


Linac-based STereotactic Arrhythmia Radioablation (STAR) of ventricular tachycardia: Case report and literature review

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Abstract

Linac-based STereotactic Arrhythmia Radioablation (STAR) is a safety and effective approach for selected patients with ventricular arrhythmias.

KEYWORDS

electrical storm - Italy, Stereotactic arrhythmia radioablation

1 | INTRODUCTION

We reported the first patient treated with STereotactic Arrhythmia Radioablation (STAR) in Italy. A 67-year-old man with electrical storm and left ventricular thrombosis. He underwent STAR with a dose of 25 Gy in one fraction (treatment plan delivered in 6 minutes). ICD interventions stopped after four months from treatment.

Cardiovascular diseases are still the first cause of mortality, despite the efficacy of new treatment and therapeutic advances for improving its prognosis. Cardiac arrhythmias are a major health burden,^{1,2} and especially ventricular arrhythmias are associated with poor prognosis and reduced quality of life. Therapeutic options include moderately effective

medication, antitachycardia pacing or shock by an implantable cardioverted defibrillator (ICD) when needed and later catheter-based ablation of arrhythmogenic substrates in the heart.

Catheter ablation aims to eliminate the electrical cells that cause cardiac arrhythmias. To date, ablative techniques use either radiofrequency (RF) energy or cryoablation. In both cases, there is tissue necrosis and consequently the inactivation of the substrate underlying arrhythmia.³

Several patients, due to their cardiac history and surgical interventions or both mitral and aortic mechanical valves or clots formations in left ventricle, could not be underwent to catheter ablation. Therefore, noninvasive therapeutic alternatives are warranted. STereotactic Arrhythmia Radioablation (STAR) with precise high dose of radiation to a well-defined

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targets potentially guided by previous cardiac diagnostic tools was used for treated these patients.¹

STAR is an advanced form of radiation therapy that delivers noninvasive, image-guided, precise high dose of radiation to targets reducing dose exposure to adjacent normal tissue and minimizing the treatment toxicity. Unlike catheter-based ablation, which utilizes either RF energy to heat tissue or freezing (cryoablation) to injure tissues, radiotherapy utilizes high dose of radiation to ablate the target. From a radiobiological point of view, the higher dose of radiation (STAR) may theoretically produce greater biological cell kill respect conventional radiotherapy. Its action mechanism is partly unknown. The tissue damage is probably a multifactorial result, due in part to the double-strand breaks in the DNA, which it leads to apoptosis, but also to vascular damage and consequent ischemic cell death.⁴

To date, there are still few studies conducted on human population.⁵⁻¹² Considering a so restricted number of treated patients, the validation of the efficacy and safety of this treatment approach still needs confirmation on a large scale, before it can be considered a standard therapeutic option in patients with cardiac arrhythmias. To date, in the STAR treatment experiences, patients were treated with a dose of 25Gy delivered in a single fraction.

Recent technological advances, especially in Linac-based stereotactic radiotherapy including Volumetric arc therapy (VMAT) and Flattening Filter Free (FFF),¹³⁻¹⁶ may enable faster and more conformal STAR treatment. Here, the first patient treated in Italy with STAR was reported.

2 | MATERIALS AND METHODS

A 67-year-old man with ischemic cardiomyopathy and low ejection fraction (25%) developed an electrical storm (44

ICD interventions in 2 months) and was evaluated by our Cardiologist Team on September 2019. More than 20 000 premature ventricular contractions (PVC)/day were recorded during therapy with amiodarone 200mg once a day and metoprolol 100mg twice a day. Catheter ablation was hampered due to left ventricular apical aneurism with thrombosis. The cardiac surgeon considered the intervention not feasible due to excessive risk. Thus, patient was enrolled for a STAR. Premature ventricular contraction morphology on 12-lead ECG was analyzed to localize the area of interest into the left ventricle myocardium (Figure 1). Twelve-lead ECG of ventricular tachycardia (VT) morphology was not available.

In order to determine the target myocardial tissue and treatment results, a merge study including PVC morphology, cardiac-gated cardiac tomography (CT), myocardial 18F-Fluorodeoxyglucose positron emission tomography (18F-FDG PET-CT) and 99mTc-Sestamibi Gated single-photon emission computed tomography (SPET-CT) was performed before the treatment. PVC morphology on 12-lead ECG was compatible with an origin from the interventricular septum (Figure 1) and, furthermore, 18F-FDG PET-CT and 99mTc-Sestamibi Gated SPET-CT were used to identify vital myocardium in that area. After these analyses, the final target area was defined on the interventricular septum (Figure 2).

For radiotherapy (RT) planning purposes, a 4-dimensional computed tomography (4-DCT) scan (2 mm slice thickness) was obtained with patients in the supine position using a personalized immobilization device. 4-DCT scan was used to the compensation of cardiac and respiratory target motion.

The diagnostic images (Cardio-CT, 18F-FDG PET-CT and 99mTc-Sestamibi Gated SPET-CT) were exported to the Eclipse® treatment planning system (Varian Medical System), and fused with the treatment planning CT. The final target volume was defined by the radiation oncologists in collaboration with electrophysiologists and radiologists. Organs

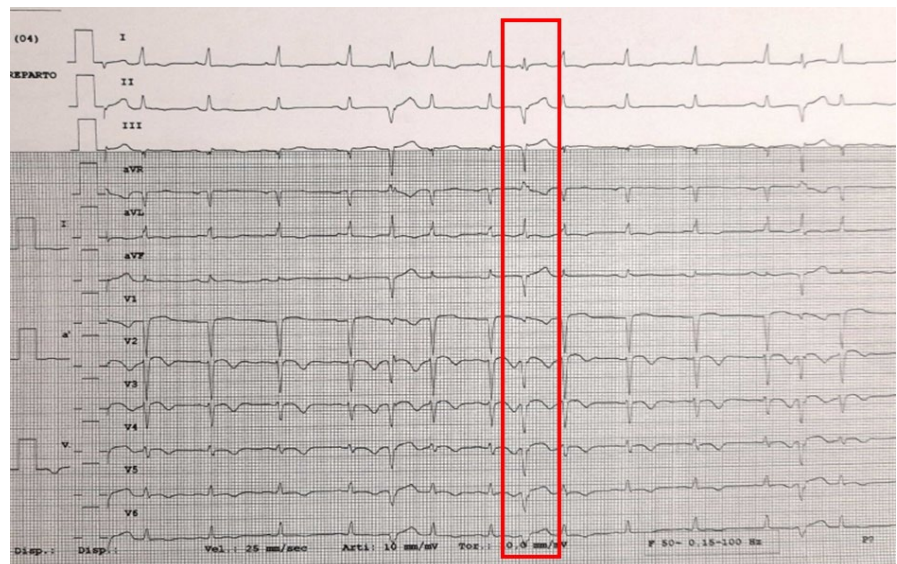


FIGURE 1 12-lead ECG showing ventricular ectopy

at risk, including the lung, heart, left coronary, esophagus, spine, and ICD, were also delineated.

A dose of 25 Gy in one fraction, optimized to have a prescription isodose line of 75%, was prescribed to the planning target volume (PTV).¹⁷ Treatment plan was generated on Varian TrueBeam™ v. 2.7, and the treatment time was only of 6 minutes (Figure 2).

3 | RESULTS

Patient was treated on 6 September 2019. IGRT (image-guided radiotherapy) with Cone Beam CT and SGRT (surface-guided radiotherapy) with Align-RT (Vision RT) were used to reduce set-up error and to monitoring patients during fraction. The treatment plan was delivered in 6 minutes.

After 3 months from radioablation, no acute side effects were registered. The patients stopped amiodarone assumption at 3 months after procedure.

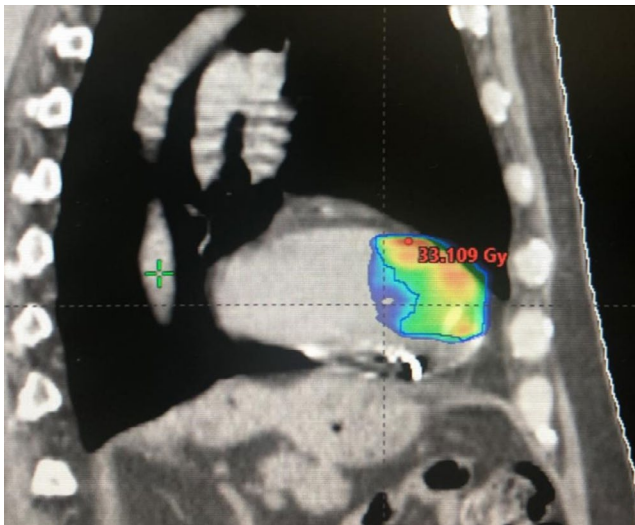


FIGURE 2 Treatment planning

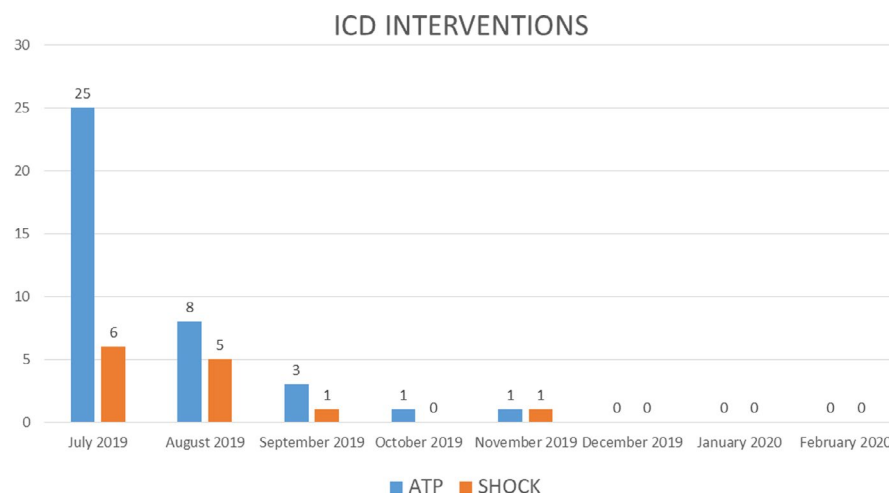


FIGURE 3 ICD interventions

At 1 month, the intracardiac defibrillator did not record VTs. The VEs decreased from 24000/24h to 123/24h. The patient had 2 sustained VT at second month from procedure, successfully interrupted by DC shock. At third month from procedure, a VT was interrupted by overdrive pacing. All these postprocedure VTs had a different cycle length when compared with the preprocedure VT.

After fourth months, the patient did not experience other ICD interventions (Figure 3). At nuclear medicine imaging, performed after six months from procedure, 18F-FDG PET-CT showed a small area of myocardial necrosis region in the site of STAR treatment and 99mTc-Sestamibi Gated SPET-CT, performed with same parameters before and after treatment, an objective improvement of kinetics and left ventricle ejection fraction (40%). After 6 months from STAR, no late side effects were registered.

4 | DISCUSSION

For cardiac arrhythmias, which are associated with poor prognosis and quality of life, therapeutic options include catheter-based ablation of arrhythmogenic substrates. Due to several patients' issues, catheter-based ablation approach could not be proposed. Therefore, noninvasive therapeutic alternatives, including STAR, are warranted.¹⁸

Preclinical and early clinical data suggest that STAR with a single dose of 25Gy could be an efficacy and safe treatment for these patients. Due to the technological improvements in Linac-based stereotactic treatments, including VMAT, IGRT, and FFF,^{19,20} the possibility of Linac-based STAR will increase in the course of the next future.

Based on the latter considerations, we reported the first patient treated with STAR in Italy. Linac-based STAR treatment plan was clinically acceptable and efficient, showing a better target coverage, sparing critical structure with a delivered

time of 6 minutes. For more precise therapy, a CBCT was performed before treatment to reduce set-up errors, while to reduce intrafraction errors SGRT was used.

To date, there are still few studies conducted on human population.^{5-7,21} In particular, these studies reported that this new strategy was associated to a low procedure risk, a reduced procedure time and a significant reduction of ventricular arrhythmias during follow-up. In several cases, cyber knife technology was used to delivered the STAR, but the here presented case with Linac-based technology showed the reduction of treatment time (6 minus vs until 70 minutes with CK); safety and efficacy of cardiac ablation for VT. In fact, in terms of safety, patient received the high dose without acute side effect registered during the first 30 days from STAR and late effects after 6 months from treatment.

In terms of clinical results, the first patients treated with STAR reported a better clinical outcome in terms of ICD interventions, ejection fraction, and drug administration. Moreover, this is the first report about use of 18F-FDG PET-CT data to plan and evaluate STAR treatment for ventricular arrhythmias.

Respect to catheter ablation, in which the reduction/absence of ventricular ectopies and VT was reported after few days from procedure, the consideration of time of the clinical results should be crucial for patients enrolled for STAR.

On the other hand, the absence of acute side effects and risk procedure was very interesting for selected patients who could be treated directly with STAR.

5 | CONCLUSIONS

Linac-based STAR is a safety and effective approach for selected patients with VT. Moreover, considering a so restricted number of treated patients, the validation of this treatment approach still needs confirmation on a large scale, before it can be considered a standard therapeutic option in patients with cardiac arrhythmias.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Fiorentino Alba, Di Monaco Antonio, Surgo Alessia, and Grimaldi Massimo: conceptualized and designed the study, and analyzed and interpreted the data. Vitulano Nicola, Gregucci Fabiana, Carbonara Roberta, Quadrini Federico, and Bonaparte Ilaria: acquired the data. Ludovico Elena: acquired the data, analyzed and interpreted the data. Rubini Giuseppe: analyzed and interpreted the data. All the authors

were involved in drafting the manuscript or revising it critically for important intellectual content; gave final approval of the version to be published; participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed 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.

ETHICAL CONSIDERATIONS

The patient signed the informed consent before the study.

DATA AVAILABILITY STATEMENT

All main data are reported in the manuscript.

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