Stereotactic Body Radiation Therapy for Ventricular Arrhythmias: Efficacy, Safety and Image Analysis-First Asian Population Study

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Abstract

Stereotactic body radiation therapy (SBRT) has been proved to be effective in refractory ventricular arrhythmia (VA). We report the first Asian series of SBRT for refractory VA in a group of Taiwanese. This study included patients with treatment-failure VA. 3D electroanatomic maps, delayed enhancement magnetic resonance imaging (DE-MRI) and dual energy computed tomography (CT) were used to identify scar substrates. The target volume was treated with a single radiation dose of 20 Gy delivered by Varian TrueBeam System. Efficacy was assessed by VA events recorded by implantable cardioverter defibrillator (ICD) or 24-hour Holter. Pre- and post-radiation therapy image studies were also performed. Adverse events were monitored during follow-up. From February 2019 to December 2019, 7 patients were enrolled. Six male and one female patients, mean age 55 years, received the treatment. Among the 7 patients with variety of cardiomyopathy, one patient died of hepatic failure. For the other 6 patients, at a median follow-up of 14.5 months, the burden of VA decreased significantly. Increased intensity of DE-MRI might be associated with lower risk of VA recurrence while the dual energy CT had lower sensitivity in the detection. No acute and minimal late adverse events were reported. We conclude that, in patients with refractory VA, SBRT was associated with a marked reduction in the burden of VA and DE-MRI might be useful to monitor treatment effect.

Introduction

Severe ventricular arrhythmia (VA) is a leading cause of sudden cardiac death (SCD) in patients with structural heart diseases. In this patient population, implantable cardioverter defibrillator (ICD) remains the treatment of choice both for primary and secondary prevention of SCD. However, ICD therapy, especially when in electric storm, is associated with excess mortality and morbidity whether the therapy is appropriate or non-appropriate [1]. Although, comparing with antiarrhythmic therapy, catheter ablation of the abnormal ventricular substrates is demonstrated to be an effective and preferable strategy for electric storm management, the outcomes are less than ideal especially in patients with nonischemic cardiomyopathy [2].

Stereotactic body radiation therapy (SBRT) as a treatment modality in radiation oncology emerged since late 1990s and flourished in recent 20 years, and has become the standard of care for inoperable early-stage non-small cell lung cancer and liver cancer [3, 4] and considered as treatment options for oligometastases in brain, lung, bone, liver, and adrenal [5]. In addition to cancer, SBRT techniques targeting benign central nervous system diseases such as arteriovenous malformations, seizure foci, and trigeminal neuralgia has demonstrated promising results. The technical and clinical advancement of SBRT include managing the respiratory motion of targets in the thorax and liver by four-dimensional computed tomography and respiratory gating facilities, defining safe radiation dosing levels for critical organs, and setting training and quality assurance standards for radiation oncology clinics globally.

The character of precise delivery of a very high radiation dose to the target tissues has enabled SBRT as a promising alternative to catheter ablation particularly for arrhythmogenic substrates that are difficult or impossible to access. Recently, SBRT has been successfully applied to severe VA with failed or contraindicated catheter ablation [6, 7]. In this study, we report the first Asian series of SBRT experience for refractory VA in a group of Taiwanese with various underlying cardiac diseases. There were several unique features of our reports. First, we reduced the radiation dose for smaller body size of Asian people. Second, we included patients with a variety of underlying cardiac diseases including ischemic cardiomyopathy (ICM), dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC). Third, the pre- and post-therapy imaging studies were also included for analyses.

Methods

Study population

The study was approved by the institutional review board of the National Taiwan University Hospital Ethics Committee. All research was performed in accordance with relevant guidelines/regulations and inform consent was obtained from all participants and/or their legal guardians. This study included patients with treatment-failure VA. Eligible patients were ≥18 years old and had ≥3 episodes of sustained ventricular tachycardias (VTs) in the past 3 months or monomorphic premature ventricular contractions (PVCs) over >20% and required failure of antiarrhythmic medication treatment and ≥1 catheter ablation (or had a contraindication to catheter ablation). In all patients, 3D electroanatomic maps of the ventricles were obtained and regions of the substrates responsible for the clinical VTs were outlined. The substrate was defined as scar by a voltage ≤ 0.5mV (normal tissue >1.5 mV), late potentials or abnormal potentials. Activation mapping was used if clinical VTs were clinically tolerable. Pace mapping during sinus rhythm was also used for assessing the exit site of clinical VTs. All patients received a detailed explanation of the risks of treatment from both the attending electrophysiologist and radiation oncologist and provided written informed consent to treatment.

Procedure workflow

The procedural workflow for SBRT is shown in Figure 1. At the planning phase of the procedure, 3D electroanatomic maps were exported from the mapping system (CARTO® 3, Biosense Webster, Israel). All patients received either ECG-gated delayed enhancement magnetic resonance imaging (DE-MRI) or dual energy computed tomography (CT) to identify the regions of scars. The CT/MRI images were compared with 3D electroanatomic maps to identify arrhythmogenic scar substrates, which were the targets of the SBRT. A contoured target volume was created together by the electrophysiologist, cardiac radiologist and the radiation oncologist. After SBRT simulation, irradiation was performed and overseen by the radiation oncologist. The patient was hospitalized on the day of radiation treatment and discharged on the other day if there was no immediate complication.

Scar substrates identification

Cardiac magnetic resonance imaging (CMR)

CMR was performed in patients with MRI-compatible implantable cardiac defibrillators (ICDs). Late gadolinium enhancement (LGE)-MRI was performed 10 minutes after gadolinium injection to detect myocardial scar. Since conventional LGE-MRI results in device-induced hyperintense artifacts that obscure ventricular images, wideband LGE-MRI was used to reduce the artifacts. The wideband LGE-MRI sequence was similar to the conventional sequence except for the bandwidth (IR sequence: TR/TE, 6.7/3.2; resolution: 1.4x2.2mm2; slide thickness: 8mm; inversion time: 250-350ms) which included a wideband inversion recovery (IR) radiofrequency pulse with frequency bandwidth and offset adjusted to minimize hyperintense artifacts. The default bandwidth of the wideband IR radiofrequency pulse was 3800Hz, and the optimal frequency offset was up to 8000Hz [19, 20].

Dual energy CT.

All patients received ECG-gated dual energy CT evaluation of myocardial scar before SBRT (Revolution HD, GE Healthcare, Milwaukee, Wis). ECG-gated noncontrast cardiac CT was performed first using prospectively gated axial scanning. Coronary CT angiography was then performed by using helical scanning with dose modulation. Multiphasic contrast injection protocol was used for better opacification of both left and right-side heart chambers. The start of scanning was determined by bolus tracking technique. Late iodine enhancement CT (LIE-CT) was performed 7 minutes later after the acquisition of coronary CT angiography.

Left ventricular scar tissue was defined as region of wall thinning, hypoattenuation, decreased perfusion or delayed enhancement on dual energy CT or CMR.

Cardiac radioablation

All patients underwent a standard SBRT simulation, immobilized using an individualized vacuum bag (BodyFIX; Elekta, Stockholm, Sweden), which limited diaphragmatic motion through external abdominal compression. A free-breathing CT and a four-dimensional (4D-CT) were acquired using a 16-slice CT scanner (Brillance Big ore CT; Philips Healthcare, Andover, MA). The gross target volume (GTV) was contoured in the treatment planning system (TPS) (Eclipse, Varian Medical Systems, Palo Alto). The internal target volume (ITV) was defined using the 4D-CT scan to account for internal motion of the GTV caused by breathing and cardiac motion. The planning target volume (PTV) was defined as ITV plus 3 to 5 mm margin to account for any residual uncertainties in patient setup, motion, and delivery.

The noninvasive cardiac radioablation treatment plan was generated in the TPS using the simultaneous integrated boost strategy to deliver 25 Gy to GTV and 20 Gy to PTV in a single fraction. 6 or 10 MV flattening filter-free photon beam and volumetric modulated arc radiotherapy (VMAT) technique was applied with multiple coplanar and non-coplanar ports, in which highly accurate and conformal radiation dose was employed by adjusting the gantry rotation speed, dose rate, and shape of a multi-leaf collimator. In order to achieve maximal coverage of the PTV region while reducing the dose to surrounding organ at risk (OAR) The resultant plan underwent physics quality assurance a day prior to delivery, to ensure accurate delivery of the dose to the patient. An example of noninvasive cardiac radioablation beam arrangement and isodose curves were shown in Figure 2.

Irradiation was performed using the image-guided radiotherapy (IGRT)- equipped linear accelerator Varian TrueBeam Radiotherapy System (Varian, Palo Alto, CA). The treatment position was verified and automatically adjusted before and during each SBRT fraction using onboard imaging device capable of acquiring volumetric images (cone beam CT, CBCT). The entire procedure was overseen by the radiation oncologist.

Outcome and adverse events assessment

After radiation therapy, patients visited the outpatient clinic at 1st and 4th week after radioablation, and every 1 month visit for unstable patients and every 3 months visit for relatively stable patients thereafter. Chest X ray and transthoracic echocardiography were arranged for possible complications, including pericardial effusion or radiation pneumonitis etc. Post radiation MRI or CT scans were arranged for eligible patients. ICD interrogation was performed at electrophysiologist's visit. For the patient with PVCs, 24-hour Holter was arranged to assess the radiation efficacy. Antiarrhythmic medications were titrating by the electrophysiologist according to the clinical condition.

We analyzed the time to recurrence of ICD therapy after 6-week of blanking period, and time to major events including mortality. The mean number of VT episodes (VT burden) and ICD therapies before and after radioablation were also recorded. Acute and late toxicities were rated according to the Common Terminology Criteria for Adverse Events version 4.0.

Results

Patient population

From February 2019 to December 2019, 7 patients were enrolled. Table 1 outlines the basic clinical characteristics. Six male and one female patients received the treatment. The mean age was 55 years (range 23-80 years). Among the seven patients, three patients had DCM, one had ICM, one had HCM, one had ARVC, and the remaining one (patient 3) had frequent PVCs with normal left ventricular ejection fraction (LVEF). The patient had delayed enhancement at basal antero-septum of left ventricle (LV) which was unlikely caused by two previous ablation procedures. The median number of

previous catheter ablations before enrollment was 2 (range, 0−4). One patient (patient 2) didn't receive catheter ablation therapy due to LV apical thrombus. Six patients were on amiodarone treatment, and four of these had >300mg daily before enrollment.

Radiation procedure

The SBRT details were showed in Table 2. Median GTV was 11.5cc (range, 4.6−64.9). Accounting for motion and conservative additional margins for setup and delivery, the median PTV was 34.4cc (range, 14.4−84.5). A median of 10 partial arcs was employed for the cardiac radioablation plan (range, 10−13), all with four non-coplanar partial arcs and a median of six coplanar partial arcs (range, 6−9). Median total monitor units were 8898 (range, 6431−12092), and the median beam-on time was 12.7 minutes (range, 9.2−17.3). No patient required sedation during the procedure. Supplement 1 included the SBRT simulation images in all patients.

Efficacy

Patient 6 (a hepatitis C virus carrier) died on post-treatment day 47 due to hepatic failure. For the other six patients, at a median follow-up of 14.5 months (range, 10-20 months), the burden of VA decreased significantly after treatment (Table 1). Three months before treatment, there were 88 episodes of ventricular tachycardia and 23 shock therapies. After blanking period (6 weeks after SBRT), there were 22 episodes of VTs during the next 91 patient-months. Only 1 patient received one shock therapy. Patient 1 with ICM had 34 episodes of VT and 5 ICD shocks three months before SBRT. Recurrent VA developed on post-treatment day 245. ICD interrogation showed 8 episodes of VTs which all terminated after one ATP treatment, and a PVC induced ventricular fibrillation (VF) with successful shock therapy, which was not the previous clinical VT. LVEF was decreased after VT recurrence (45% to 33%). Patient 2 with DCM had 14 episodes of VT and 3 ICD shocks three months before SBRT. VT recurred on post-treatment day 366 with presentation of chest pain. Standard ECG showed slow VT with a heart rate of 96bpm, which was also not the previous clinical VT. No ICD therapy was delivered to this patient since the VT cycle length was out of the VT zones of ICD programming. Patient 4 with DCM had a significant clinical response. Before treatment, 6980 episodes of non-sustained VTs 3 months before treatment were recorded by ICD; after treatment, only 391 episodes of non-sustained VT was recorded and every episode was less than 1 second. Post-treatment LVEF improved 6 months after treatment (30% to 68%). Patient 5 with ARVC had 6 episodes of VT, all needed shock therapy, three months before SBRT. Amiodarone dosage was reduced right after SBRT. Recurrent VTs occurred on post-treatment day 105. All the episodes were less than 10 seconds and no ICD shock was required. No more VTs were detected 8 months after SBRT. Patient 7 with DCM also had a significant clinical response. Three months before SBRT, he had 31 episodes of VT and 8 ICD shocks. No more VT was recorded by ICD after treatment. For the patient with frequent PVCs (patient 3), the baseline PVC burden was 35%, and the burden remained similar (35%) 6 weeks after SBRT and increased to 44% in the 4th month, but decreased to 9% in the 7th and 0.2% in the 12th month during follow-up.

Imaging comparison

Four patients (patient 3, 4, 5 and 7) received pre- and post-treatment CMR. The others didn't receive CMR study since their ICDs were not MRI compatible. For patients who cannot received MRI study, pre- and post-treatment dual energy CT was arranged. Patient 6 didn't have post-treatment imaging study due to mortality. The median time of post-treatment imaging was 7 months after SBRT (range 3-12 months). Five out of six patients showed increased scar areas in the post-treatment images compared with the pre-treatment ones (one example was demonstrated in figure 3). Both CMR and dual-energy CT demonstrated the effects of SBRT but dual-energy CT seemed to be less sensitive in detecting the effects. The SBRT effects of the other two patients, patient 4 and 5 were less obvious. In patient 4, the DCM patient, pre-treatment CMR and dual-energy CT didn't identify obvious scar. The contoured target volume was created by the electrophysiologist according to the 3D electroanatomical mapping. Only 4.6cc of PTV and 14.4cc GTV were given, and the post-treatment images didn't identify the scar either. In patient 5, the ARVC patient, pre-treatment CMR showed diffuse delayed enhancement at RVOT, free wall and inferior of RV myocardium, and patchy delayed enhancement over RV basal septum. According to previous 3D electroanatomical mapping, SBRT target was targeted to the RV basal septum. After treatment, no scar enlargement was noted. All pre- and post-treatment images were shown in Supplement 2.

Adverse events

No immediate complications occurred during the treatment or hospitalization. All patients were discharged the next day after treatment. No ICD dysfunction including battery longevity, lead thresholds, or lead impedances was observed after treatment. Grade 1 pericardial effusion was noticed in patient 2 around 6 months after SBRT. Grade 5 hepatic failure developed in patient 6, which was unlikely caused by the radiation therapy.

Discussion

Chronic therapy of patients with sustained VA included ICD, antiarrhythmic drugs, catheter ablation, and/or surgery. For patients with recurrent VA refractory to antiarrhythmic medication therapy, current guideline recommended radiofrequency catheter ablation.

The VISTA randomized multicenter trial showed that an extensive substrate-based ablation approach is superior to ablation targeting only clinical and stable VTs in patients with ICM presenting with tolerated VTs [8]. Systematic review and meta-analysis of non-randomized trials suggested significantly lower rates of recurrent VT following a combined endocardial/epicardial ablation compared with endocardial ablation alone [9]. Therefore, comprehensive and extensive substrate elimination is the best catheter ablation strategy for recurrent VT. However, there are some potential etiologies that might lead to failure of catheter ablation, for example, inability to accurately identify VT substrate, extensive substrate not amenable for ablation,

or inaccessible VT substrates, such as mid-myocardial, LV summit or intraseptal area. In patients who failed with catheter ablation, SBRT is an emerging treatment under investigation.

To our knowledge, this is first reported case series in Asia-Pacific which included 7 patients with 5 different VA etiologies. This case series is also the first one to compare pre-treatment and post-treatment imaging.

The first reported case series of five patients who received noninvasive cardiac radiation for VT have suggested the efficacy of cardiac radioablation for VT using SBRT [6]. The same group published the first prospective phase I/II trial of electrophysiology-guided noninvasive cardiac radioablation for VT (ENCORE VT study) of 19 patients, which showed that the procedure was safe and well-tolerated and markedly reduced VT burden [7]. These 2 studies used noninvasive electrocardiographic imaging to map the VT circuit. In our study, every patient received 3D electroanatomic mapping either by activation mapping during VTs or voltage mapping for hemodynamically unstable VTs or polymorphic VTs. To identify the substrates accurately, in additional to 3D electroanatomic mapping, every patient received pre-treatment contrast enhanced dual energy CT and DE-MRI (unless contraindicated) to identify the scar areas in order to delineate the target region precisely. The fundamental concept of this approach is to eliminate the potential arrhythmogenic substrates thoroughly rather than just the exit site and adjacent areas of clinical VTs which might be far from the critical isthmus.

Regarding the SBRT, compared with the published studies, our report is different in several aspects. First, we used simultaneous integrated boost strategy to deliver 25 Gy to GTV and 20 Gy to PTV in a single fraction, while other studies prescribed a single dose of 25 Gy to the PTV [6, 7, 10]. Our clinical results demonstrated that this strategy in treating refractory VT is as effective as previous studies. Second, we used linear accelerator Varian TrueBeam System with flattening filter-free photon beam, which is similar to ENCORE VT study [7] (16% treated by Varian TrueBeam and 84% by Varian Edge) but different from Neuwirth study [11] in which the robotic treatment system CyberKnife was used. According to published reports [7, 11, 13], CyberKnife system however contributed to smaller planning target volume (22.2cc in Neuwirth CyberKnife study vs. 98.9cc in ENCORE VT study vs. 52.0cc in our study) and lesser Gr3+ late toxicities (10% late cardiac late toxicity in Neuwirth CyberKnife study vs. 39% late cardiac or pulmonary toxicity in ENCORE VT study) and caused longer treatment time (68.0 min in Neuwirth CyberKnife study vs 15.3 min in ENCORE VT study vs 12.7 in our study). As yet, linear accelerator−based radiotherapy system is currently the main strategy for treating refractory VT in our facility.

In all previously reported case series [6, 7, 10-12] VT episodes decreased significantly after 6-week blanking period. In our study, VT episodes decreased 91%, and ICD shock therapy decreased 86%. All patients responded to SBRT. Besides, all VT patients showed acute effect of SBRT with no recurrence in blanking period. In previous reports, three studies [6, 7, 10] with linear accelerator Varian TrueBeam System revealed better efficacy on VT reduction than the other two studies [11, 12] with CyberKnife system. In TrueBeam system group, 94% of patients responded to SBRT in ENCORE VT study [7]; 87.5% of patients responded to SBRT in Lloyd study [10]. In CyberKnife system group, 80% of patients responded to SBRT and 20% of patients showed delayed effects in Neuwirth study [11]; all patients (5 patients) experienced clinically significant mid- to late-term VA recurrence in Gianni study [12]. Delivering ablative dose to heart by TrueBeam system seems more effective than by Cyberknife system. However, dosimetry study comparing the two systems and quality assurance study approving consistency between delivered doses and planned doses should be carried out, in order to reasoning a suggestion to use TrueBeam system as the major delivery strategy.

In ENCORE VT study, 2 patients with PVC-related cardiomyopathy were enrolled and 1 showed an increased PVC burden at 6-week and decreased in the 3-month during follow-up. In our patient 3, the PVC burden was stationary at 6-week, increased in the 4th month and decreased in the 7th and 12th month. The effect of SBRT to PVC was more delayed than the previous study. Since the response on PVC burden to radioablation was less reported, it needs further study to clarify the time course of response after SBRT.

Previous studies have demonstrated the radiobiological mechanisms of SBRT. Recent evidence indicates that SBRT causes direct cell death due to DNA damages and indirect cell death through vascular damage [13]. Garcia-Barros et al. [14] reported that irradiation of tumors with doses higher than 8-10 Gy rapidly caused ceramide-mediated apoptotic death in endothelial cells, thereby leading to vascular occlusion and tumor cell death. Cuculich et al. [6] demonstrated the first postmortem cardiac samples 3 weeks after SBRT, which showed prominent ectatic blood vessels at the interface of dense scar and viable myocardium (scar border zone). This study is the first report to compare pre- and post-SBRT images. Images of most of the patients showed denser or more extensive scar after SBRT as expected. In patient 4, both pre-and post-treatment images didn't identify obvious scar. This patient received SBRT with only 4.6cc of PTV and 14.4cc GTV. Although CMR theoretically could detect the myocardium scar as little as 1 cm^3, it was probable that the biological effects prompted by exposure to radiation cannot be precisely predicted, and the scar might be too small to be detected by CMR in this patient. In patient 5, post-treatment scar at RV basal septum was stationary without enlargement. The radiation effects may be correlated with the nature of exposure and their extents, and also the microenvironment of the target tissues. Whether the septum (thicker myocardium) is more radioresistant and needs higher doses is unknown.

No severe acute adverse event was reported by previous studies [6, 7, 10-12]. Radiation pneumonitis and pericardial effusions were most common reported clinical relevant adverse events. In our study, no radiation pneumonitis was noted by post-treatment chest X ray and CT. In patient 2, the post treatment CT 6 months after SBRT revealed Grade 1 pericardial effusion, which was absent in the previous follow-up transthoracic echocardiography. The pericardial effusion persisted in the latest transthoracic echocardiography follow-up.

Patient 6 in this study died of hepatic failure. He was a HCV carrier without previous follow up history. His baseline liver function was normal. One month after SBRT, he came to ER due to progressive jaundice and dyspnea. HCV viral load was 205000 IU/mL. GTV of this patient was 35.5 cc and PTV was 83.4 cc. The liver mean dose was 41.5 cGy. Radiation related hepatic failure was not likely. Heart failure symptoms and slow VT (in blanking

period) were also presented at ER. Heart failure with comorbid hepatitis C was proposed to be related to his hepatic failure. In the 2 largest reports [7, 10], most of the mortality cases were related to heart failure, and none was radiation related.

In our study, the mean age was young (mean 55 years, range 23-80 years). We enrolled young patients because that patients receiving SBRT reported overall good quality of life in general, associated with better global health status and lower indirect costs of productivity loss [15, 16], which are much more important in young rather than old patients. In children and young adults, SBRT prolonged overall survival without significant toxicities [17]. The maturation of SBRT contributed to decades of technical and clinical advancement, including managing cardiac and respiratory motions, defining safe radiation dosing levels for critical organs, and setting quality assurance standards globally. Before large-scale long-term follow-up data emerges, we recommended that SBRT could be given to patients only with life-threatening or severely symptomatic VAs refractory to medications and traditional ablation procedures. As long as the SBRT organs at risks (OARs) constraints by the report of AAPM Task Group 101 were cautiously satisfied [18], we could minimize long-term complications in patients undergoing SBRT.

Limitation

This is a small, single-center, retrospective analysis with limited follow-up time. The long-term efficacy and safety of this treatment is still not known.

Conclusion

In conclusion, in patients with medication and catheter ablation refractory VT of variable etiologies, SBRT for cardiac radioablation was associated with a marked reduction in the burden of VA.

Declarations

Author contributions

L-YL is responsible for the overall content as a guarantor, contributed to the conception and design of the work, acquisition and interpretation of the data and critical revision of the manuscript for important intellectual content. L-TH and JL-YC contributed to the conception and design of the work, analysis and interpretation of data for the work, drafting of the manuscript and revising the manuscript. H-MC, Y-CH, M-YS, S-HK, Y-CC, J-LL and W-JC contributed to the conception or design of the work and the acquisition of data for the work. W-JL contributed to the conception and design of the work, interpretation of the data and critical revision of the manuscript for important intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

Compliance with ethical standards

Competing interests

The authors declare that they have no competing interests

Ethical approval

The study was approved by the Institutional Review Board of the National Taiwan University Hospital Ethics Committee.

Informed consent

The study was approved by the institutional review board of the National Taiwan University Hospital Ethics Committee. All research was performed in accordance with relevant guidelines/regulations and inform consent was obtained from all participants and/or their legal guardians.

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Tables

Table 1. Patients clinical characteristics and treatment details							
Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Clinical characteristics							
Age (years old)	58	56	49	47	23	72	80
Sex	Female	Male	Male	Male	Male	Male	Male
Indication	Ischemic cardiomyopathy	Dilated cardiomyopathy	Frequent PVCs	Dilated cardiomyopathy	Arrhythmogenic right ventricular cardiomyopathy	Hypertrophic cardiomyopathy	Dilated cardiomyopathy
LVEF before treatment (%)	45	20	66	30	69	42	43
Anti-arrhythmic drugs	Amiodarone	BB+Amiodarone	BB+Mexiletin	BB+Amiodarone	BB+Amiodarone	BB+Amiodarone	BB+Amiodarone
Amiodarone dosage (mg/d)	300	400	0	100	400	400	200
No. of catheter ablation	1	0	2	1	4	2	2
No. of episodes of VT 3 months before treatment	34	14	PVC 35%	3	6	3	31
No. of ICD shocks	5	3	-	1	6	2	8
Treatment							
Target region	Infero-posterior wall	Anterior wall	Basal antero-septum	RVOT	RV basal septum	Apex	Antero- to infero-septum
Volume (cc)							
GTV	15.4	40.9	9.4	4.6	11.5	35.3	33.5
PTV	52.1	80.5	23.9	14.4	34.4	83.4	92.6
Time (min)	12.7	17.3	14.4	9.2	10.9	12.5	12.5
No. of episodes of VT after treatment	9	1	PVC 0.2%	0	13	5	0
No. of ICD shocks after treatment	1	0	-	0	0	0	0
Time to recurrence (days)	245	366	-	0	105		
LVEF after treatment (%)	33	22	72	68	65	42	33

PVC=premature ventricular complex; BB=beta-blocker; LVEF= left ventricular ejection fraction; VT=ventricular tachycardia; ICD=implantable cardioverter-defibrillator; RVOT=right ventricular outflow tract; GTV= gross target volume; PTV= planning target volume

Table 2. Stereotactic body radiotherapy treatment details

Median target volume, cc (range)	
Gross target volume	15.4 (4.6−40.9)
Planning target volume	52.0 (14.4−92.6)
SBRT energy, n (%)	
6MV FFF	2 (28.5)
10 MV FFF	5 (71.5)
SBRT employed partial arcs, number (range)	
Total arcs	10 (9−13)
Coplanar arcs	6 (5−9)
Non-coplanar arcs	4 (4−4)
Median SBRT monitor units, MU (range)	8898 (6431−12092)
Median SBRT treatment time, min (range)	12.7 (9.2−17.3)

SBRT = Stereotactic body radiotherapy; FFF = flattening filter-free photon beam

Figures

3D electroanatomic mapping

DE-MRI/dual energy CT for identifying substrates

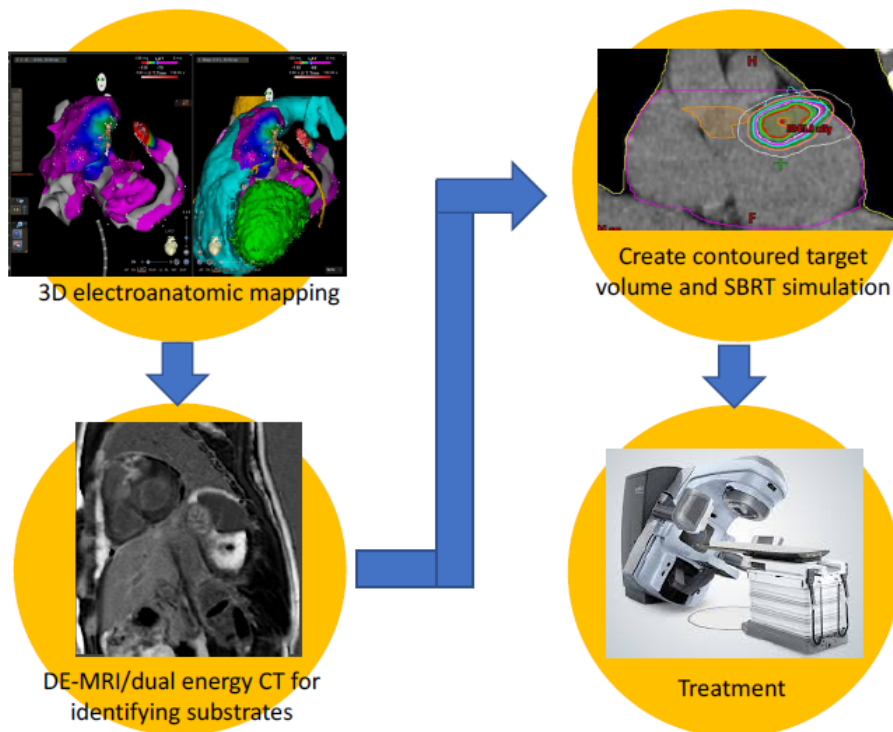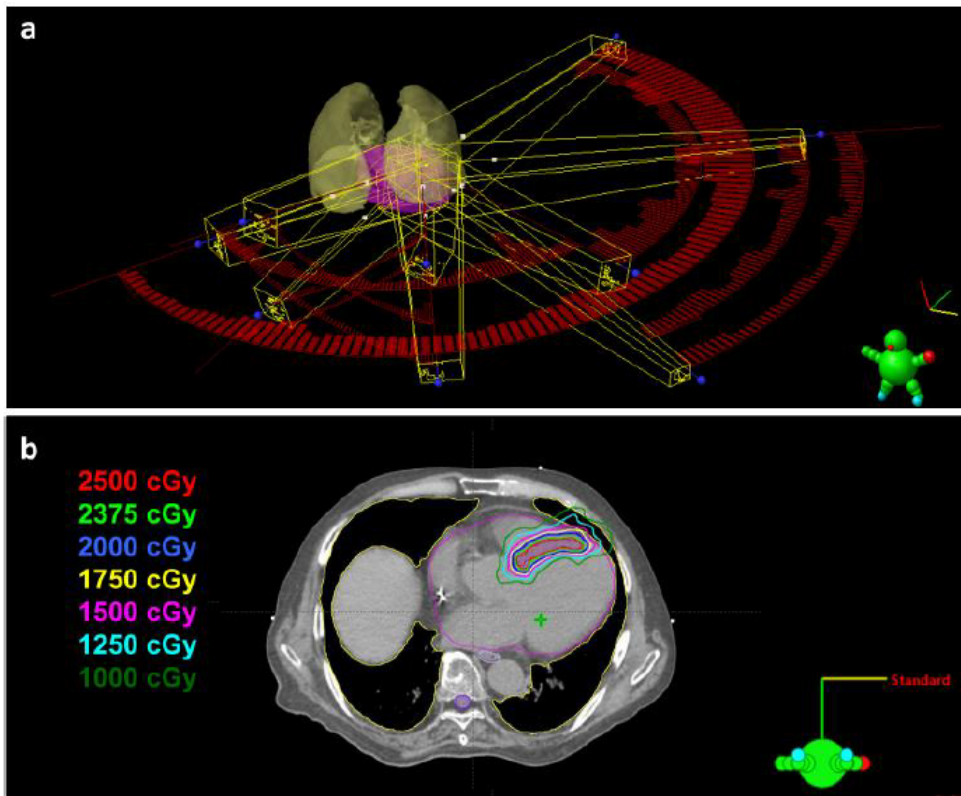Create contoured target volume and SBRT simulation

Treatment

Figure 1

Workflow for stereotactic body radiation therapy of cardiac radioablation

Figure 2

Noninvasive cardiac radioablation beam arrangement and isodose distributions Patient 7 underwent noninvasive cardiac radioablation via 6 MV flattening filter-free photon beam and stereotactic volumetric modulated arc radiotherapy technique. A total of 25 Gy was prescribed to gross target volume (GTV) and 20 Gy to planning target volume (PTV) in a single fraction by simultaneous integrated boost strategy. Shown are (a) beam arrangement in noninvasive cardiac radioablation plan, and (b) dose distributions on the axial view. The color-washed areas indicate the following: red, the GTV; and blue, the PTV. The orange, red, light green, blue, yellow, pink, indigo, and dark green lines represent isodose curves of 3000, 2500, 2375, 2000, 1750, 1500, 1250, and 1000 Gy, respectively.
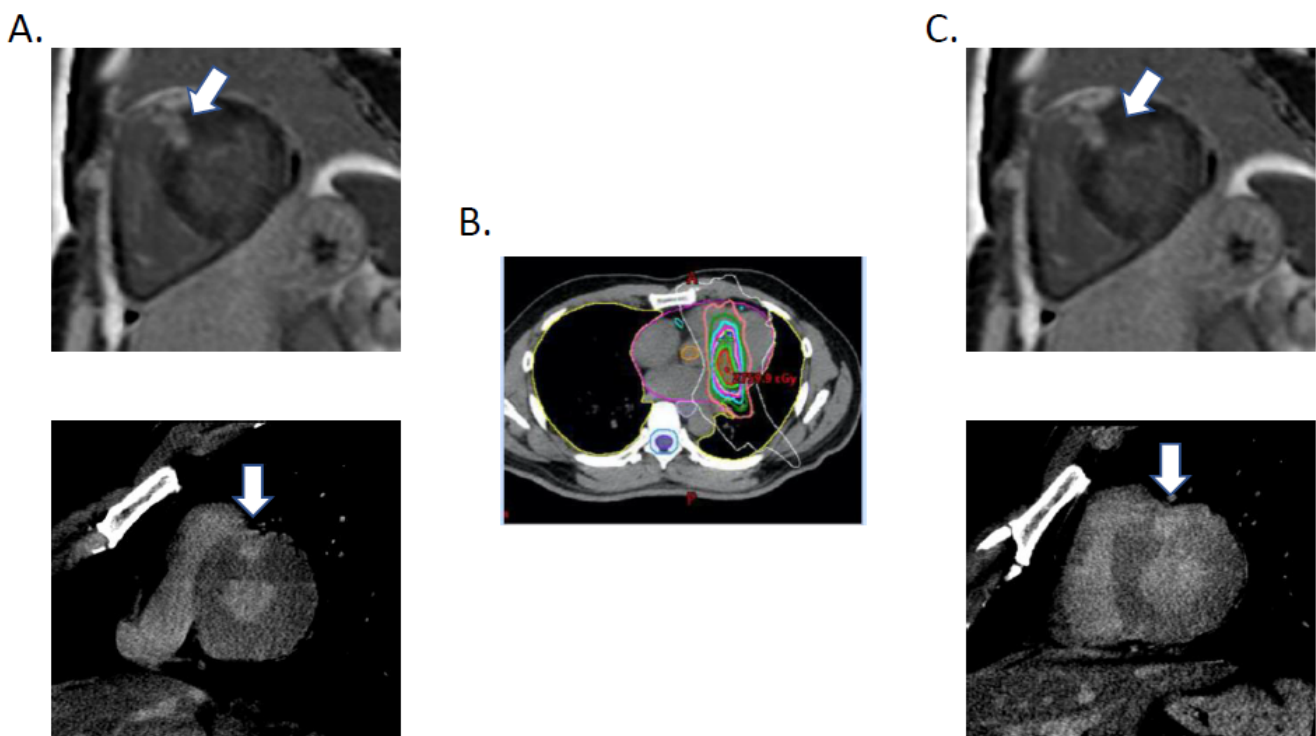
Figure 3

Pre- and post- treatment imaging comparison A.Pre-treatment CMR (upper part) and dual-energy CT (lower part) of patient 3 showed delayed hyperenhancement of basal antero-septum (white arrow). B.SBRT contour of patient 3. C.Post-treatment CMR (upper part) and dual-energy CT (lower part) of patient 3 showed mildly increased delayed hyperenhancement of basal antero-septum (white arrow).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- S1.pdf
- S2.pdf