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

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Abstract

The EU Horizon 2020 Framework-funded standardized Treatment Platform for Stereotactic Therapy Of Re-entrant tachycardia by a Multidisciplinary (STOPSTORM) consortium has been established as a large research network for investigating STereotactic Arrhythmia Radioablation (STAR) for ventricular tachycardia (VT). The aim is to provide a pooled treatment database to evaluate patterns of practice and outcomes of STAR and finally to harmonize STAR within Europe. The consortium comprises 31 clinical and research institutions. The project is divided into nine work packages (WPs): (i) observational cohort; (ii) standardization and harmonization of target delineation; (iii) harmonized prospective cohort; (iv) quality assurance (QA); (v) analysis and evaluation; (vi, ix) ethics and regulations; and (vii, viii) project coordination and dissemination. To provide a review of current clinical STAR practice in Europe, a comprehensive questionnaire was performed at project start. The STOPSTORM Institutions’ experience in VT catheter ablation (83% ≥ 20 ann.) and stereotactic body radiotherapy (59% > 200 ann.) was adequate, and 84 STAR treatments were performed until project launch, while 8/22 centres already recruited VT patients in national clinical trials. The majority currently base their target definition on mapping during VT (96%) and/or pace mapping (75%), reduced voltage areas (63%), or late ventricular potentials (75%) during sinus rhythm. The majority currently apply a single-fraction dose of 25 Gy while planning techniques and dose prescription methods vary greatly. The current clinical STAR practice in the STOPSTORM consortium highlights potential areas of optimization and harmonization for substrate mapping, target delineation, motion management, dosimetry, and QA, which will be addressed in the various WPs.

Keywords

- Stereotactic arrhythmia radioablation
- Ventricular tachycardia
- Cardiac arrhythmias
- Stereotactic body radiotherapy
- Consortium
- EU Horizon 2020

Introduction

Cardiovascular disease is one of the leading causes of death in Europe (45%).1 In patients with structural heart disease (SHD), ventricular tachycardia (VT) and ventricular fibrillation play a decisive role in sudden cardiac death, and anti-arrhythmic medication and implantable cardioverter-defibrillators (ICDs) are used to minimize the risks.2 Patients with refractory VT often undergo minimally invasive catheter ablation. However, many patients with advanced heart disease have secondary diagnoses that make invasive procedures difficult or impossible. Another limitation for performing ablation is the accessibility of the corresponding VT region. Deep intramural areas or subepicardial locations, especially in the vicinity of structures such as coronary arteriess, make effective ablation difficult so that ~20–50% of the patients develop recurrent VT after catheter ablation.3,4 For refractory VT patients without other interventional options, cardiac stereotactic body radiation therapy (SBRT), called STereotactic Arrhythmia Radioablation (STAR), is now a new promising form of therapy.5,6 Preclinical studies on STAR were already realized in 2010, while the first clinical STAR treatments for VT were accomplished as early as 20127 and 2014.8 STAR treatments are based on a complex, interdisciplinary interaction of various diagnostic procedures, as well as quality assurance (QA) methods, and require a great amount of clinical experience in the respective areas.9 A schematic presentation of the STAR process is shown in Figure 1. First, pre-planning takes place, in which an electrophysiologist defines the VT substrate. This is usually done based on electroanatomical mapping (EAM) data, which can be obtained, for example, from previous ablation procedures or dedicated non-invasive mapping systems, combined with anatomical scar imaging. The latter is performed through the assessment of echocardiography.
computed tomography (CT), magnetic resonance imaging (MRI), and/or positron emission tomography (PET)/scintigraphy imaging. The defined VT substrate must then be transferred to the contrast-enhanced cardiac CT and the planning CT for delineation of the target volume (TV) by the radiation oncologists for treatment planning. Radiotherapy treatment delivery is another challenge in the case of STAR treatments because of respiratory and cardiac motion of the target area. Furthermore, the indication for STAR treatment is often given at a short notice due to incessant VT or electrical storm.

Little is currently known about the possible acute and late radiation-related effects of STAR on the whole heart or on individual substructures. Furthermore, the exact radiobiological processes in healthy as well as diseased cardiac tissue are also not yet fully understood, though recent data suggest that STAR at lower doses (20–25 Gy) may quickly induce reprogramming of cardiac conduction, whereas radioablation at higher doses (>30 Gy) may induce scar formation. These different mechanisms further complicate accurate recommendations for the prescription dose, desired dose (inhomogeneity) and the maximum dose. Nevertheless, the first clinical data for STAR showed promising results with markedly reduced VT burden after treatment. The first prospective clinical trial by Robinson et al. (NCT 02919618) evaluated the safety and efficacy of STAR. Limited acute toxicities were observed, with a 1-year survival rate which is comparable with survival rates of similar patients and an improvement in quality of life (QoL) over time with a marked reduction in VT burden.

That said, the complexity of STAR with regard to substrate identification by EAM, target volume delineation, cardiac and respiratory motion management, and the application of high-dose single-fraction irradiation requires a high-quality standard for optimal safety and efficacy. Further multi-centre evaluation of this novel procedure is urgently needed, despite several ongoing clinical trials for STAR currently recruiting in Europe (e.g. NCT 03867747, NCT 04642963, and NCT 04066517). A novel programme investigating STAR is 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). The aim of this project is to establish a pooled STAR treatment database to evaluate efficacy and safety and to eventually harmonize STAR within Europe. Herein, in the first part of the article, we present an outline of the STOPSTORM project, followed by a review of current clinical STAR practice in Europe based on a comprehensive survey of the participating centres.

STOPSTORM consortium

The STOPSTORM consortium comprises 31 clinical and research institutes in Europe (see https://stopstorm.eu/en/consortium). These include 24 electrophysiology (EP) and 22 radiation oncology (RO) departments. Additionally, five institutes have recently joined the consortium as participating centres, and participation remains open throughout the project to all centres in the European Union that want to or are already performing STAR treatments.

The main objectives of the STOPSTORM consortium project are as follows:

1. To implement a European registry infrastructure for collecting STAR data from all patients treated non-invasively for refractory VT:
   (a) Observational data collection from patients who have been treated before the launch of the prospective validation cohort and from patients treated throughout the project who do not meet the selection and quality criteria of the prospective validation cohort.
To meet these goals, the project is divided into nine work packages (WPs) (Figure 2) in order to work on optimal solutions for certain aspects of STAR: (i) observational validation cohort; (ii) standardization of target delineation; (iii) prospective validation cohort; (iv) QA of clinical structure delineation, treatment planning, and treatment delivery; (v) analysis and evaluation; (vi) clinical ethics and regulations; (vii) dissemination, exploitation, and communication; (viii) project coordination and management; and (ix) EU project ethics requirements. Within the framework of WP 1 and 3, comprehensive patient data will be collected using an electronic data capture database (Castor EDC, Ciwit B.V., Amsterdam, The Netherlands) either retrospectively or prospectively of all STAR treatments performed by the consortium member institutions. For this purpose, regulatory and infrastructure prerequisites based on a definition of harmonized methods (STOPSTORM protocol) and parameters (electronic case report forms) are derived and used for setting up national prospective clinical trials and the STOPSTORM database. The full cohort will be split into two cohorts by the credentialing and audit committee based on a detailed treatment review audit of each case (WP 4) and based on defined selection and quality criteria (see the next section) and specified STAR quality guidelines from WP 2 and WP 4. In WP 2 (EP, target delineation) and WP 4 (RO, treatment delivery), dedicated benchmark studies and audits for target delineation based on invasive and non-invasive mapping, target transport methods from mapping to RO systems, critical structure contouring, radiation treatment planning, and radiation dose delivery (including an assessment on the impact of target motion) will be established and used as a base for early STAR quality guidelines and for accreditation of each participating centre in order to be enabled to submit data into the project database. Furthermore, WP 2 and WP 4 also contain the development of a dedicated STAR software solution to perform the standardized, centralized multi-centre multi-platform case review of the credentialing and audit committee and to facilitate a secondary independent means of treatment QA for each centre. Finally, the main implementation of harmonizing and optimizing STAR in Europe will come from the patient data evaluation of the two cohorts including dose–effect and outcome modelling in WP 5, where we hypothesize that the prospective cohort would demonstrate superior outcomes in terms of safety and efficacy. The result at the end of the project

Figure 2 Presentation of the different WPs in the STOPSTORM project and their relationships. The early retrospective data collected in WP 1 will serve as base for several other WPs in order to develop workflows and guidelines in WP 2 and sequentially WP 4 and WP 6/9 and sequentially WP 3. WPs 2 and 4 are responsible for benchmarks and audits, credentialing and centralized treatment reviews for QA, while the fully clinical data collected and analysed in WP 1, 3, and 5 are used to establish harmonized quality criteria for STAR in Europe. WP 6–9 are responsible for project management and communication and for clinical and project ethics and other regulatory needs for the prospective validation cohort (WP3) and the accompanying national clinical trials.
will be a patterns-of-care analysis and according to consensus recommendations for STAR based on the collected clinical data and its analysis. Supporting the project, WP 6–9 are responsible for project organization, clinical and project ethical guidance, patient involvement, and other regulatory needs including the establishment of national observer groups.

**STAR treatment registry**

At the time of the project start in May 2021, many patients have already been treated within the STOPSTORM consortium. Based on previous STAR treatments and ongoing clinical trials in Europe, at least 317 patients are expected to be observationally/retrospectively (n = 100) and prospectively (n = 217) entered into the STAR treatment registry over the project period. All VT patients of age ≥18 treated with STAR at the consortium member institutions will be included in the registry, which comprises retrospective cases treated before the project start (observational validation cohort) as well as prospectively treated cases ideally included in ongoing approved local/national clinical trials with their trial protocols harmonized with the STOPSTORM consortium registry protocol (protocol number BASEC-2021-01730, approved by the Medical Ethical Committee of the Canton Zurich, Switzerland, 14 December 2021). The STOPSTORM consortium registry has been designed to include as many patients as possible, while allowing for data set uniformity and sufficient analytical power to determine the safety and efficacy of STAR. For this purpose, a specific set of selection criteria for the harmonized prospective validation cohort has been set for the STOPSTORM consortium registry, while all other cases that do not meet the following criteria will be added to the observational cohort:

- SHD: ischaemic cardiomyopathy (ICM) and/or non-ischaemic cardiomyopathy (dilative cardiomyopathy/hypertrophic cardiomyopathy).
- Implantable cardioverter-defibrillator (ICD) and/or cardiac resynchronisation therapy defibrillator.
- At least one sustained monomorphic VT recurrence under optimized anti-arrhythmic medication without demonstration of acute myocardial infarction, primary electrical disease (channelopathy), reversible and treatable cause (e.g. drug-induced or intoxication) that can be adequately addressed otherwise.
- Prior ≥1 failed the catheter ablation procedure to control ≥1 sustained monomorphic VT or catheter ablation not feasible based on currently recommended mapping and ablation techniques.
- No evidence of active systemic, pulmonary, or pericardial inflammation that has required systemic treatment during the past 6 months (e.g. treatment with disease-modifying agents, corticosteroids, or immunosuppressive drugs).
- No uncontrolled cancer or chemo/immune therapy, either during the past month or planned within 1 month.
- Data acquisition performed prospectively (ideally within a prospective national clinical trial) with the
  - Target precisely defined based on the STOPSTORM quality requirements for STAR and
  - Target safely treated based on established STOPSTORM dose constraints and planning guidelines.

For the prospective cohort, all patients meeting the selection and quality criteria that signed written consent for pseudonymized data sharing in agreement with the European Union’s General Data Protection Regulation will be registered in the STOPSTORM consortium STAR treatment registry before treatment and will undergo harmonized diagnostics, pre-treatment imaging, and at least 24 months of follow-up (*Table 1*). In addition, dedicated questionnaires before and after treatment, comprehensive treatment documentation, and data collection will enrich the STOPSTORM consortium database.

**National clinical trials**

The STOPSTORM consortium comprises a STAR treatment registry but is not an actual interventional clinical trial. However, the project specifically supports national clinical trials through a dedicated STOPSTORM consortium ethics advisory board and through ethical and regulatory guidelines for STAR. Furthermore, in order to assign a STAR case to the harmonized prospective treatment registry, treatment within a clinical trial or according to a quality-assured STAR protocol with prospective registration and follow-up according to the standards of the STOPSTORM protocol is mandated. An overview of ongoing clinical trials for STAR in participating STOPSTORM centres is provided in *Table 2*.

**Quality assurance**

To enable harmonization, standardization, and optimization of STAR treatments within the STOPSTORM consortium, a comprehensive QA programme including mandatory benchmark studies (target definition and contouring of cardiac substructures, treatment planning, and delivery) and audits (treatment unit quality audits and STAR case audits) and a dedicated STAR case review software for secondary QA has been established within the project, with detailed results being reported with the progress of the project. The QA programme and a case-by-case audit of each prospective STAR case are steered by an elected credentialing and audit expert committee. Due to the heterogeneity within the STOPSTORM consortium with varying expertise in STAR treatments in various countries in Europe, we performed a comprehensive survey through a questionnaire on patterns of practice for STAR. The QA programmes regarding catheter ablation and stereotactic radiotherapy were enquired at the beginning of the project, and the results are presented and discussed in the following sections.

**Patterns of practice for STAR**

**STOPSTORM consortium survey**

For the survey on the patterns of practice of STAR, a comprehensive questionnaire was developed which was divided into three sections: cardiology/EP (18 items), RO (24 items), and medical physics (23 items). The cardiology/EP section included questions about the organization, experience, and technical equipment of the departments for catheter ablation of VT, as well as specific inquiries on STAR (patient selection, mapping, and imaging techniques). The RO section consisted of questions on organization, experience with SBRT, as well as specific inquiries on STAR (number of treatments performed, ongoing clinical trials, contouring, TV definition, treatment specifications, and delivery). Questions about radiotherapy equipment, corresponding quality controls, dosimetry, and QA were clarified in the medical physics section of the questionnaire. The full questionnaire can be found in *Supplementary material online, Appendix S1*.

The survey was developed by the management board of the consortium consisting of 17 electrophysiologists, radiation oncologists, and medical physicists using a three-staged agreement process. The survey was then sent to the representatives of each STOPSTORM partner site at the beginning of the project to be filled out by the site’s specialists. The evaluation was done using Excel and descriptive statistics (Version 2207, Microsoft 365, Microsoft Corporation, Redmond, USA).

**Cardiology/electrophysiology**

The majority of the STOPSTORM consortium cardiology/EP departments are participating in multi-centre clinical trials for VT ablation (23/24, 96%), and more than two-thirds perform 20–100 VT ablations per year (17/24, 71%), while three centres (3/24, 13%) perform annually more than 100 ablations in SHD. Also, more than two-thirds of the
departments use EAM for preprocedural imaging of the VT substrate for STAR within their institutional protocol (17/24, 71%). In contrast, non-invasive ECG-based mapping (ECGI)\[^{18,20}\] so far found little use clinically (3/24, 13%), for research purposes (2/24, 8%), and for evaluation of the STAR procedure (1/24, 4%). Nuclear imaging has little application within the consortium (PET: 8/24, 33%; single photon emission CT (SPECT): 3/24, 13%). General quality audits for ablation are rarely implemented in the participating centres (9/24, 37%). Detailed information on the RO and medical physics sections participating sites, end-to-end tests are integrated specifically for SBRT (17/22, 77%). Detailed information on the RO and medical physics sections of the questionnaire can be found in Supplementary material online, Tables S3–S6.

### Radiation oncology and medical physics

More than three-quarters of the RO departments have more than 10 years of experience in SBRT (18/22, 82%), and the majority have already participated in multi-centre clinical trials (21/22, 95%). About three-quarters of the radiotherapy systems are calibrated according to small-field dosimetry guidelines (17/22, 77%), mainly in reference to the International Atomic Energy Agency (IAEA) report 483 (11/17, 65%).\[^{27}\] Furthermore, more than half of these centres perform small-field dosimetry for absolute dose calibration (10/17, 59%). External audits and dosimetry audits are not yet performed in all departments (13/22, 59%; and 16/22, 73%, respectively). In three-quarters of participating sites, end-to-end tests are integrated specifically for SBRT (17/22, 77%). Detailed information on the RO and medical physics sections of the questionnaire can be found in Supplementary material online, Tables S3–S6.

### STAR treatment

At the start of the STOPSTORM project in May 2021, almost three-quarters of the STOPSTORM consortium members reported having already performed STAR (16/22, 73%), with a total number of 84 patients treated. For more than two-thirds of the centres performing STAR, treatments were based on a dedicated STAR protocol or on a running clinical trial (11/16, 69%). Prerequisites as indication and contraindications for STAR treatments of the STOPSTORM consortium members are shown in Table 3.

Most of the centres perform dedicated EAM procedures before STAR treatments (17/24, 71%) while almost two-thirds merge their

### Table 1 STOPSTORM.eu data collection theme

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RT, radiotherapy; M, mandatory; O, optional; ECG, electrocardiography; EP, electrophysiology; FDG, fludeoxyglucose; PET, positron emission tomography; SPECT, single photon emission computed tomography; MRI, magnetic resonance imaging; CT, computed tomography; NIPS, non-invasive programmed stimulation; ICD, implantable cardioverter-defibrillator; CTCAE, Common Terminology Criteria for Adverse Events; PROMS, patient-recorded outcome measures; EQ5D, standardized measure of health-related quality of life.
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*Harmonized with the STOPSTORM protocol.
mapping data with CT or MRI images during the procedures (15/24, 63%). Furthermore, three-quarters of the centres perform motion compensation during EAM (18/24, 75%), while only few departments implemented QA methods for these processes (5/18, 28%).

For TV definition for the VT substrate, dedicated interdisciplinary STAR teams are installed in all centres. However, the methods of TV delineation and transport from the EAM to the radiotherapy planning systems vary greatly. The basis for TV delineation is mainly mapping during VT (23/24, 96%), and also pace mapping (18/24, 75%), voltage mapping (15/24, 63%), late ventricular potentials/fragmented potentials mapping (18/24, 75%), and other methods (5/24, 21%) such as scar imaging on CT/MRI (1/5, 20%), evoked delayed potentials such as scar imaging on CT/MRI (1/5, 20%), presumable channels on CT/MRI wall-thinning maps (1/5, 20%), and isochronal late activation mapping (18/24, 75%), while all centres allow underdosage in the PTV for sparing critical structures such as the stomach or oesophagus. The most commonly used radiation technique is intensity-modulated arc therapy (16/22, 73%) with standard c-arm linear accelerators (linac) or MRI linacs, followed by robotic-based CyberKnife radiosurgery (5/22, 23%) and intensity-modulated particle therapy with protons (1/22, 5%).

### Discussion

**STOPSTORM consortium**

Reports on STAR for patients with refractory VT with limited treatment options so far demonstrated high efficacy in terms of reduction of VT burden and associated ICD interventions, with low toxicity in the majority. However, these reports are mostly small single-centre experiences with varying methods and techniques, relatively short follow-up, and the overall number of treated patients is still low in Europe and worldwide. To optimize this novel treatment modality early on despite the limited number of patients, the STOPSTORM consortium was successfully founded to create a Europe-wide pooled STAR treatment database with accompanying harmonization and QA projects.
The founding STOPSTORM consortium members represent a large variety of experienced research and treatment institutions for VT ablation, SBRT, and STAR across Europe. Most importantly, the project is open for further centres for participation. With 84 STAR treatments and several ongoing national clinical trials at project start, the STOPSTORM consortium has a solid basis for high-quality scientific analysis and clinical evaluation of STAR. Besides having established the observational and harmonized prospective treatment registry, we also present the most comprehensive review of the current patterns of STAR practice which will serve as a baseline for further harmonization and standardization of this novel treatment. In the following sections, we will discuss the current STAR practice in terms of treatment indications and technical considerations.

Patterns of STAR practice in Europe
Cardiology/electrophysiology
One of the major challenges of novel treatments is patient selection, and not surprisingly, the survey showed significant heterogeneity in terms of patient selection for STAR across Europe. Recently, a modified Delphi process from selected German and Swiss centres on recommendations for STAR practice was published.\textsuperscript{37} Comparing these recommendations (≥ 20% difference = distinct, < 15% difference = agreement), distinctly fewer STOPSTORM consortium members consider SHD to be a prerequisite for STAR (67% vs. 100% of the survey and Delphi consensus participants, respectively). This is in stark contrast to the selection criteria for the prospective STAR cohort and could potentially originate from differences in experience and availability of catheter ablation, radiation therapy, and STAR in each centre and the very early stage of the STOPSTORM project where no consensus discussions have been performed. The different opinions on STAR prerequisites are also distinct on electrical storm (50% vs. 85%), contraindications to catheter ablation (63% vs. 100%), and the presence of an ICD (71% vs. 92%), while agreement seems to be on one or more previous failed catheter ablations (92% vs. 100%), optimal anti-arrhythmic and heart failure medication (88% vs. 100%), and recurrent sustained monomorphic VT (79% vs. 85%) as a prerequisite. There is also a distinct difference between the Delphi recommendations and the STOPSTORM consortium members on contraindications for STAR, predominantly on polymorphic VT/ventricular fibrillation (42% vs. 62%) and life expectancy <6 months (54% vs. 15%). On the other hand, there was an agreement with respect to channellopathies/genetic causes (75% vs. 77%), eligibility for catheter ablation (83% vs. 77%), pregnancy (100% vs. 85%), temporary causes for VT (92% vs. 77%), and breastfeeding (83% vs. 85%). Interestingly, advanced heart failure (NYHA Class IV; 38% vs. 15%) and prior chest irradiation (13% vs. 31%) seem not to be a major contraindication in both the consensus statement and the STOPSTORM consortium (albeit differently weighted), although this was defined as an exclusion criterion for the harmonized prospective cohort.

While there are, of course, significant differences between a multidisciplinary Delphi consensus process with four discussion rounds,\textsuperscript{37} and a comprehensive survey with a single-disciplinary, uni-directional questionnaire with prior knowledge of and partly participation in the consensus recommendations, we still find some differences in preferences of the prerequisite and contraindication worthwhile highlighting. It seems that within the STOPSTORM consortium, STAR is used less in more severe or terminal patients (e.g. with limited life expectancy or advanced heart failure), while patients without an SHD may also be considered for STAR. This is interesting insomuch, as patients with severe conditions such as electrical storm do seem to benefit from STAR as the last resort bail-out procedure.\textsuperscript{38,39} Nevertheless, it should be mentioned that specific inclusion/exclusion criteria for current clinical trials are considerably stricter than the answers of the presented survey may imply.\textsuperscript{23,24,37} Further pooled treatment data analysis will hopefully shed some light on optimal patient selection.

Another challenge for STAR is the paradigm change between catheter-ablation and the specific TV definition of the underlying VT substrate for stereotactic radiotherapy treatment planning. Functional information through EAM in combination with anatomical imaging is most often used for STAR. Interestingly, non-invasive ECGI is rarely used within the STOPSTORM consortium at the time, potentially due to limited availability, despite well-documented clinical evidence from the worldwide first case series and the first clinical trial on STAR.\textsuperscript{18,20} The STOPSTORM consortium members predominantly use invasive EAM for TV definition. However, the specifics of the EAM procedures including image integration or even the EAM data format itself are very heterogeneous in clinical practice.

The more data are available, the more likely an estimation of which patients benefit most from STAR, and thus a better definition of the prerequisites and contraindications can be made. Also, more data and additional longer follow-up times will show what needs to be defined as TV. Hence, one of the major WP 2 of the STOPSTORM consortium project is designated to the harmonization of TV definition as this is currently the largest uncertainty of STAR.\textsuperscript{10,13,16,17}

Functional imaging such as PET and SPECT, which can easily be co-registered to the radiotherapy planning CT, might be helpful to characterize the VT substrate in patients with non-ICM or show derived scar maps that correlate with the voltage maps.\textsuperscript{40,41} Additionally, scar imaging derived from CT or MRI may also be helpful to further increase the TV delineation accuracy for STAR\textsuperscript{18} as additional information from functional imaging has demonstrated knowledge increase about the pathophysiology of ventricular arrhythmias and improvement in the outcomes of catheter ablation.\textsuperscript{40,41} The STOPSTORM consortium is split between the question of either targeting the whole scar substrate or solely the re-entrant VT channels if specifically identifiable. In the aforementioned consensus recommendations for STAR, functional imaging was not judged to be a minimum requirement for STAR\textsuperscript{18} and STOPSTORM consortium members rarely perform PET/SPECT. If available though, most if not all clinicians would use the data additionally alongside the EAM.

Another aspect of the STOPSTORM consortium project is the establishment of QA measures for STAR. In our survey, we found that general audits for EP and especially EAM are not common within the STOPSTORM consortium (EP: 38%, EAM: 28%), although they would enhance the development of standards and increase the treatment quality.\textsuperscript{13} Furthermore, the clinical practice guidelines of the European Society of Cardiology for ventricular arrhythmias and the prevention of sudden cardiac death do also not contain any recommendations regarding QA or audits,\textsuperscript{44} although the benefits of audits have already indeed been demonstrated in other cardiological indications\textsuperscript{45,46} or for imaging and image registration procedures by other societies.\textsuperscript{47}

Radiation oncology
One of the crucial aspects of stereotactic radiotherapy is the precise definition and delineation of gross tumour volume (GTV) and clinical tumour volume (CTV), internal target volume, and OAR on time-resolved (respiratory and cardiac motion)\textsuperscript{13,15} contrast- and non-contrast-enhanced TPI.\textsuperscript{26,48} Contrary to RO treatments, there is generally no visible tumour on the TPI (MRI, CT) for STAR except for scar visualization in a subset of patients. Thus, the GTV/CTV is mainly defined based on the invasive or non-invasive EAM within dedicated EP mapping systems whose data formats are incompatible with current radiotherapy TPSs. A standardized and quality-controlled transfer method between the two working spaces is urgently needed, which is one of the major challenges for STAR.\textsuperscript{10,12} A clinical-validated software specifically for this task currently does not exist. The EAM-to-TPS TV transfer is predominantly carried out manually via visually and anatomically assisted transfer.
of the surface-based EAM-determined TV to the cross-sectional TPI in the TPS. Unfortunately, such approach undoubtedly introduces a major potential for inaccuracies and target misses. Several approaches are already under development; however, due to the novelty of STAR, this issue remains to be resolved.29

Customized, in-house or open-source, software-aided tools for this process are hence investigated in many centres, which may have the potential to reduce user-dependent variability in the transfer and interpretation of the TV in the TPS. That said, these tools are used heterogeneously throughout the STOPSTORM consortium creating an environment where treatments would not be reproducible and difficult to compare. Two approaches have been reported so far: (i) anatomical cardiology presentation of the left ventricle in the TPS and (ii) joint EAM-TPI data presentation in tertiary software. The first is achieved by overlaying the commonly used AHA 17-segment model over the left ventricle in the TPS.28,29 The benefit is that this method is well standardized even allowing the estimation of the target region based on ECG. The downside is that the larger segments may create unnecessary large treatment volumes, despite a higher technical accuracy in terms of dose delivery with SBRT. The second approach is the specific EAM data representation in either in-house or open-source software.11,30–32 The data formats are mostly specific to the software versions used in each centre and hence limiting broad dissemination. Furthermore, the EAM and TPS data may be also not easily registered, and validation of those methods has only just begun.11 Hence, we urge to use such software with great care and only as additional QA tools. The upside, however, is the joint display of EP and RO data. A platform-independent joint EAM-TPS data display tool will be developed within the STOPSTORM consortium to enable standardized display and evaluation of TV determination for STAR treatments.

Besides TV definition, OAR delineation and dose constraints are heterogeneous within the STOPSTORM consortium. While large efforts are being made for harmonization of OAR delineation19 and dose constraints20 for SBRT, only limited information exists on cardiac substructures for STAR.21 Contouring, as well as dosimetry for OARs, is already being harmonized through ongoing consensus-oriented benchmarks. Similarly, respiratory and cardiac motion compensation strategies for STAR and their comparability will be addressed.22–24 The experience in catheter ablation, stereotactic radiotherapy, and STAR within the STOPSTORM consortium is adequate, while the survey clearly showed areas of harmonization and optimization need for complex moving targets such as in STAR. Implementing QA standards for STAR will be a key aspect of WP 4 in the consortium.

STOPSTORM provides the necessary basics to answer the open questions regarding STAR. Simply more patient data are needed in many cases, which can be collected via the STOPSTORM registry.

Limitations
The limitation of the questionnaires and their representation of European EP and RO departments is that only consortium members were surveyed without prior consensus discussion and with varying clinical expertise in catheter ablation, radiation therapy, and STAR. Thus, the results cannot be considered as a general measure of the quality and experience of all European facilities. The guidelines developed through the survey and subsequently in the STOPSTORM project over the next few years can serve as a recommendation for departments worldwide and thus bring harmonization to a larger number of users.

Conclusion
The experience in catheter ablation, stereotactic radiotherapy, and STAR within the STOPSTORM consortium is adequate, while the survey clearly showed areas of harmonization and optimization need for substrate mapping, target delineation, motion management, dosimetry, and QA, which will be addressed in the respective STOPSTORM project WPs. The STOPSTORM project is also open for new participating centres within the European Union.

Supplementary material
Supplementary material is available at Europace online.

Data availability
Detailed survey data is available upon reasonable request to the lead authors.

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References
