting of the VT substrate.

Timeline

Index date	A 66-year-old man with coronary artery disease was admitted for recurrent episodes of slow ventricular tachycardia (VT) requiring implantable cardioverter-defibrillator interventions
1, 5, 11 months	Repeated catheter VT ablations that were not successful due to arrhythmia intramural origin
1 year and 6 months	The first stereotactic radiotherapy without effect
2 years and 10 months	Remapping after the first radiotherapy
3 years and 2 months	The second stereotactic radiotherapy
4 years and 2 months	Last follow-up visit. After 3 months blanking period no recurrences of any arrhythmia

Case presentation

A 66-year-old man was referred for recurrent episodes of slow VT (108 b.p.m.) requiring interventions of implantable cardioverter-defibrillator (ICD) (*Figure 1A*). The patient had a history of ischaemic heart disease and underwent coronary artery bypass graft surgery 12 years ago (three grafts to the left anterior descending artery, the posterior descending artery and the marginal branch). The arrhythmia was terminated by repeated sequences of antitachycardia pacing, no shocks were delivered. However, both VT and antitachycardia pacing were highly symptomatic with palpitations and chest pain. Amiodarone (200 mg/day) and metoprolol (75 mg/day) failed to suppress the arrhythmia. Physical examination was unremarkable.

Echocardiography showed eccentric left ventricular hypertrophy (the thickness of the interventricular septum was 14 mm) with hypokinesis of the apex and anterior wall. The left ventricular ejection fraction was calculated to 35%. Coronary angiography did not reveal any appropriate lesion for revascularization. During the electrophysiology study, clinical VT was located below the base of the posteromedial papillary muscle. The earliest endocardial activation preceded the QRS complex only by 5 ms with an initial far-field component (*Figure 1C*). The normal uni/bipolar voltages suggested the absence of a larger scar in the area. Despite three endocardial ablation procedures, the VT remained inducible. As the clinical VT originated from hypertrophic myocardium with high voltage and endocardial catheter ablation failed to abolish the arrhythmia, we hypothesize that the VT originated deep within the left ventricular wall. An attempt for percutaneous epicardial approach failed because of adhesions from previous cardiac surgery. No suitable vessel was identified that could be used for transcoronary or coronary venous alcohol ablation. Thus, the patient was referred for SBRT. During the first SBRT, the planned target volume (PTV) was determined by a visual alignment of the presumed origin of VT from electroanatomical maps and computer tomography (CT) images. Twenty-five Gy was delivered to the PTV (21 mL) using Cyberknife (Accuracy) as described previously.[2]

However, the first SBRT session failed to suppress VT. The patient continued to have highly symptomatic episodes of VT treated with antitachycardia pacing (around 20 episodes/month). Treatment with amiodarone (200 mg/day) was continued throughout the period of 20 months. VT episodes were of the same electrocardiogram (ECG) morphology and the patient underwent a re-do electrophysiology study. An electroanatomical map of the left ventricle showed a new, sharply demarcated, low voltage area. The detectable scar was larger on unipolar (size of 16 cm^2) than on bipolar (size of 7 cm^2) map. Interestingly, the earliest endocardial activity during VT overlapped with the area of low unipolar voltage, but not with a low bipolar voltage region (*Figure 2*). Additional ablation again failed to suppress VT inducibility. At this stage, we used a new integration strategy for the selection of PTV (see Supplementary material online and *Figure 3*)[6] and planned the second SBRT. The new PTV was highlighted at the site of the earliest endocardial activation during VT and radiation dose was again 25 Gy. Thanks to the precise identification of the target, the PTV was only 12 ml. This allowed an expansion of the PTV by 3 mm towards the ventricular cavity and epicardium (resulting in a final PTV of 18 ml) to ensure transmural lesion. The Dice overlap of the PTVs from both SBRT sessions was 0.68. Acutely, an increase in VT recurrences was observed (30 episodes during the first month), which gradually disappeared over 3 months period. During 1-year follow-up, no VTs were noted clinically, by ICD interrogation or by Holter ECG monitoring. No complications related to SBRT were observed, the left ventricular ejection fraction remained unchanged at 35%. No dysfunction of the implanted device was noted.
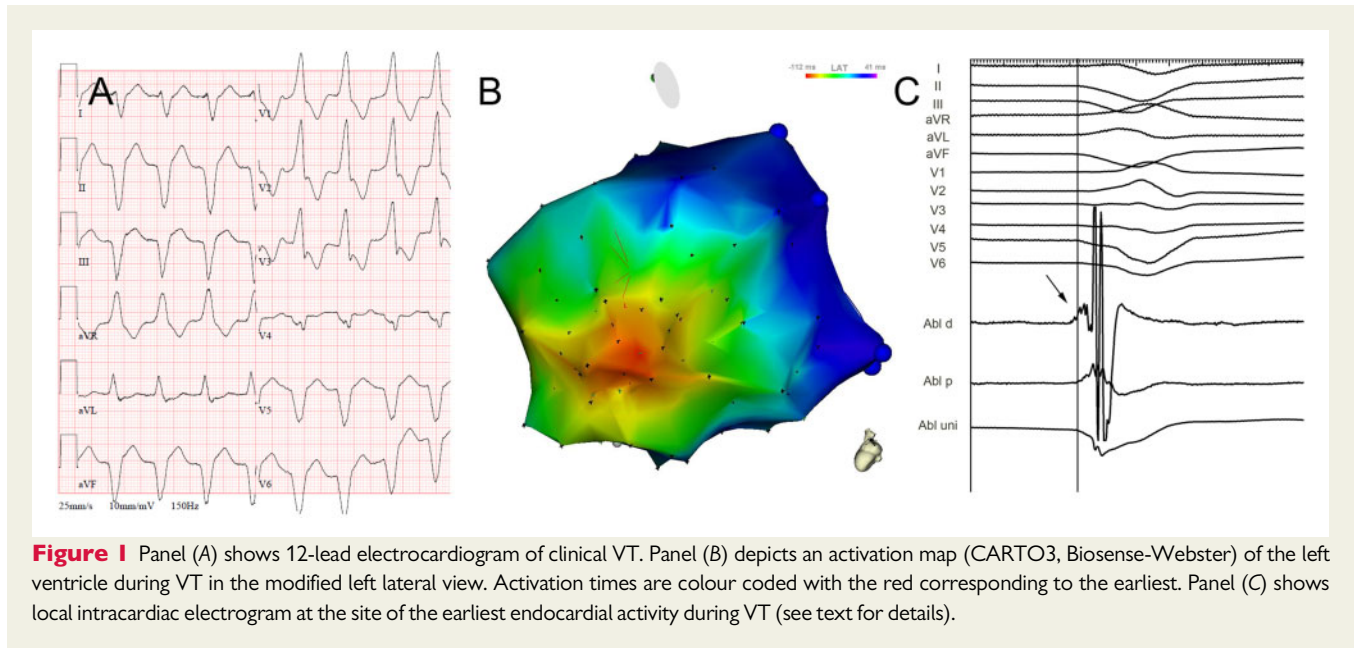
Figure 1 Panel (*A*) shows 12-lead electrocardiogram of clinical VT. Panel (*B*) depicts an activation map (CARTO3, Biosense-Webster) of the left ventricle during VT in the modified left lateral view. Activation times are colour coded with the red corresponding to the earliest. Panel (*C*) shows local intracardiac electrogram at the site of the earliest endocardial activity during VT (see text for details).

Discussion

Stereotactic body radiotherapy emerged as a promising therapeutic option for patients with recurrent VT that failed catheter ablation. However, many aspects related to SBRT are currently unknown. Here, we present the case documenting the effect of repeated SBRT on otherwise refractory VT. It underscores the importance of precise delineation of the target for SBRT and describes a method for direct integration of the electrophysiology data on the pre-SBRT planning CT study. Finally, it is the first case to document in-vivo, by serial voltage mapping, the development of a myocardial lesion created by SBRT. The latter provides an important mechanistic proof of the efficacy of SBRT.

Several factors could have contributed to the success of the second SBRT session. Above all, we believe that the precise integration of electroanatomical mapping data with CT enabled to target part of the substrate that was critical to the VT. Remapping after the first SBRT showed a newly formed area with low bipolar and unipolar voltage. This contrasted with the absence of new detectable scarring after the initial ablation sessions. Although the voltage was attenuated by catheter ablation, it did not fall below the standard criteria of 1.5 mV (bipolar) or 8.3 mV (unipolar). This probably reflects limited ability of current ablation catheters to deliver large lesions in hypertrophic ventricular myocardium. The fact that low unipolar voltage, but not bipolar voltage was seen at the earliest activation site indicate that the first SBRT did not lead to the homogeneous transmural lesion. While bipolar electrograms have a limited field of view and reflect characteristics of adjacent tissue, unipolar voltage mapping provides further range,[7] and low unipolar voltages may indicate regions of epicardial/intramural involvement. Based on this, we may hypothesize that portion of midmyocardium was still spared at the target site. Such interpretation should be, however, taken with caution considering the complexity of scar creation by radiotherapy. Additionally, it is our practice to use point-by-point mapping, which limits the number of points in voltage maps. The use of the multipolar mapping catheter could have increased the mapping density and improve delineation of low voltage areas. Nevertheless, the remapping indicated that the maximum scarring after the first SBRT missed the desired target. We believe that a more precise definition of the target during the first SBRT session could have prevented the need for the second SBRT.

Another important fact is that the precise integration of the electrophysiology-derived target resulted in a significantly smaller target volume (12 vs. 21 ml). This allowed for adding a 3-mm margin to the PTV increasing the chance of achieving transmural lesion. Adding such a margin was not possible during the first SBRT session because of the limiting volume of the non-selectively delineated PTV. Whether the precise identification of the target for SBRT could improve the safety of SBRT by reducing the PTV has to be verified by future studies.

Precision required for targeting in SBRT also suggests that it is questionable whether non-invasive body surface mapping[3] could replace the invasive strategy for image integration. One reason is the spatio-temporal variability of recovered electrograms that limits the precise localization of arrhythmia circuits from the body surface.[8] The other reason is that critical isthmus of re-entry or site of origin in focal arrhythmias may not correlate with the site of the earliest epicardial breakthrough.[9]

We cannot exclude the possible effect of a cumulative dose of the repeated SBRT (2 × 25 Gy), as there was an overlap between the PTVs. Nonetheless, we would strongly discourage from routine SBRT at such high doses because of the risk of complications. Oncology studies have reported the manifestation of cardiac toxicity several years after chest radiotherapy.[10] When high doses (70–90 Gy) are used for lung cancer treatment, cardiac adverse events may be observed in 23% of cases with a median of 26 months to the first event.[11] In our case, the repeated SBRT was justified by recurrent VT episodes that significantly impaired the patient's quality of life.
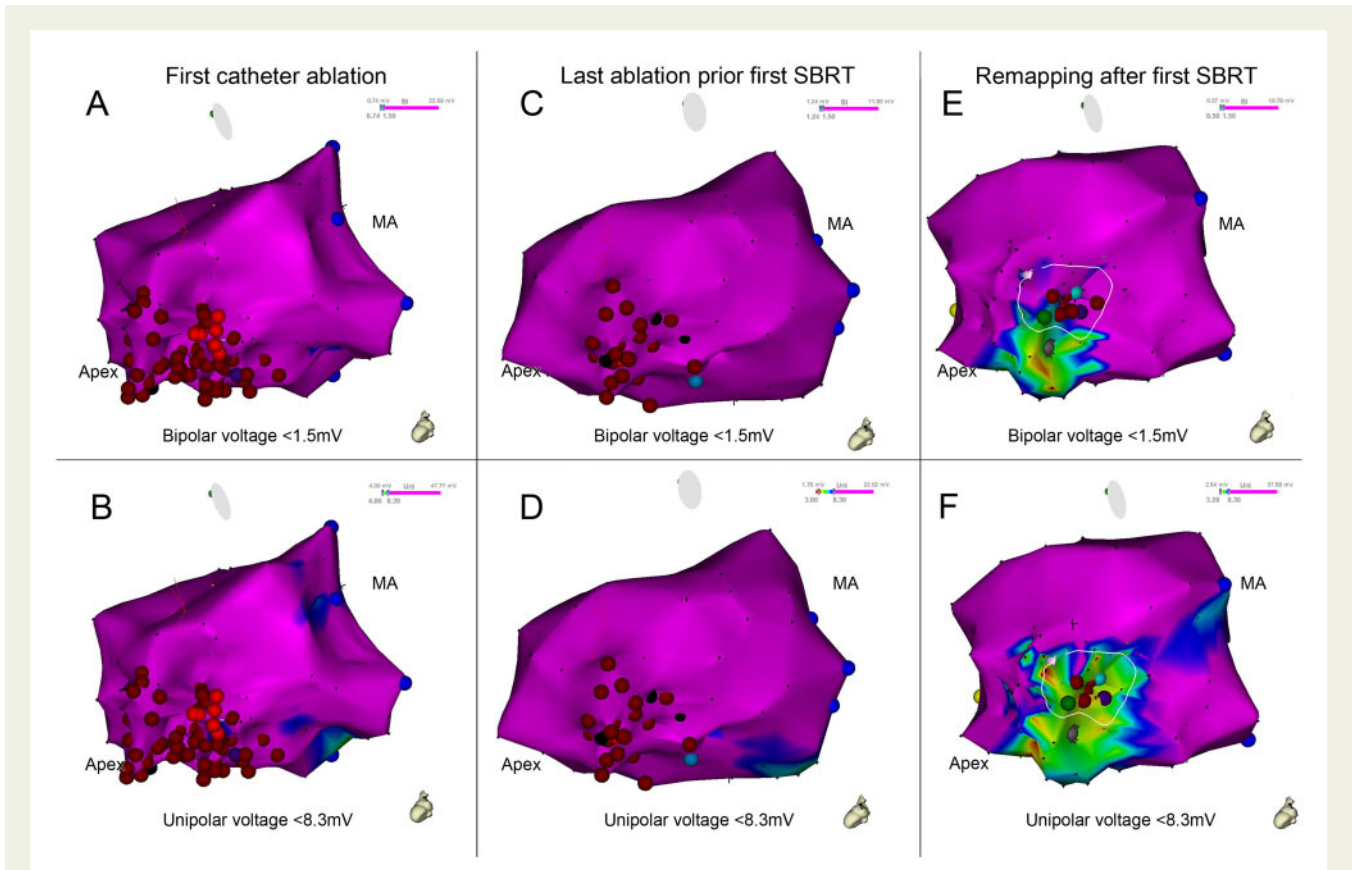
Figure 2 Electroanatomical bipolar and unipolar voltage maps depicting left ventricle in the left lateral view obtained during the first ablation procedure (*A*, *B*), before the first SBRT (*C*, *D*), and prior the second SBRT (*E*, *F*). Voltage is colour-coded, cut-off values for scar detection were set to 1.5 mV and 8.3 mV for bipolar and unipolar voltage, respectively. Note the absence of a new detectable scarring after the first ablation session despite numerous radiofrequency applications. Interestingly, the earliest endocardial activity during VT (white circle) overlapped with the area of low unipolar voltage, while it was only neighbouring the low bipolar voltage region. This indicates that the maximum scarring after the first SBRT occurred only adjacent to the desired target. MA, mitral annulus.
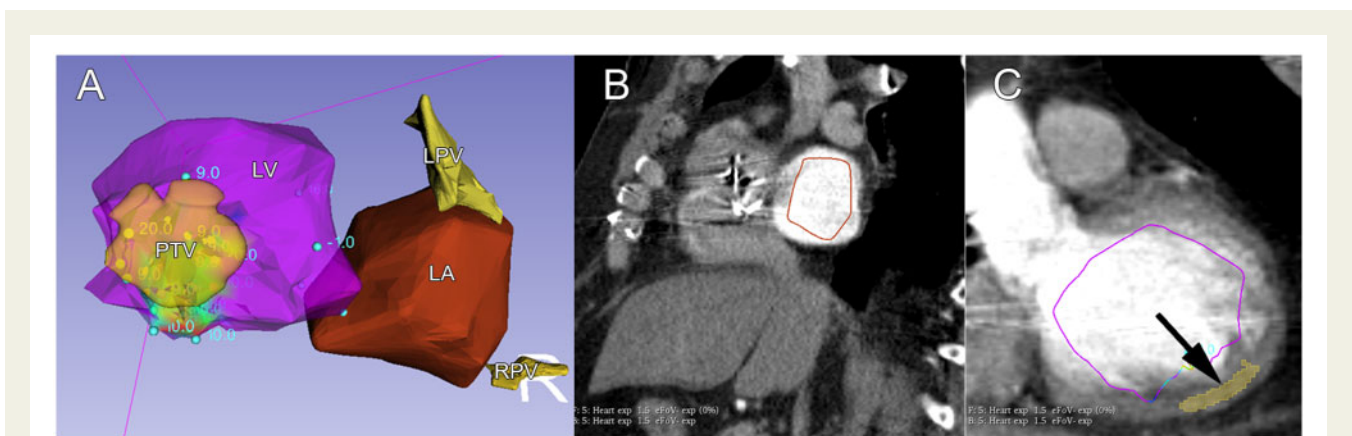

Figure 3 Overview of PTV selection for the second SBRT using the image integration (see text for details). Panel (*A*) shows a 3D model of the LV and LA imported from the electroanatomical mapping system in dedicated software (slicer.org). Panels (*B*) and (*C*) depict endocardial contours of the LA and LV projected onto the raw CT images confirming proper registration. The PTV is projected on the CT slice by yellow colour (arrow). 3D, three dimensional; CT, computed tomography; LA, left atrium; LV, left ventricle; LPV, left-sided pulmonary veins; PTV, planned target volume; RPV, right-sided veins.

At present, the exact mechanisms of myocardial injury induced by SBRT are still unclear. Besides cell death from ionization and free radical production, which leads to the accumulation of double-strand breaks in DNA, there may be additional indirect mechanisms through damage to the tissue vasculature.[12] Of note, the second SBRT in our case led acutely to a temporary increase in VT episodes, which may be explained by a radiation-induced inflammatory reaction. Although there are anecdotal cases of an acute effect of SBRT on suppression of electric storm,[13,14] our case demonstrates potential risks of SBRT for patients with a high degree of electrical instability. In our patient, the therapeutic effect was noted only after three months. In an earlier case report, we observed the disappearance of VT episodes within 6 months after SBRT in a patient with cardiac myxoma.[5] These observations are in line with animal studies showing the delayed effects of radiation therapy on the atrioventricular node.[15]

Lead author biography

Assoc. Prof. Petr Peichl graduated at Charles University in Prague and completed his training in electrophysiology under direction of Prof. Josef Kautzner. His research focus on the catheter ablation of ventricular tachycardia and utility of intracardiac echocardiography during ablation procedures. He currently holds the position of the Head of catheter ablation programme in IKEM, Prague. He is author of more than 80 medical publications in leading journals.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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