ESC European Society of Cardiology

European Heart Journal - Case Reports (2024) **8**, ytae541
https://doi.org/10.1093/ehjcr/ytae541

GRAND ROUND
Electrophysiology

3D-targeted, electrocardiographic imaging-aided stereotactic radioablation for ventricular tachycardia storm: a case report

Yeşim S. Kaya [1], Job Stoks [1], Colien Hazelaar [2], Wouter van Elmpt [2], Suzanne Gommers [3], Paul G.A. Volders [1], Karolien Verhoeven[2], and Rachel M.A. ter Bekke [1]*

[1]Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center+, Postbus 5800, 6202 AZ Maastricht, The Netherlands; [2]Department of Radiation Oncology (Maastro), GROW Research Institute for Oncology and Reproduction, Maastricht University Medical Centre+, Doctor Tanslaan 12, 6229 ET Maastricht, The Netherlands; and [3]Department of Radiology and Nuclear Medicine, Maastricht University Medical Center+, Postbus 5800, 6202 AZ Maastricht, The Netherlands

Received 29 May 2024; revised 13 August 2024; accepted 17 September 2024; online publish-ahead-of-print 30 September 2024

Background Stereotactic arrhythmia radioablation (STAR) is a promising non-invasive therapy for patients with ventricular tachycardia (VT). Accurate identification of the arrhythmogenic volume, or clinical target volume (CTV), on the radiotherapy (RT) 4D planning computed tomography (CT) scan is key for STAR efficacy and safety. This case report illustrates our workflow of electro-structural image integration for CTV delineation.

Case summary A 72-year-old man with ischaemic cardiomyopathy and VT storm, despite two (endocardial and epicardial) catheter-based ablations, was consented for STAR. A 3D electro-structural arrhythmia model was generated from co-registered electroanatomical voltage and activation maps, electrocardiographic (ECG) imaging, and the cardiac CT angiography scan (in ADAS 3D), pinpointing the VT isthmus and inferoapical VT exit. At this location, an area with short recovery times was found with ECG imaging. A multidisciplinary team delineated the CTV on the transmural ventricular myocardium, which was fused with the 4D planning CT scan using a digital images and communication in medicine (DICOM) radiotherapy file. The CTV was 63% smaller compared with using the conventional American Heart Association 17-segment approach (11 vs. 24 cm^3). A single fraction of 25 Gy was delivered to the internal target volume. After an 8-week blanking period, no VT recurrences or radiation-related side-effects were noted. Eight months later, the patient died from end-stage heart failure.

Discussion We report a novel workflow for 3D-targeted and ECG imaging-aided CTV delineation for STAR, resulting in a smaller irradiated volume compared with segmental approaches. Acute and intermediate outcome and safety were favourable. Non-invasive ECG imaging at baseline and during induced VT holds promise for STAR guidance.

Keywords Ventricular tachycardia • Catheter ablation • Stereotactic radiotherapy • Case report • Image integration

ESC curriculum 2.1 Imaging modalities • 5.6 Ventricular arrhythmia

* Corresponding author. Tel: +31 (0)43 3877095, Email: rachel.ter.bekke@mumc.nl
Handling Editor: Stefano Bordignon
Peer-reviewers: Michael Waight; Francisco Moscoso Costa
Compliance Editor: Nicolo Sisti

Learning points

- Pre-procedural 3D electro-structural characterization of the arrhythmogenic substrate and its integration into the planning 4D CT scan is feasible and accurate for stereotactic arrhythmia radioablation (STAR), using ADAS 3D.
- Non-invasive electrocardiographic imaging during baseline rhythm and (non-invasively induced) ventricular tachycardia (VT), on top of invasive contact mapping, pinpoints areas of interest for STAR planning, including VT exit sites adjacent to regions with short recovery times.

Introduction

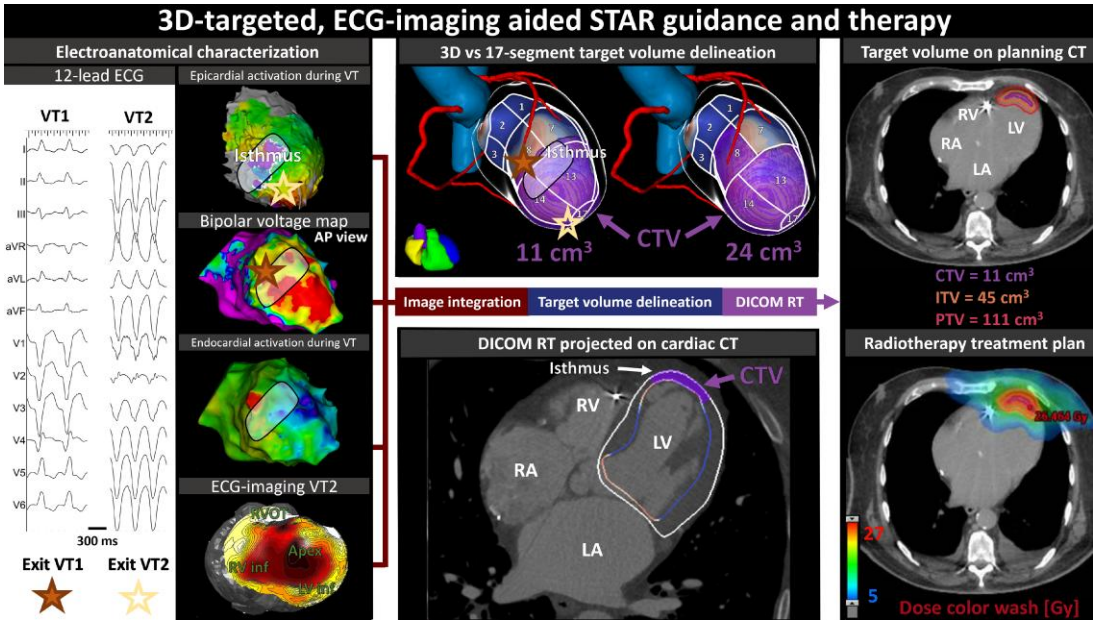
Ventricular tachycardia (VT) most commonly occurs in patients with structural heart disease and imposes an increased risk of sudden death. The dominant VT mechanism is scar-related re-entry.[1] Conventional anti-arrhythmic therapy consists of drugs (beta-blockers, sotalol, amiodarone, procainamide, or mexiletine), cardiac defibrillation/antitachycardia pacing, and/or invasive catheter-based ablation. Unfortunately, drug-induced (proarrhythmic) side-effects and suboptimal ablation lesion formation have led to undesirable VT recurrences.[2] Bail-out strategies, like needle-, bipolar-, transcoronary alcohol-, and surgical VT-substrate ablation, have been developed to improve the durability of ventricular lesion formation.

Stereotactic arrhythmia radioablation (STAR) has emerged as a non-invasive and transmural treatment option for VT. By directing radiation to the arrhythmogenic substrate volume, or clinical target volume (CTV), significant reductions of VT burden and implantable cardioverter-defibrillator (ICD) shocks have been reported.[3,4] Long-term results on the safety and efficacy of radiation-related effects are currently being evaluated in large registries. The EU-funded Standardized Treatment and Outcome Platform for Stereotactic Therapy Of Re-entrant tachycardia by a Multidisciplinary project (STOPSTORM consortium, Horizon 2020, GA No. 945119) aims at providing a pooled database for the evaluation of practice and outcomes of STAR and ultimately at harmonizing STAR within Europe.[5]

Accurate delineation of the arrhythmic target substrate is key for effective and safe STAR delivery.[6–8] The CTV usually encompasses the (presumed) protected VT isthmus and its exit and is confined to scarred myocardium [from electroanatomical mapping (EAM), computed tomography (CT), cardiac magnetic resonance imaging (MRI), echocardiography, or single-photon emission CT]. This EAM-annotated 2D target can be transferred to a 3D CT volume using various approaches. Brownstein *et al.*[7] proposed an atlas based on the American Heart Association (AHA) 17-segment model for all imaging modalities. An AHA 17-segment heat map is constructed incorporating all electro-structural targets, which is subsequently transferred to the 4D planning CT scan. Others have utilized the free open-source 3D slicer[9] or the ADAS 3D (ADAS 3D Medical SL, Barcelona Spain) software[10,11] that registers all electro-structural imaging modalities including the cardiac CT scan. The CTV is directly demarcated on the cardiac CT scan. Next, the CTV on the cardiac CT scan is co-registered to the 4D planning CT scan.

In this case study, we aimed to outline our clinically used workflow for 3D precision delineation of the arrhythmogenic substrate for STAR delivery. This involved the 3D co-registration of critical electrical VT properties derived from contact activation/voltage mapping and the panoramic electrical data from electrocardiographic (ECG) imaging, as well as scar imaging from CT/MRI, in ADAS 3D. The CTV, colour coded as a ventricular volume on the cardiac CT scan, was directly exported as a digital images and communication in medicine (DICOM) radiotherapy (RT) file and served as the basis for RT treatment planning and delivery.

Summary figure



The workflow for the determination of the target volume using the 3D precision method.

Case presentation

A 72-year-old patient, with ischaemic cardiomyopathy [LV (left ventricular) ejection fraction 35%] due to an old anterior wall myocardial infarction, was transferred to our centre because of VT storm. He had received three appropriate ICD shocks whilst on sotalol therapy. Upon presentation, his heart rate was 140 b.p.m. with a blood pressure of 106/59 mm Hg; respiratory rate and oxygen saturation were within normal limits. The 12-lead ECG showed a sustained monomorphic VT with a left bundle branch block-like morphology in lead V1, leftward axis, and precordial transition in lead V4 (VT1; *Figure 1A*). Based on the Andreu algorithm,[12] the VT exit was most likely located in the mid-anteroseptal segment 8 (*Figure 1B*). Laboratory data showed normal electrolytes and lactate, a decreased glomerular filtration rate of 37 mL/min/1.73 m^2 (>90 mL/min/1.73 m^2), and elevated high-sensitivity troponin of 455 ng/L (<14 ng/L) and creatine kinase of 1184 U/L (<225 U/L). VT1 persisted despite intravenous administration of procainamide and amiodarone, as well as multiple external electrical cardioversions. The patient was intubated, and a veno-arterial extracorporeal membrane oxygenation (ECMO) was installed. Transthoracic echocardiography and CT angiography confirmed the presence of a large anterior-apical myocardial infarction and aneurysm formation (*Figure 1C*), without signs of hypervolaemia. A known chronic occlusion of the left anterior descending coronary artery was found on coronary angiography.

Because of incessant VT1, an emergency endocardial catheter ablation was performed during ECMO support (*Figure 2*). Using the OCTARAY™ mapping catheter (Biosense Webster, Irvine, CA, USA), an extensive anteroapical area of reduced peak-to-peak voltage was characterized (*Figure 2A*). Activation mapping of VT1 pinpointed the endocardial VT exit site to the LV anteroseptal border zone. Despite extensive mapping, a substantial part of the critical isthmus remained missing, as shown in *Figure 2B–E* and Supplementary material online, *Video S1*. Radiofrequency energy delivery [40 W, 42°C, ThermoCool SmartTouch catheter (Biosense Webster, Irvine, CA, USA)], targeted at the VT exit site and the presumed juxtaposed endocardial localization of the mid/epicardial isthmus, did not result in VT termination (*Figure 2D*). Therefore, an ECMO-assisted epicardial ablation was performed (*Figure 3*). During mapping of the isthmus region, the VT1 circuit was interrupted, provoking a second VT (VT2) with an exit from the apico-anterior segment 15 (*Figure 3*; Supplementary material online, *Video S2*). The epicardial VT isthmus, opposite to the endocardial area of interest, was successfully ablated (*Figure 3B*), terminating both VTs and rendering the patient non-inducible for any VT. The procedure was uneventful. The patient was easily weaned from ECMO and discharged.

Two months later, the patient was readmitted because of recurrent sustained monomorphic VT with a similar morphology as VT2 (see Supplementary material online, *Figure S1*). Since the patient was optimally treated with medical heart failure therapy and amiodarone, and because he was considered ineligible for heart transplantation or LV assist device, STAR was proposed.

After informed consent, as part of the ELectroanatomic substrate-guided STereotactic Ablative Radiotherapy for refractory Ventricular Tachycardia (ELSTAR-VT, NL9339/NL77235.068.21) study at Maastricht University Medical Center+, non-invasive programmed electrical stimulation from the right ventricular ICD lead was performed

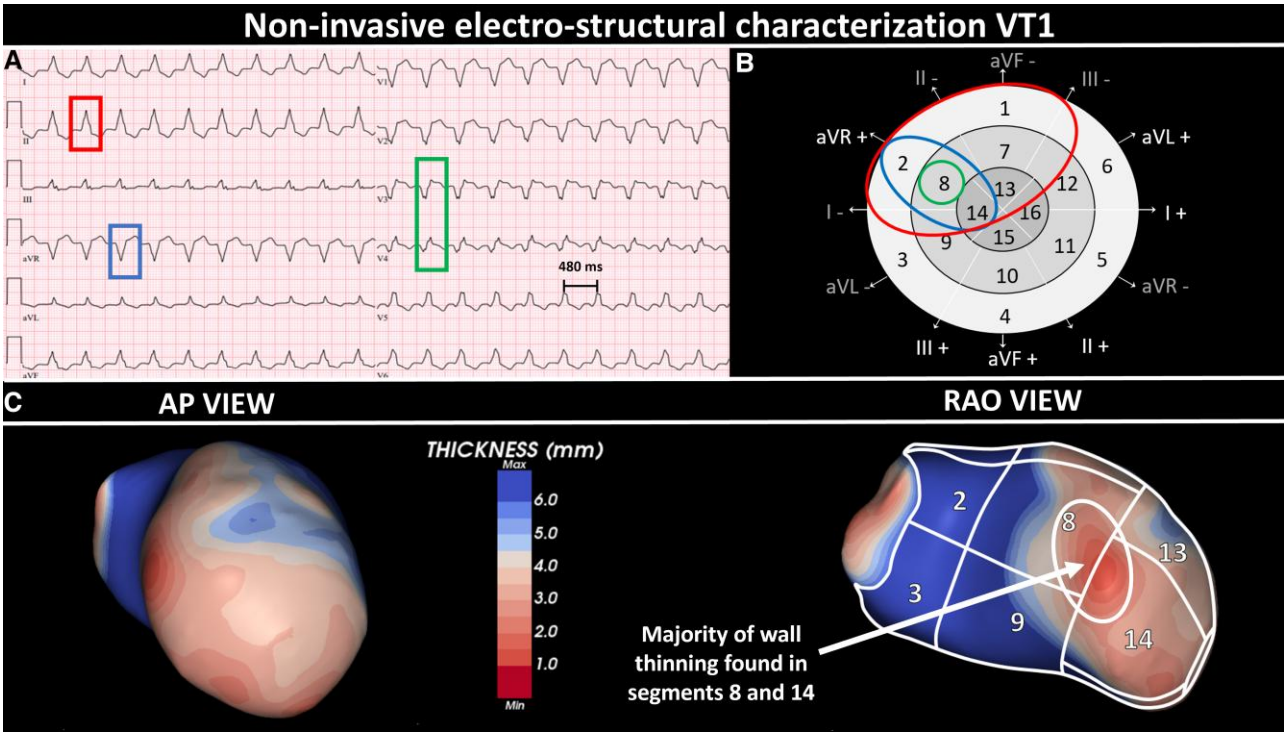


Figure 1 Non-invasive electrostructural characterization of VT1. (*A*) Twelve-lead electrocardiogram showing a sustained monomorphic ventricular tachycardia with a left bundle branch morphology in lead V1, left-ward axis, and precordial transition in lead V4. (*B*) Based on the Andreu algorithm,[12] the exit of this ventricular tachycardia is most likely located in the mid-anteroseptal segment 8. (*C*) The wall thickness 3D model of the left ventricle based on the computed tomography angiography scan in anterior-posterior and right anterior oblique view, showing the most prominent areas of wall thinning in segments 8 and 14, corresponding to the VT1 exit site. AP, anterior-posterior; RAO, right anterior oblique.

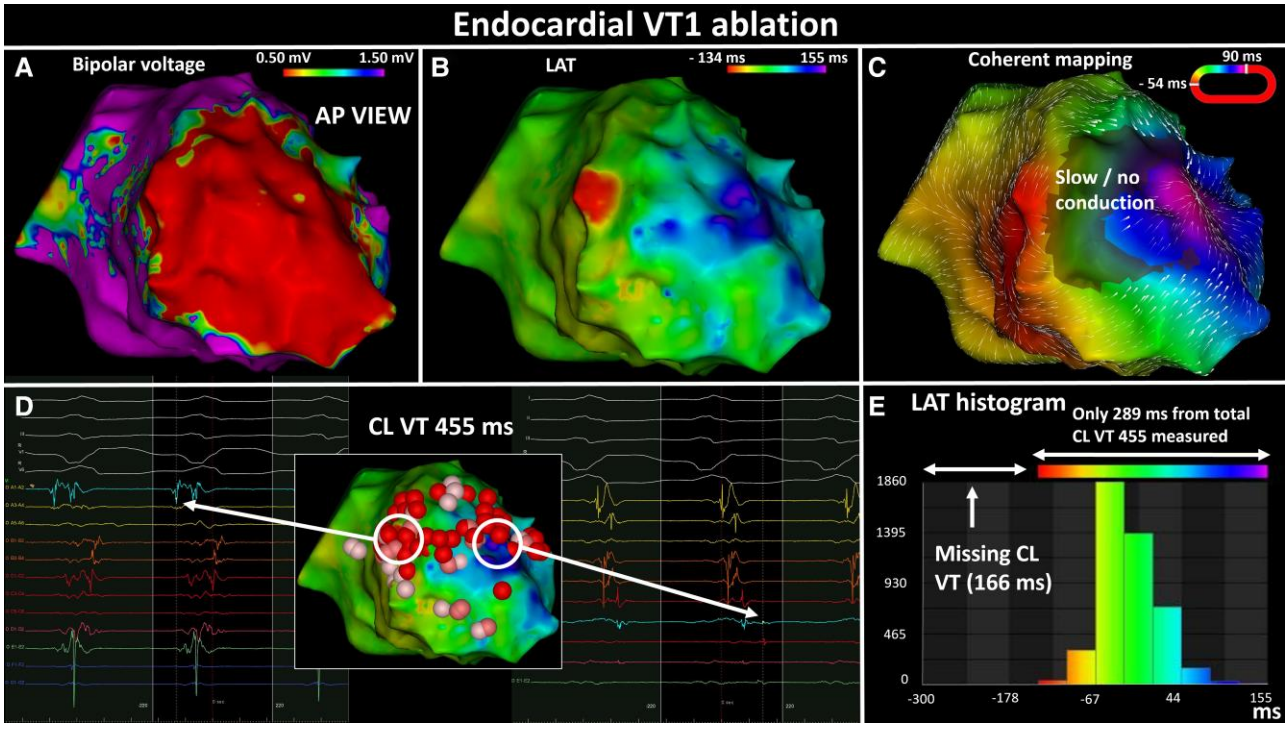


Figure 2 Endocardial VT1 ablation. (*A*) Bipolar voltage map of the left ventricle in the anterior-posterior view. An extensive scar area can be seen at the anteroapex (voltage < 1.5 mV). (*B*) Local activation time mapping during VT1 shows an area of early activation (−134 ms) at the anteroseptal border zone and late activation (155 ms). (*C*) Coherent mapping reveals an area of slow/no conduction in between the areas of early and late activation. (*D* and *E*) The cycle length of the ventricular tachycardia during the procedure was 455 ms. A large part of the cycle length was missing endocardially, suggesting a mid/epicardial isthmus. *D* additionally shows the ablation lesion set (dots). AP, anterior-posterior; CL, cycle length; LAT, local activation time; VT, ventricular tachycardia.

during simultaneous ECG imaging (BioSemi, Active Two, Amsterdam). VT2 was easily induced (see Supplementary material online, *Figure S2*). By combining electroanatomical information from the 224-electrode body surface potential map and the contrast-enhanced CT scan, the reconstructed local activation of the clinically documented VT was pinpointed to the intersection of segments 14, 15, and 17 (*Figures 4* and *5*). Interestingly, local recovery times adjacent to this area were short during atrial fibrillation and coincided with high recovery time gradients during both ventricular pacing and atrial fibrillation, suggesting regional vulnerability for unidirectional block and re-entry.[13]

Clinical target volume delineation was performed by the integration of available invasive and non-invasive electro-structural substrate characteristics into a single 3D DICOM model using ADAS 3D. First, CT-derived anatomical structures like the ascending aorta, aortic root, and LV endocardium were carefully segmented and co-registered to corresponding landmarks from the EAM and ECG imaging maps (see Supplementary material online, *Figure S3*). Manual image integration of invasive EAM and CT endocardial geometry led to a mean Euclidean node-to-node distance 2.60 ± 2.33 mm. On the aligned 3D electro-structural models, for each modality, the areas of interest (scar area, VT exit, and VT isthmus) were identified (*Figure 5*).

A multidisciplinary team of experienced radiation oncologists, cardiologists, and radiologists determined the arrhythmogenic CTV for STAR on this 3D model. The CTV was directly colour coded onto the 3D LV wall thickness model using a research software application in ADAS 3D (*Figure 5*; Supplementary material online, *Video S3*). Using this precision targeting approach, a CTV of 11 cm^3 was calculated, (partly) incorporating AHA segments 8, 13, 14, 15, 16, and 17. For comparison, a segmental heat map approach would have resulted in a 63% larger CTV of 24 cm^3. The 3D precision CTV was exported as a DICOM RT file, imported in the RT treatment planning software (Eclipse version 16.1, Varian Medical Systems, Palo Alto, CA, USA), and co-registered with the 50% exhale phase of the respiration-correlated (4D) planning CT scan. Margins incorporating respiration and cardiac motion were defined based on the respiratory motion of all phases of the 4D planning CT scan in six different directions (cranial 7 mm, caudal 6 mm, ventral 1 mm, dorsal 4 mm, medial 3 mm, and lateral 3 mm) to generate the internal target volume (ITV). To account for, amongst others, cardiorespiratory motion as described by Stevens *et al.*,[14,15] residual uncertainties, positioning, and movement of the patient, an isotropic margin of 5 mm was added to the ITV, based on standard practice, to derive the planning target volume (PTV). Nearby organs at risk were defined. The accuracy of the transfer of the planned CTV from ADAS 3D to the 4D planning CT scan was assessed by exporting the final irradiated CTV from the 4D planning CT scan back into ADAS 3D. The 4D planning CT scan and cardiac CT scan were merged based on the above-described landmarks. A mean Euclidean node-to-node distance of 1.41 ± 1.03 mm was found between the two CTVs, indicating high transfer accuracy even after two co-registrations.

A single fraction with a total dose of 25 Gy to the ITV and 20 Gy to the PTV was delivered using three coplanar half (205°) volumetric

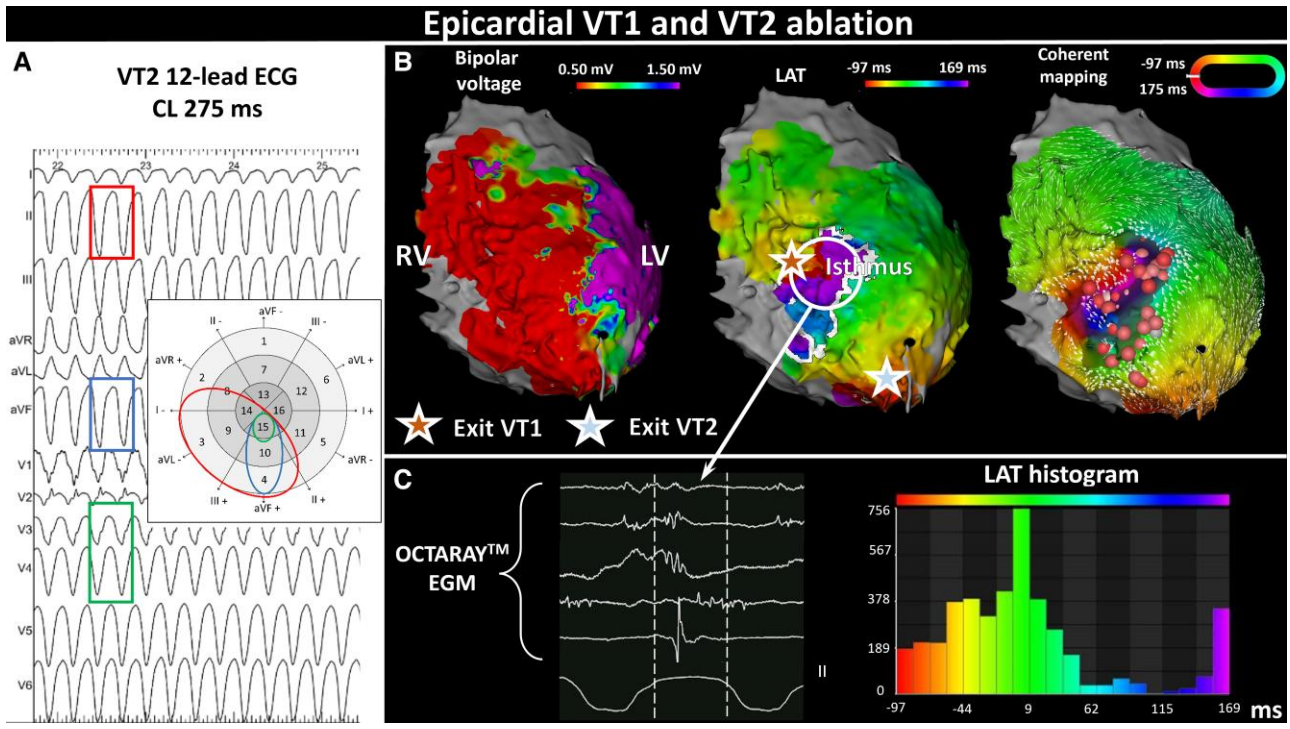


Figure 3 Epicardial VT1 and VT2 ablation. (*A*) Twelve-lead electrocardiogram showing a second ventricular tachycardia (VT2) with a cycle length of 275 ms and a presumed exit from the apico-anterior segment 15. (*B*) The bipolar voltage, local activation time and coherent mapping are respectively shown from left to right. A large scar area on bipolar mapping was mapped with a clear VT isthmus, opposite to the endocardial area of interest, as seen on the local activation time and coherent mapping. The exits of VT1 and VT2 are indicated with the stars. (*C*) The electrogram recorded with the OCTARAY™ at the isthmus spanning the diastolic interval. EGM, electrogram; LAT, local activation time; LV, left ventricle; RV, right ventricle; VT, ventricular tachycardia.

modulated arc therapy arcs and 6 MV flattening filter-free beams using a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA, USA; *Figure 6A*). The total delivery time from first to last monitor unit was 11 min. No acute complications were noted. Within the blanking period of 8 weeks, two episodes of sustained monomorphic VT occurred that were successfully converted to sinus rhythm. After the blanking period, no VTs were recorded with the ICD during the follow-up period, compared with 20 sustained VT episodes and 12 ICD shocks before STAR (monitor zone 100 b.p.m.; *Figure 6B*). The amiodarone dose was reduced from 400 to 200 mg daily. No radiation pneumonitis was observed. Eight months after STAR, the patient died from end-stage heart failure without having shown VT recurrence. A relation between the STAR and the worsening of heart failure was not deemed likely.

Discussion

In this case report, we have fused for the first-time non-invasive 3D ECG imaging with conventional imaging modalities including endocardial and epicardial EAM as well as CT angiography aiming to enhance our understanding of arrhythmia formation and guide STAR. This extends our existing image integration pipeline[16] to prospective (non-invasive) therapies. In ADAS 3D, the integrated models intuitively displayed the multiple critical components of both VTs including the protected isthmus and VT exit sites with short recovery times that may allow re-entrant excitation to exit the scar area. The colour-coded CTV was easily contoured in ADAS 3D and exported as DICOM RT in order to be imported into the RT treatment planning system, avoiding the need for replication or re-delineation of the target volume in the STAR planning software. This may reduce the inter-observer variabilities between the cardiologist and radiation oncologist. Our approach led to a 63% reduction of the CTV compared with the traditional segmental approach. Intermediate-term outcome was favourable without VT recurrences or radiation-related side-effects. Moreover, ADAS 3D allowed the 'backloading' of the targeted CTV from the 4D planning CT scan into the 3D electro-structural arrhythmia model, demonstrating a high transfer accuracy of 1.41 ± 1.03 mm.

Since the first case series described by Cuculich *et al.*,[3] STAR is increasingly being embraced as a bail-out strategy for VT that is persistent after conventional ablative therapies. One of the challenges is the accurate and reproducible delineation and transfer of the arrhythmogenic volume from various combined imaging modalities onto the planning CT scan. This is partly because of the lack of agreement between experienced electrophysiologists on the identification of the CTV using a standard EAM data set,[17] but also because of the divergence of methods employed for CTV delineation and transfer to the planning CT scan. These encompass manual annotation, registration of EAM map in CT, and AHA 17-segment and research software approaches.[7,17] The accuracy of segment-guided annotation on a cardiac CT scan appeared poor with high inter-observer variability.[8] Alternatively, Hohmann *et al.*[9] manually annotated the 2D arrhythmogenic area from the EAM, which was rendered into a 3D volume, on the cardiac CT scan using the open-source 3D slicer software with a customized plug-in. The CTV was subsequently merged with the planning CT scan.

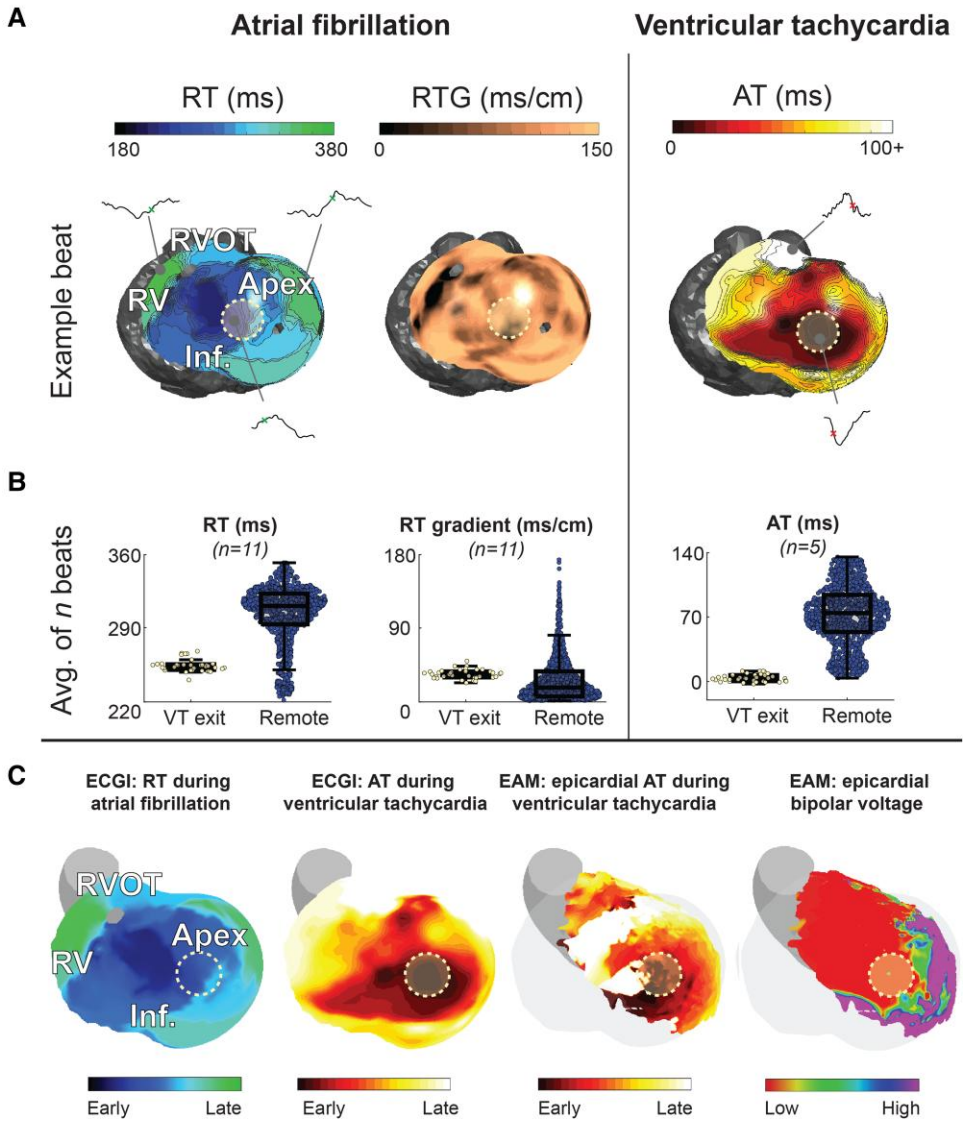


Figure 4 Electrocardiographic (ECG) imaging for stereotactic arrhythmia radioablation workup. (*A*) Representative example beats of recovery time and spatial recovery time gradients during atrial fibrillation (left) and activation time during VT2 (right). The dashed circle indicates a 15 mm radius around the VT2 exit. (*B*) Averaged over multiple beats: during atrial fibrillation, recovery time was relatively early and recovery time gradients were high near the VT2 exit, compared with remote areas (left). During ventricular tachycardia, activation time was relatively early near the VT2 exit (right). (*C*) Comparison of ECG imaging and electroanatomical mapping: early recovery time during atrial fibrillation (ECG imaging) coincides with early activation during ventricular tachycardia (ECG imaging and electroanatomical mapping) and was close to the border of the low-voltage area (electroanatomical mapping). AT, activation time; RT, recovery time; RTG, recovery time gradients; VT, ventricular tachycardia.

Santos-Ortega *et al.*[10] first described the use of ADAS 3D for multimodal imaging integration and therapy planning for STAR delivery. Compared with 3D slicer, ADAS 3D allows for the integration of all electrical and imaging modalities, including MRI, CT, EAM, and ECG imaging, on the same CT scan. Furthermore, scar models with heterogeneous tissue corridors or wall thickness architectures from MRI and CT scan, respectively, provide additional information on arrhythmia formation. The STAR tags positioned on the EAM can be easily visualized, facilitating CTV delineation. In our case, the integration of panoramic ECG imaging, visualizing both baseline electrophysiology and the non-invasively induced VT (by programmed stimulation performed from the dwelling right ventricular ICD lead), co-located the VT exit site to the EAM-derived epicardial exit site. Already during baseline rhythm, this VT exit site was surrounded by an area of shortened recovery time and higher spatial gradients thereof, both indicative of a higher vulnerability to re-entry.[13] From high-density contact mapping, it is known that these parameters may predispose to a lower re-entry vulnerability index, pinpointing to VT sites of origin.[18]

To the best of our knowledge, this is the first report on the comprehensive integration of ECG imaging-derived electrical signatures into conventional multimodal imaging techniques. The added value of non-invasive ECG imaging to guide STAR delivery, however, needs to be investigated in larger patient populations.

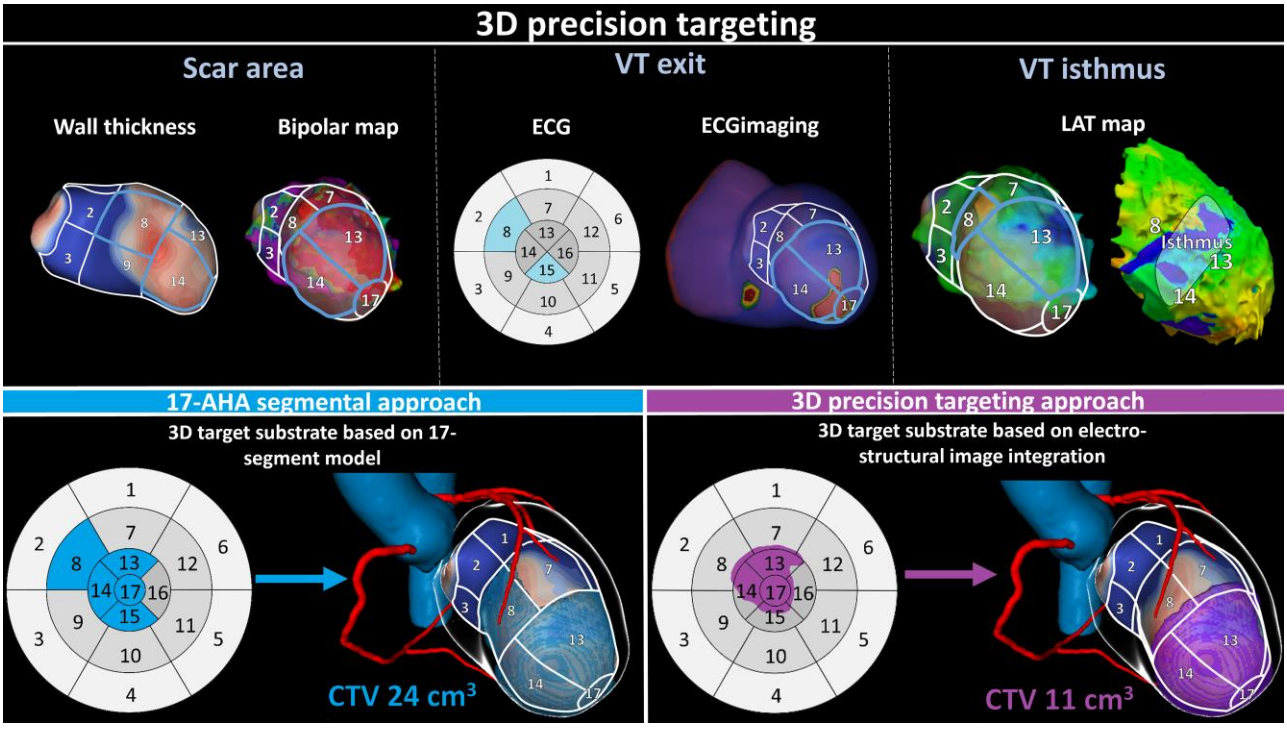


Figure 5 Clinical target volume delineation. The scar area, ventricular tachycardia exit, and isthmus depicted with the American Heart Association 17-segment method or through the 3D precision targeting. With accentuated lines, the relevant segments for targeting are shown for the American Heart Association 17-segment method. For both methods, the clinical target volumes projected with the American Heart Association 17-segment model and the 3D precision approach on the left ventricle are shown (blue for American Heart Association 17-segment method and purple for the precision targeting method). AHA, American Heart Association; CTV, clinical target volume; LAT, local activation time; VT, ventricular tachycardia.

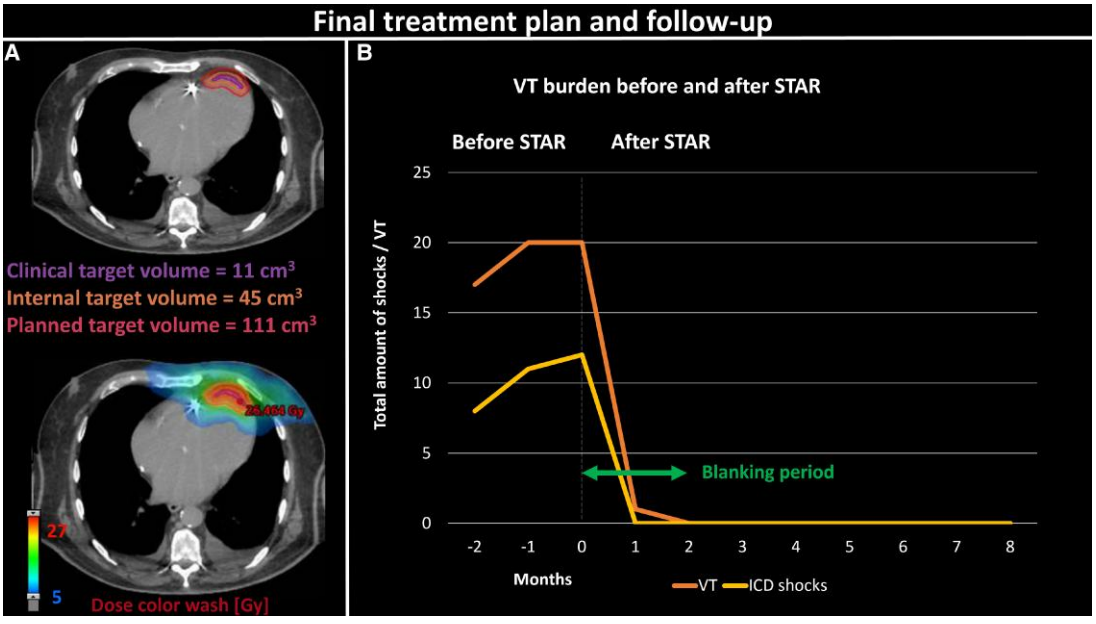


Figure 6 Target volume and follow-up. (*A*) The target volume is composed of a clinical target volume of 11 cm^3, an internal target volume of 45 cm^3 and a planning target volume of 111 cm^3. (*B*) Ventricular tachycardia burden as registered from the patient's implantable cardioverter-defibrillator, depicting the occurrence of two sustained monomorphic ventricular tachycardias in the blanking period after stereotactic arrhythmia radioablation treatment, with no other ventricular tachycardia episodes afterwards. STAR, Stereotactic arrhythmia radioablation; VT, ventricular tachycardia.

Patient's perspective

Our patient was interviewed allowing him to share his experience with STAR. Quote from the interview: 'If you have no choice left, RT is a great solution for people with ventricular arrhythmias…. My wife and I look back gratefully, we were well-guided and -treated by the doctors and nurses'.

Conclusion

3D-targeted, ECG imaging-aided cardiac stereotactic radioablation was effective and safe in this patient with refractory VT storm in the setting of ischaemic cardiomyopathy. Non-invasive ECG imaging during baseline rhythm and (non-invasively induced) VT pinpointed critical areas for STAR delivery including the VT exit site and regions with short recovery times. All electro-structural details of the arrhythmogenic substrate were co-registered, leading to a reduced target volume and an accurate transfer of the CTV to the planning CT scan compared with the AHA 17-segment method.

Lead author biography

Yeşim S. Kaya is a physician scientist at the Department of Cardiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center+, the Netherlands. She focuses on the electro-structural mechanisms and treatment of ventricular tachycardia using multimodal mapping. Her ambition is to become a cardiologist-electrophysiologist with a subspeciality in ventricular arrhythmias.

Supplementary material

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

Acknowledgements

The authors would like to thank all members of the STOPSTORM consortium (see https://stopstorm.eu/en/consortium). The workflow of STAR treatment operates seamlessly owing to our team of dedicated professionals. We express gratitude to all professionals from the Departments of Cardiology, Radiology, and Radiation Oncology who assisted with the creation of our STAR workflow and the treatment administered to our patients. Furthermore, we thank Professor Phillip S. Cuculich, Washington University School of Medicine, St. Louis, MO, for the expert advice.

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

Conflict of interest: None declared.

Funding: This study is part of the project 'Standardized Treatment and Outcome Platform for Stereotactic Therapy of Re-Entrant Tachycardia by a Multidisciplinary (STOPSTORM) Consortium' that has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 945119. YSK received the Harry Struijker-Boudier award for talented academics (HS-BAFTA) from the Cardiovascular Research Institute Maastricht (CARIM). RtB received a Veni grant from the Netherlands Organization for Scientific Research (NWO/ZonMw 0915016181013).

Data availability

The data underlying this case report can be made available upon reasonable request to the corresponding author.

References

1. Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Blom NA, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2022;**43**:3997–4126.
2. Santangeli P, Muser D, Maeda S, Filtz A, Zado ES, Frankel DS, et al. Comparative effectiveness of antiarrhythmic drugs and catheter ablation for the prevention of recurrent ventricular tachycardia in patients with implantable cardioverter-defibrillators: a systematic review and meta-analysis of randomized controlled trials. *Heart Rhythm* 2016;**13**:1552–1559.
3. Cuculich PS, Schill MR, Kashani R, Mutic S, Lang A, Cooper D, et al. Noninvasive cardiac radiation for ablation of ventricular tachycardia. *N Engl J Med* 2017;**377**:2325–2336.
4. Robinson CG, Samson PP, Moore KMS, Hugo GD, Knutson N, Mutic S, et al. Phase I/II trial of electrophysiology-guided noninvasive cardiac radioablation for ventricular tachycardia. *Circulation* 2019;**139**:313–321.
5. Grehn M, Mandija S, Miszczyk M, Krug D, Tomasik B, Stickney KE, et al. Stereotactic arrhythmia radioablation (STAR): the Standardized Treatment and Outcome Platform for Stereotactic Therapy Of Re-entrant tachycardia by a Multidisciplinary consortium (STOPSTORM.eu) and review of current patterns of STAR practice in Europe. *Europace* 2023;**25**:1284–1295.
6. Ohri N, Shen X, Dicker AP, Doyle LA, Harrison AS, Showalter TN. Radiotherapy protocol deviations and clinical outcomes: a meta-analysis of cooperative group clinical trials. *J Natl Cancer Inst* 2013;**105**:387–393.
7. Brownstein J, Afzal M, Okabe T, Harfi TT, Tong MS, Thomas E, et al. Method and atlas to enable targeting for cardiac radioablation employing the American Heart Association segmented model. *Int J Radiat Oncol Biol Phys* 2021;**111**:178–185.
8. van der Ree MH, Cuculich PS, van Herk M, Hugo GD, Balt JC, Bates M, et al. Interobserver variability in target definition for stereotactic arrhythmia radioablation. *Front Cardiovasc Med* 2023;**10**:1267800.
9. Hohmann S, Henkenberens C, Zormpas C, Christiansen H, Bauersachs J, Duncker D, et al. A novel open-source software-based high-precision workflow for target definition in cardiac radioablation. *J Cardiovasc Electrophysiol* 2020;**31**:2689–2695.
10. Santos-Ortega A, Rivas-Gándara N, Pascual-González G, Seoane A, Granado R, Reyes V. Multimodality imaging fusion to guide stereotactic radioablation for refractory complex ventricular tachycardia. *HeartRhythm Case Rep* 2022;**8**:836–839.
11. Brett CL, Cook JA, Aboud AA, Karim R, Shinohara ET, Stevenson WG. Novel workflow for conversion of catheter-based electroanatomic mapping to DICOM imaging for non-invasive radioablation of ventricular tachycardia. *Pract Radiat Oncol* 2021;**11**:84–88.
12. Andreu D, Fernández-Armenta J, Acosta J, Penela D, Jáuregui B, Soto-Iglesias D, et al. A QRS axis-based algorithm to identify the origin of scar-related ventricular tachycardia in the 17-segment American Heart Association model. *Heart Rhythm* 2018;**15**:1491–1497.
13. Cluitmans MJM, Bayer J, Bear LR, ter Bekke RMA, Heijman J, Coronel R, et al. The circle of reentry: characteristics of trigger-substrate interaction leading to sudden cardiac arrest. *Front Cardiovasc Med* 2023;**10**:1121517.
14. Stevens RRF, Hazelaar C, Bogowicz M, ter Bekke RMA, Volders PGA, Verhoeven K, et al. A framework for assessing the impact of cardiac and respiratory motion for stereotactic arrhythmia radioablation (STAR) using a digital phantom with a 17-segment model—a STOPSTORM.eu consortium study. *Int J Radiat Oncol Biol Phys*. 2024;**118**:533–542.
15. Stevens RRF, Hazelaar C, Fast MF, Mandija S, Grehn M, Cvek J, et al. Stereotactic arrhythmia radioablation (STAR): assessment of cardiac and respiratory heart motion in ventricular tachycardia patients—a STOPSTORM.eu consortium review. *Radiother Oncol* 2023;**188**:109844.
16. Stoks J, Hermans BJM, Boukens BJD, Holtackers RJ, Gommers S, Kaya YS, et al. High-resolution structural-functional substrate-trigger characterization: future roadmap for catheter ablation of ventricular tachycardia. *Front Cardiovasc Med* 2023;**10**:1112980.
17. Boda-Heggemann J, Blanck O, Mehrhof F, Ernst F, Buergy D, Fleckenstein J, et al. Interdisciplinary clinical target volume generation for cardiac radioablation: multicenter benchmarking for the RAdiosurgery for VENtricular TAchycardia (RAVENTA) trial. *Int J Radiat Oncol Biol Phys* 2021;**110**:745–756.
18. Orini M, Graham AJ, Srinivasan NT, Campos FO, Hanson BM, Chow A, et al. Evaluation of the reentry vulnerability index to predict ventricular tachycardia circuits using high-density contact mapping. *Heart Rhythm* 2020;**17**:576–583.