



## Review Article

# Stereotactic Arrhythmia Radioablation (STAR): Assessment of cardiac and respiratory heart motion in ventricular tachycardia patients - A STOPSTORM.eu consortium review



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## ABSTRACT

**Aim:** To identify the optimal Stereotactic Arrhythmia Radioablation (STAR) strategy for individual patients, cardiorespiratory motion of the target volume in combination with different treatment methodologies needs to be evaluated. However, an authoritative overview of the amount of cardiorespiratory motion in ventricular tachycardia (VT) patients is missing.

**Methods:** In this STOPSTORM consortium study, we performed a literature review to gain insight into cardiorespiratory motion of target volumes for STAR. Motion data and target volumes were extracted and summarized.

**Results:** Out of the 232 studies screened, 56 provided data on cardiorespiratory motion, of which 8 provided motion amplitudes in VT patients (n = 94) and 10 described (cardiac/cardiorepiratory) internal target volumes (ITVs) obtained in VT patients (n = 59). Average cardiac motion of target volumes was < 5 mm in all directions, with maximum values of 8.0, 5.2 and 6.5 mm in Superior-Inferior (SI), Left-Right (LR), Anterior-Posterior (AP) direction, respectively. Cardiorespiratory motion of cardiac (sub)structures showed average motion between 5–8 mm in the SI direction, whereas, LR and AP motions were comparable to the cardiac motion of the target volumes. Cardiorespiratory ITVs were on average 120–284% of the gross target volume. Healthy subjects showed average cardiorespiratory motion of 10–17 mm in SI and 2.4–7 mm in the AP direction.

**Conclusion:** This review suggests that despite growing numbers of patients being treated, detailed data on cardiorespiratory motion for STAR is still limited. Moreover, data comparison between studies is difficult due to inconsistency in parameters reported. Cardiorespiratory motion is highly patient-specific even under motion-compensation techniques. Therefore, individual motion management strategies during imaging, planning, and treatment for STAR are highly recommended.

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Ventricular tachycardia (VT) arising on structural heart disease is a re-entrant arrhythmia that can result in sudden cardiac death [1]. Initial treatment of VT consists of placement of an Implantable Cardioverter-Defibrillator (ICD) and anti-arrhythmic drugs [2]. If patients continue to suffer from VT, they qualify for an invasive radiofrequency cardiac ablation procedure that aims to homogenise the arrhythmogenic substrate. Unfortunately, these treatments fail to control the arrhythmia in 30–50% [3–5] of the patients, and alternative options are needed.

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The delivery of high-dose stereotactic radiotherapy to the arrhythmogenic substrate within the left ventricle, called STereotactic Arrhythmia Radioablation (STAR), is a new treatment option for refractory VT that has shown promising results [6–10].

To deliver STAR, the target volume, i.e., the arrhythmogenic substrate, needs to be determined using imaging modalities, such as electro-anatomical mapping (EAM), cardiac computed tomography (CT), or magnetic resonance imaging (MRI). Following common radiotherapy nomenclature, this target volume is often denoted as the clinical target volume (CTV). However, note that this CTV is typically not obtained by expanding a prior identified (gross) target volume. Subsequently, the target volume must be transferred to a treatment planning CT on which organs at risk

(OARs) are delineated. Next, the treatment plan is optimized taking into account possible uncertainties, e.g., set-up errors and treatment delivery inaccuracy, by creating margins from the predefined target volume to a Planning Target Volume (PTV). During treatment, patients must be positioned on the treatment couch in the same position as during the planning CT. However, delivering the total radiation dose (typically 20–25 Gy) in a single fraction to the target while avoiding surrounding healthy tissues can be challenging because of target and organ motion due to breathing and cardiac contraction. It is therefore important to assess and manage motion of the target (and OARs) during target volume delineation, treatment planning, and treatment delivery [11].

Cardiac and respiratory motion during treatment can be managed using, amongst others, an Internal Target Volume (ITV) approach based on time-resolved imaging, gating techniques, or tracking of the target or surrogate structures. The impact of cardiorespiratory motion of the target, in combination with different motion management options, on STAR is unknown and needs to be evaluated to deliver the best possible treatment [12]. A first step towards a better understanding of the impact and the optimization of STAR could be to model combined respiratory and cardiac motion in either physical or digital phantom studies. Such phantom studies could provide a thorough evaluation of the impact of motion because the ground-truth motion is known (prescribed) and because phantoms allow the investigation of different treatment scenarios while keeping other parameters unchanged/controlled. To set up such phantom studies, an overview of the motion amplitudes in patients is needed. However, a comprehensive overview of movement of the target area and heart under different motion management strategies in VT patients is missing.

In this Standardized Treatment and Outcome Platform for Stereotactic Therapy Of Re-entrant tachycardia by a Multidisciplinary consortium study (STOPSTORM.eu, Horizon 2020, GA No. 945119), we performed a narrative literature review to obtain an overview of cardiac and respiratory motion of STAR targets in the left ventricle and other relevant cardiac (sub)structures in combination with different motion management strategies. This overview includes both cardiac and cardiorespiratory motion amplitudes, as well as CTV, ITV, and PTV values that were used to assess the impact of motion on the treatment volume and can be used as a starting point for future studies investigating the impact of motion on STAR. Furthermore, advice will be given about reporting the amount of cardiorespiratory motion for future studies.

## Materials and methods

### Search strategy and inclusion criteria

In April 2023, a PubMed search was performed using the following search strategies: (“Tachycardia, Ventricular” [MeSH Terms] OR “Atrial Fibrillation” [MeSH Terms]) AND Humans [MeSH Terms] AND (Motion [MeSH Terms] OR Respiration [MeSH Terms]) AND (“Cardiac Imaging Techniques” [MeSH Terms] OR “Diagnostic Imaging” [MeSH Terms]). The keyword “Atrial Fibrillation” was included to have a comprehensive overview of all articles describing cardiac motion in arrhythmia patients. This “cardiology-focused” search was complemented with a “radiotherapy-focused” search: (Cardiac Radioablation) OR (Stereotactic Arrhythmia Radioablation) OR (Stereotactic Body Radiotherapy AND Ventricular Tachycardia). Search results were limited to publications after the year 2000 to ensure modern methodologies.

After removing duplicate findings, the remaining entries were screened. Articles were included if they were written in English, performed in humans, and available via the institution's library access. Furthermore, articles had to report either 1) cardiac, respi-

ratory, or cardiorespiratory motion amplitudes of the heart or cardiac (sub)structures in healthy subjects or patients suffering from atrial fibrillation (AF) or VT, or 2) Clinical, Internal, or Planning Target Volumes during STAR in VT patients. Subsequently, references within articles eligible for data extraction were examined and added if they fulfilled the inclusion criteria.

### Data extraction

The final set of articles was analysed and the following information was extracted: 1) study population and number of subjects, 2) image modality used to determine motion, 3) motion assessment method, 4) breathing type, i.e., breath-hold, abdominal compression or free-breathing, 5) organ/structure investigated, 6) motion type, i.e., cardiac motion only, respiratory motion only, or cardiac and respiratory motion combined, 7) motion amplitudes, i.e., mean, range, min/max, and direction of the motion, i.e., Superior-Inferior (SI), Left-Right (LR), Anterior-Posterior (AP), and/or 3D trajectory, 8) treatment methodology, i.e., ITV approach, tracking, or gating, and 9) CTV, ITV, PTV, and CTV/ITV to PTV margins.

### Data analysis

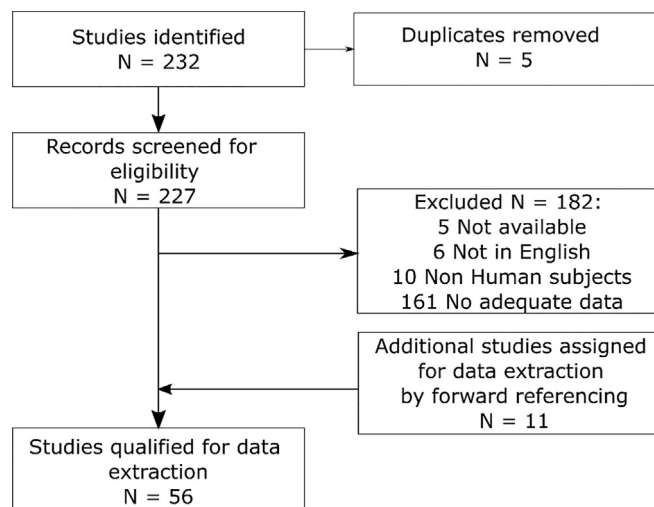
After extraction, the motion data, i.e., motion amplitudes for the SI, LR, and AP directions and 3D trajectories, were categorized with respect to study population, organ/structure investigated, motion type, and image modality and motion management technique. Missing values were calculated, whenever possible. CTV, ITV, and/or PTV volumes were sorted according to treatment methodology and data for individual patients averaged per study.

The results were compared among different categories to gain insight into cardiac and respiratory motion of cardiac (sub)structures in combination with different motion management techniques.

## Results

### Search results

A total of 232 (search 1: 64 + search 2: 168) citations were identified based on the PubMed search. After removing duplicates (N = 5), the remaining records were screened. A total of 182 articles were excluded because they did not comply with our inclusion criteria (Fig. 1). After screening the references of the remaining 45



**Fig. 1.** Decision tree showing the number of articles included and excluded in the literature review.

articles, 11 referenced articles were added, resulting in a total of 56 articles eligible for data extraction.

From the 56 articles that presented data related to movement of the target or other cardiac (sub)structures, 20 articles provided cardiac or cardiorespiratory motion amplitudes, whereas 32 articles provided target volumes, i.e., CTV, ITV, or PTV. Four articles provided both motion amplitudes and target volumes.

#### Data on motion amplitudes

From the 24 articles that provided motion amplitudes, 7 publications investigated motion within VT patients, 8 in AF patients, and 7 in healthy subjects. In addition, one article reported motion data on VT patients and healthy subjects (McLeish et al. [13]), whereas one study described motion in healthy volunteers and

AF patients (Lydiard et al. [14]). Included studies provided data obtained from a total of 94 VT patients, 186 AF patients, and 57 healthy subjects. Motion amplitudes of 16 different cardiac structures were reported, divided over the three subject groups, making the final data set sparse. Therefore, only motion of the target volume (or surrogate), left ventricle, right ventricle, left atrium, or the heart for VT patients and healthy subjects are reported in this review. A complete overview of motion data obtained for the remaining structures and AF patients can be found in the [supplementary material \(Table S1\)](#).

Techniques used to assess cardiac and/or respiratory movement are shown in [Table 1 and 2](#). The most used methodology to assess cardiac motion was cardiac-gated MRI (N = 3) in combination with breath-hold [14–16]. MRI in combination with breath-holds at different levels (N = 2) [13,17] or respiratory-binned 4D-CT during

**Table 1**  
Overview of the studies that report motion amplitudes for VT patients.

Article	Number of subjects	Structure	Motion	Motion [mm] Mean ± SD [min max]			Motion management technique (modality; motion assessment; motion management)
				SI	LR	AP	
Prusator 2021 [18]*	11	Target volume	C	4.1 ± 2.0 [1.4 8.0]	3.4 ± 1.1 [1.0 4.8]	4.3 ± 1.2 [2.6 6.5]	Cardiac (ECG)-binned CT (10 phases); Manual delineation on each phase/ Register shift during rigid registration of cardiac structures from each phase to the diastolic phase; EBH
	11		C & R	4.7 ± 2.0 [2.2 7.9]	6.9 ± 2.6 <sup>3D</sup> 3.9 ± 1.6 [1.7 6.9]	4.1 ± 0.8 [2.2 5.4]	Respiratory-binned CT (10 phases); Manual delineation on each phase/ Tracking of shift needed to register cardiac structures from each phase to the end IBH image; Abd. Comp. FB
Knutson 2019 [19]*	16	Target volume	C & R	3.0 [1.0 7.2]	sagittal plane <sup>2D</sup> 4.4 [3.0 11.3] [1.6 12.0] coronal plane <sup>2D</sup>	axial plane <sup>2D</sup> 4.7	Respiratory-Gated CT; Delineation of target on reference phase/ Manual measurements of motion by overlaying reference target on the 4D CT/ denoted as median maximum GTV to ITV distance; Abd. Comp. FB
Harms 2022 [20]	8	Target Volume	C	2.1 [0.4 4.6]	1.7 [0 5.2]	2.4 [0.5 3.9]	Respiratory-binned and ECG-gated 4D-CT; magnitudes of deformable registration vector fields; FB
Thosani 2021 [15]	1	Septum (around TV)	C	< 3.0	< 3.0	< 3.0	Cardiac MRI; Manual delineation based on EAM, and cardiac MRI; BH
	1		R	< 4.0	< 4.0	< 4.0	Respiratory-binned 4D-CT; Manual delineation based on EAM, and cardiac MRI; FB
Knybel 2021 [22]	20	ICD lead (RV septal)	C & R	5.0 ± 2.6 [3.2 7.3]	3.4 ± 1.9 [2.0 6.8]	3.1 ± 1.6 [2.1 4.9]	Synchrony Respiratory Tracking system (CyberKnife); Tracking of the ICD lead; FB
Roujol 2013 [21]	27	Left ventricle	C		10.2 ± 2.7 [5.5 16.9] <sup>3D</sup>		Electro-anatomical mapping; Cardiac and respiratory motion components were extracted from catheter location using multi-band filters and averaged over all mapping points; FB
	27		C & R	7.0 ± 1.8	3.3 ± 1.2	3.6 ± 1.2	See description above
Harms 2022 [20]	27	Left ventricle	C & R		8.8 ± 2.3 [4.3 14.8] <sup>3D,**</sup>		See description above
	8		C	2.7 [0.6 5.7]	0.8 [0.3 2.0]	1.3 [0.4 3.2]	Respiratory-binned and ECG-gated 4D-CT; magnitudes of deformable registration vector fields; FB
Harms 2022 [20]	8	Left atrium	C	3.1 [0.1 11.0]	1.1 [0 1.9]	1.3 [0.2 2.3]	Respiratory-binned and ECG-gated 4D-CT; magnitudes of deformable registration vector fields; FB
McLeish 2002 [13]	10	Heart	C & R	8.3 ± 3.9 [3.8 14.3] <sup>***</sup>	1.0 ± 0.7 [0.2 2.1] <sup>***</sup>	1.8 ± 1.2 [0.3 4.4] <sup>***</sup>	Respiratory-gated MRI (at least EBH and IBH); Manual structure segmentation in EBH/ Rigid followed by deformable registration of other phases to the EBH phase; BH at EBH and IBH
Krug 2019 [23]	1	Heart	C & R	< 10.0	< 3.0	< 3.0	ECG-triggered and Respiratory-binned CTs; Manual structure segmentation based on EAM and ECG-triggered CT; FB

\*Overlap in patient cohort; \*\*Underestimation of respiratory component due to limited temporal window; \*\*\*Absolute values; RV = Right Ventricle; Abd. Comp. = Abdominal Compression; IBH = Inspiration Breath-hold; EBH = Expiration Breath-hold; FB = Free-Breathing; C = Cardiac Motion only; C & R = Cardiorespiratory motion; <sup>2D</sup> 2D motion vector; <sup>3D</sup> 3D motion vector; SI = Superior-Inferior; LR = Left-Right; AP = Anterior-Posterior; Values calculated from data provided in the original article are denoted in italic.

**Table 2**

Overview of studies that report motion amplitudes for healthy subjects.

Structure & Article	LV Apex	Number of subjects	Motion	Motion [mm] Mean $\pm$ SD [min max]			Methods (modality; motion assessment; motion management)
				SI	LR	AP	
<b>LV Apex</b>							
Wang 1995 [17]*	10	C & R	16.0 $\pm$ 7.1	-	3.0 $\pm$ 2.8	Prospective ECG-gated MRI (diastolic phase); MRI; Manual tracking of anatomic landmarks; BH at different levels	
<b>LA</b>							
Nehrke 2001 [49]	10	C & R	15.0	-	-	2D gradient-echo MRI; Navigator pulses; FB	
Lydiard 2021 [14]	10	C	4.6 $\pm$ 1.5	4.3 $\pm$ 1.8	3.7 $\pm$ 1.4	MRI retrospective ECG-gating (25–32 phases); manual delineation on each phase/Tracking centroids; EBH	
Ipsen 2016 [16]	4	C		3.9 $\pm$ 0.6 [3.3 4.5] <sup>3D</sup>		MRI retrospective ECG-gating (10 phases); manual delineation on each phase; End-EBH	
	4	C & R	16.5 $\pm$ 8.0	3.1 $\pm$ 1.1	5.8 $\pm$ 3.5	MRI retrospective ECG-gating; Tracking isocenter shift determined by matching 2D cardiac templates created during End-EBH; FB	
Ipsen 2014 [50]	6	C & R	10.2 $\pm$ 3.0	2.0 $\pm$ 1.2	2.4 $\pm$ 1.4	Cardiac cine MRI; Tracking template shift of manually contoured structures; FB	
<b>Heart</b>							
McLeish 2002 [13]	8	C & R	16.4 $\pm$ 4.5 [11.6 23.5]**	3.8 $\pm$ 1.3 [2.1 6.1]**	7.1 $\pm$ 3.1 [2.4 11.5]**	MRI; Tracking template shift of manually contoured structures; Different levels of BH between EBH and IBH	
Wang 1995 [17]*	10	C & R	15.0	-	-	Prospective ECG-gated MRI (diastolic phase); Tracking anatomic landmarks; BH at different levels	
Akdag [51]	1	C	9.2	5.9	2.7	3D cine MRI; Segmentation using cross-correlation with a reference image	
	1	C	15.3	-	-	2D cine MRI; Segmentation using cross-correlation with a reference image	
Wang 2006 [52]	5	C & R	S:11.1 $\pm$ 6.1; I:10.1 $\pm$ 1.3	L:11.0 $\pm$ 9.3; R:14.7 $\pm$ 11.8	A:11.1 $\pm$ 3.3; P:12.9 $\pm$ 7.6	MRI (no gating); Margins along the SI, LR, and AP directions; FB	
	5	C	S:7.9 $\pm$ 2.5; I:8.4 $\pm$ 5.0	L: 6.9 $\pm$ 2.4; R:10.4 $\pm$ 7.1	A: 7.1 $\pm$ 1.3; P: 8.6 $\pm$ 2.0	Respiratory-gated MRI; Margins along the SI, LR, and AP directions; FB	
	5	-	S:5.0 $\pm$ 3.3; I:5.7 $\pm$ 2.1	L: 5.6 $\pm$ 1.1; R: 4.5 $\pm$ 2.3	A: 3.7 $\pm$ 1.2; P: 5.7 $\pm$ 1.8	Respiratory- & cardiac-gated MRI; Margins along the SI, LR, and AP directions; FB	

\*Overlap in patient cohort; \*\*Absolute values; RV = Right Ventricle; Abd. Comp. = Abdominal Compression; IBH = Inspiration Breath-hold; EBH = Expiration Breath-hold; FB = Free-Breathing; C = Cardiac Motion only; C & R = Cardiorespiratory motion; <sup>2D</sup> 2D motion vector; <sup>3D</sup> 3D motion vector; SI = Superior-Inferior; LR = Left-Right; AP = Anterior-Posterior; Values calculated from data provided in the original article are denoted in *italic*.

abdominal compression (N = 2) [18,19] were the most used methods to assess cardiorespiratory motion.

#### Motion amplitudes in VT patients

Table 1 shows the motion of cardiac (sub)structures within VT patients as a result of either cardiac contraction on its own, or in combination with respiratory motion.

Motion of the target induced by cardiac contraction was on average 2–4 mm [18,20]. For individual patients, however, Prusator et al. [18] reported values as high as 8.0 mm in the SI direction under breath-hold conditions. Although Roujol et al. [21] reported 3D cardiac motion of the left ventricle that is larger compared to the target motion reported by Prusator et al [18], i.e., 10.2  $\pm$  2.7 mm versus 6.9  $\pm$  2.6 mm, left ventricular motion reported by Harms et al. [20] was much smaller (< 3 mm).

Cardiorespiratory motion of the target under abdominal compression free-breathing conditions was on average 4–5 mm [18,19], which is slightly higher than cardiac motion of the target volume. Although this indicates that abdominal compression is also effective in reducing target motion due to breathing, both abdominal compression and breath-hold techniques might not be tolerated by all VT patients because of their poor clinical condition. Cardiorespiratory motion during free-breathing of a right ventricular septal ICD lead [22] and the left ventricle [21] in the SI direction were 5.0  $\pm$  2.6 mm and 7.0  $\pm$  1.8, respectively. Motion in the LR and AP direction were on average around 3.0–3.5 mm for both structures [21,22]. Finally, cardiorespiratory motion of the heart was larger in SI direction (up to 14.3 mm) compared to motion of cardiac substructures, whereas motion in the LR and AP directions appeared smaller [13,23].

#### Motion amplitudes in healthy subjects

Table 2 shows an overview of the methods and motion data obtained from the literature on healthy subjects. Comparison of the motion of VT patients (Table 1) and healthy subjects (Table 2) showed that average motion of the LA due to cardiac contraction seemed to be somewhat larger in healthy subjects, especially in the AP direction, i.e., 4.6, 4.3, and 3.7 mm [14] versus 3.1, 1.1, and 1.3 mm [20], in the SI, LR, and AP direction, respectively.

Left ventricular motion due to both breathing and cardiac motion in healthy subjects was approximately two times higher in the SI direction (16.0  $\pm$  7.1 mm and 15.0 mm [17] versus 7.0  $\pm$  1.8 mm [21]), whereas motion in the AP direction was similar, i.e., 3.0  $\pm$  2.8 mm [17] versus 3.6  $\pm$  1.2 mm [21] (data on LR motion was not reported). Finally, cardiorespiratory motion of the heart as a whole was also higher in healthy subjects [13] compared to VT patients [13], with average motion reaching values up to approximately two to three times higher, i.e., 16.4  $\pm$  4.5 mm versus 8.3  $\pm$  3.9 mm in the SI direction, 3.8  $\pm$  1.3 mm versus 1.0  $\pm$  0.7 mm in the LR direction, and 7.1  $\pm$  3.1 mm versus 1.8  $\pm$  1.2 mm in the AP direction.

#### Target volume

Only the combination of CTV together with ITV or PTV yields insight into cardiac or cardiorespiratory motion of the target. Therefore, only articles reporting this combination are shown in Table 3. As a consequence of these selection criteria, a number of studies were excluded from this volume analysis. This included some CyberKnife studies that did not use a CTV to ITV expansion. However, the complete overview of target volumes extracted from

**Table 3**

Overview of studies that report CTV/ITV/PTV data for STAR treatment.

Article	Number of patients	Volumes [cc] Mean (Median) [min max]			ITV-PTV Margin	Methods (ITV construction; motion management)
		CTV	ITV	PTV		
Bellec 2022 [12]	4	33 [15 78]	50 [22 110]* 71 [25 150]	120 [47 250]	3 mm	Cardiorespiratory motion obtained from cardiac-gated and respiratory-binned 4D-CT; FB
Robinson 2019 [7]	19	(25) [6 89]	(31) [18 129]	(99) [61 299]	5 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB during Abdominal Compression
Knutson 2019 [19]	16	(25) [12 55]	(30) [18 82]	(98) [66 209]	5 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB during Abdominal Compression
Krug 2019 [23]	1	8	- <sup>#</sup>	42	5 mm	Cardiorespiratory motion obtained from ECG-triggered and respiratory-binned 4D-CT; FB
Mayinger 2020 [8]	1	74 74	155 -	269 115	5 mm 2 mm AP/LR; 3 mm SI	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB CTV without additional margin; Tracking with MR-linac during respiratory-gated FB and Expiration-Breath-Hold
Widesott 2020 [31]	1	18	27	70	5 mm	Cardiac motion obtained from retrospective cardiac-gated 4D-CT + respiratory motion from multiple breath-hold CTs; Inspiration Breath-hold
Gerard 2021 [24]	2	30 [17 42]	-	85 [66 103]	3 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB
Carbucchio 2021 [25]	7	39 [14 53]	111 [54 146]	183 [88 225]	Not reported	Cardiorespiratory motion obtained from a respiratory-binned 4D-CT; FB
Levis 2022 [26]	1	26	32	89	5 mm	Cardiorespiratory motion obtained from a respiratory-binned 4D-CT; FB
Ninni 2022 [53]	17	29 [7 109]	-	63 [20 186]	3 mm	CTV without additional margin; CyberKnife ICD lead tracking during FB
Nasu 2022 [27]	1	8	-	29	5 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB
Scholz 2019 [33]	1	33	55.8	82	2 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; Mechanical ventilation
Abdel-Kafi 2020 [30]	2	25 [24 25]	-	93 [85 100]	5 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB
Huang 2022 [54]	1	2	-	4	0 mm	CTV + 2 mm; CyberKnife ICD lead tracking during FB
Chang 2023 [28]	6	20 [1 79]	-	84 [9 247]	Not reported	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB
Harms 2022 [20]	8	26 [1 82]	-	46 [9 140]	0–5 mm	CTV + manual margin; FB
Amino 2023 [32]	3	20 [8 24]	45 [30 66]	67 [50 96]	2 mm	CTV + 3 mm based on heart rate and respiratory variability; FB
Ree 2023 [29]	6	46 [15 87]	77 [41 211]	187 [93 372]	5 mm	Cardiorespiratory motion obtained from respiratory-binned 4D-CT; FB

#cardiac motion < 10 mm in SI direction & < 3 mm in all other directions; \*Cardiac ITV; Values calculated from data provided in the original article are denoted in italic. FB = Free-Breathing.

all articles (161 VT patients) can be found in the [supplementary material \(Table S2\)](#).

For the 18 articles (97 VT patients) that reported CTV in combination with ITV or PTV, most used treatment strategies were free-breathing using an ITV based on cardiorespiratory motion obtained with either respiratory-binned 4D-CT scans (N = 8) [8,24–30] or both cardiac (ECG)-gated and respiratory-binned 4D-CT scans (N = 2) [12,23].

Ten studies reported both CTV and ITV. Knutson et al. [19] reported CTV and ITV together with cardiorespiratory motion of the target. Target motion of 4.4, 4.7, and 3.0 mm in the axial, coronal, and sagittal plane, respectively, resulted in a 20% increase of CTV to ITV. Bellec et al. [12] reported the ITV as a result of cardiac motion as well as resulting from cardiorespiratory motion. Compared to the CTV, the ITV increased by 39%–75% due to cardiac contraction and by 76%–249% due to cardiac and respiratory motion combined in this study. Average increases of CTV to ITV due to cardiorespiratory motion reported in the other eight studies ranged between 20–184% [7,8,25,26,29,31–33].

## Discussion

To deliver the best possible STAR, the impact of cardiorespiratory motion of the target and surrounding structures for a specific treatment methodology needs to be evaluated. Phantom studies could provide insight into the impact of motion and facilitate the further optimization of STAR. To steer such phantoms, representative cardiac and cardiorespiratory motion patterns are needed.

Unfortunately, an overview of the cardiac and respiratory motion of the target and cardiac (sub)structures in VT patients in combination with different motion management techniques is not available, making research towards personalized STAR difficult. In this study, we conducted a literature review to create an overview of the cardiac and respiratory motion of arrhythmic regions that are targeted during STAR, as well as the motion of other cardiac (sub)structures in VT patients and healthy subjects, to generate a starting point for future studies investigating the impact of motion on STAR.



Collected motion amplitudes showed average displacement of the target due to cardiac contraction to be 2–4 mm in each direction in VT patients. Compared to cardiac motion on its own, VT patients showed larger cardiorespiratory motion of cardiac (sub)structures during free-breathing in the SI direction. Compared to motion in VT patients, the cardiorespiratory motion of cardiac (sub)structures was larger in healthy subjects in the SI direction, with average values of 10–17 mm. Motion in the LR and AP direction was more comparable to the motion in VT patients in most studies. Nevertheless, McLeish et al. [13] showed larger differences for the whole heart in all directions. However, a direct comparison of motion between healthy subjects and patients might not be trivial, as reported motion data from volunteers was acquired using MRI whereas patient motion was mostly assessed using 4D-CT.

Cardiac motion resulted in an average increase of 51% of the target volume compared to the CTV, whereas cardiac and respiratory combined motion resulted in an average increase of 115% in one study [12]. Other studies reported average increases due to combined cardiac and respiratory motion of 20 to 184%. Therefore, incorporating both cardiac and respiratory motion might be of crucial importance in the clinical treatment plan design, depending on the treatment strategy.

As becomes clear from the results, large variations in motion were seen between patients from different studies and between patients within the same study. A possible explanation for the intra-study variation in cardiac motion between patients is that most VT patients suffer from heart failure, hence, differences in anatomy, position, cardiac contraction, and resulting motion patterns are expected [22]. Fuchs et al. [34] have shown that patients with chronic heart failure present reduced rotation during contraction of the left ventricular apex and base, which manifests itself, among others, as a reduced ejection fraction. Indeed, studies performed in patients suffering from VT or AF report ejection fractions ranging from 35% [22] up to 60% [35].

Interstudy variations might be explained by differences in image modalities, motion management techniques, and motion assessment methodologies used. For example, nonrigid image registration can yield physiological results but is difficult to validate without gold standards (e.g., implanted fiducials). Rigid registration, on the other hand, might be easier and more robust to carry out, but might not yield physiological motion [36]. Cardiac motion is in the order of a few millimeters and adequate image resolution is necessary to accurately assess the motion. Moreover, cardiorespiratory motion is a complex movement pattern (including out-of-plane motion) with a fast cardiac and a slower respiratory component, and capturing it also requires adequate temporal resolution [21,37]. Many studies use respiratory-binned 4D-CTs to capture cardiorespiratory motion resulting in blurred images due to cardiac contraction [38,39], which might lead to inaccurate motion assessment. Other studies use breath-hold at different breathing levels (e.g., inspiration and expiration) to estimate the respiratory motion within a subject. However, studies have shown that (repeated) inspiration breath-holds without visual feedback can lead to patients breathing in deeper compared to normal tidal breathing resulting in an overestimation of the respiratory motion compared to free-breathing [13]. In addition, intra-breath-hold variations might result in a different position of the heart and other organs compared to normal tidal breathing due to relaxing of muscles [13,40]. Nevertheless, even with adequate spatial and temporal resolution, most techniques only provide a snapshot in time yielding motion that might not represent the motion displayed during treatment due to day-to-day variations.

Some centers track and assess (cardio)respiratory motion in real-time during treatment using, for example, the CyberKnife system. Such systems do not need a respiratory ITV, although a small margin is often used to compensate for cardiac motion. As a result,

the amount of healthy tissue being irradiated could be less compared to conventional treatment machines where an ITV-approach is used. However, these systems can often only track a surrogate structure, e.g., an ICD-lead, which may monitor (cardio)respiratory motion that might differ from the actual target motion [22].

At this moment the accuracy of cardiac and respiratory motion required to plan/deliver adequate STAR is not known yet and heavily depends on the equipment available at the institute. It is however warranted that in future publications, all motion related data that is acquired during the preparation and treatment phase is reported. Eventually, future dosimetric analysis could then give recommendations on how to best perform cardiac and/or respiratory motion management strategies.

Although we included the search term “AF” in case such articles reported motion data on the LV, we were unable to compare motion in AF patients with motion in VT patients due to the sparsity of the data. Furthermore, we did not include healthy subjects in our initial search term. We did, however, allow the inclusion of data on healthy subjects via the reviewed articles and via forward referencing.

Although more articles on motion in healthy subjects and/or AF patients could have been included, the most impeding factor is the limited amount of motion data on VT patients found in literature as this limits the extent of analyses that can be performed. Few studies investigated motion amplitudes of the target or cardiac (sub)structures in VT patients and many radiotherapy studies only report ITV-PTV margins and total volume treated, but do not report CTV or ITV. Performing analyses with motion data categorized and compared based on assessment technique/modality would be ideal. Furthermore, it would be interesting to compare motion of targets located in different regions of the heart to investigate the feasibility of regional treatment margins, as some studies mention that cardiac motion, especially in the fibrotic region, might be smaller in VT patients in comparison with healthy volunteers [21,22]. To aid in optimization of STAR, the quality of motion data for STAR needs to be improved.

Therefore, future studies on STAR should not only report the target volume's location, using for example the American Heart Association (AHA) 17-segment model [41], but also the CTV, ITV, and cardiac and respiratory motion amplitudes (in SI, LR, and AP direction) on which the CTV-ITV expansions are based. Moreover, studies should provide detailed information about metrics that describe the cardiac hemodynamic function of patients, such as ejection fraction.

Due to the limited patient numbers per centre, a common multi-centre database is needed to better understand the biological effects of STAR [42,43], to determine which patients benefit most from STAR, and to define quality requirements for treatment preparation, e.g., target identification and motion assessment, and delivery [44]. Therefore, the Standardized Treatment and Outcome Platform for Stereotactic Therapy Of Re-entrant tachycardia by a Multidisciplinary consortium (STOPSTORM.eu, Horizon 2020, GA No. 945119) started in May 2021. The project aims are the establishment of a pooled STAR database for efficacy and safety evaluation and the harmonisation of STAR across Europe [45].

In conclusion, a literature review was performed to obtain information on cardiac and cardiorespiratory motion of cardiac (sub)structures within VT patients and healthy subjects that could be used as future references for studies on STAR. Unfortunately, motion data in VT patients is limited and results are often poorly reported. Based on data collected in this review it appears that motion, even under motion management techniques, is highly patient-specific [18,39], and therefore individual motion assessment is desired for STAR. Nevertheless, collection of well-documented motion data in currently ongoing clinical trials [46–

48] or multicentre treatment databases (e.g., STOPSTORM.eu) is of the utmost importance for the safe and widespread introduction of this treatment technique.

### CRedit authorship contribution statement

**Raoul R.F. Stevens:** Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft. **Colien Hazelaar:** Supervision, Conceptualization, Methodology, Validation. **Martin F. Fast:** Funding acquisition. **Joost J.C. Verhoeff:** Funding acquisition. **Oliver Blanck:** Conceptualization, Methodology, Funding acquisition. **Wouter van Elmp:** Supervision, Conceptualization, Methodology, Validation.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.radonc.2023.109844>.

### References

- [1] Tang PT, Shenasa M, Boyle NG. Ventricular arrhythmias and sudden cardiac death. *Curr Electrophysiol Clin* 2017;9:693–708. <https://doi.org/10.1016/j.ccep.2017.08.004>.
- [2] Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, et al. 2019 HRS/EHRA/APHS/LAHS expert consensus statement on catheter ablation of ventricular arrhythmias. *Europace* 2019;21:1143–4. <https://doi.org/10.1093/europace/euz132>.
- [3] Tung R, Vaseghi M, Frankel DS, Vergara P, Di Biase L, Nagashima K, et al. Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: An International VT Ablation Center Collaborative Group study. *Heart Rhythm* 2015;12:1997–2007. <https://doi.org/10.1016/j.hrthm.2015.05.036>.
- [4] Kuck KH, Tilz RR, Deneke T, Hoffmann BA, Ventura R, Hansen PS, et al. Impact of substrate modification by catheter ablation on implantable cardioverter-defibrillator interventions in patients with unstable ventricular arrhythmias and coronary artery disease: Results from the multicenter randomized controlled SMS (Substrate). *Circ Arrhythmia Electrophysiol* 2017;10:1–9. <https://doi.org/10.1161/CIRCEP.116.004422>.
- [5] Sapp JL, Wells GA, Parkash R, Stevenson WG, Blier L, Sarrazin J-F, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. *N Engl J Med* 2016;375:111–21. <https://doi.org/10.1056/nejmoa1513614>.
- [6] 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;377:2325–36. <https://doi.org/10.1056/nejmoa1613773>.
- [7] 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;139:313–21. <https://doi.org/10.1161/CIRCULATIONAHA.118.038261>.
- [8] Mayinger M, Kovacs B, Tanadini-Lang S, Ehrbar S, Wilke L, Chamberlain M, et al. First magnetic resonance imaging-guided cardiac radioablation of sustained ventricular tachycardia. *Radiother Oncol* 2020;152:203–7. <https://doi.org/10.1016/j.radonc.2020.01.008>.
- [9] van der Ree MH, Dieleman EMT, Visser J, Adam JA, de Bruin-Bon RHA, de Jong RMAJ, et al. Direct clinical effects of cardiac radioablation in the treatment of a patient with therapy-refractory ventricular tachycardia storm. *Adv Radiat Oncol* 2022;7. <https://doi.org/10.1016/j.adro.2022.100992>.
- [10] Miszczyk M, Jadczyk T, Gołba K, Wojakowski W, Wita K, Bednarek J, et al. Clinical evidence behind stereotactic radiotherapy for the treatment of ventricular tachycardia (STAR)—A comprehensive review. *J Clin Med* 2021;10:1238. <https://doi.org/10.3390/jcm10061238>.
- [11] Guckenberger M, Baus WW, Blanck O, Combs SE, Debus J, Engenhart-Cabillie R, et al. Definition and quality requirements for stereotactic radiotherapy: consensus statement from the DEGRO/DGMP Working Group Stereotactic Radiotherapy and Radiosurgery. *Strahlentherapie Und Onkol* 2020;196:417–20. <https://doi.org/10.1007/s00066-020-01603-1>.
- [12] Bellec J, Rigal L, Hervouin A, Martins R, Lederlin M, Jaksic N, et al. Cardiac radioablation for ventricular tachycardia: Which approach for incorporating cardiorespiratory motions into the planning target volume? *Phys Med* 2022;95:16–24. <https://doi.org/10.1016/j.ejmp.2022.01.004>.
- [13] McLeish K, Hill DLG, Atkinson D, Blackall JM, Razavi R. A study of the motion and deformation of the heart due to respiration. *IEEE Trans Med Imaging* 2002;21:1142–50. <https://doi.org/10.1109/TMI.2002.804427>.
- [14] Lydiard S, Pontré B, Lowe BS, Ball H, Sasso G, Keall P. Cardiac radioablation for atrial fibrillation: Target motion characterization and treatment delivery considerations. *Med Phys* 2021;48:931–41. <https://doi.org/10.1002/mp.14661>.
- [15] Thosani A, Trombetta M, Shaw G, Oh S, Sohn J, Liu E. Stereotactic arrhythmia radioablation for intramural basal septal ventricular tachycardia originating near the His bundle. *Heart Case Reports* 2021;7:246–50. <https://doi.org/10.1016/j.hrcr.2021.01.012>.
- [16] Ipsen S, Blanck O, Lowther NJ, Liney GP, Rai R, Bode F, et al. Towards real-time MRI-guided 3D localization of deforming targets for non-invasive cardiac radiosurgery. *Phys Med Biol* 2016;61:7848–63. <https://doi.org/10.1088/0031-9155/61/22/7848>.
- [17] Wang Y, Riederer SJ, Ehman RL. Respiratory motion of the heart: Kinematics and the implications for the spatial resolution in coronary imaging. *Magn Reson Med* 1995;33:713–9. <https://doi.org/10.1002/mrm.1910330517>.
- [18] Prusator MT, Samson P, Cammin J, Robinson C, Cuculich P, Knutson NC, et al. Evaluation of motion compensation methods for non-invasive cardiac radioablation of ventricular tachycardia. *Int J Radiat Oncol Biol Phys* 2021. <https://doi.org/10.1016/j.ijrobp.2021.06.035>.
- [19] Knutson NC, Samson PP, Hugo GD, Goddu SM, Reynoso FJ, Kavanaugh JA, et al. Radiation therapy workflow and dosimetric analysis from a phase 1/2 trial of noninvasive cardiac radioablation for ventricular tachycardia. *Int J Radiat Oncol Biol Phys* 2019;104:1114–23. <https://doi.org/10.1016/j.ijrobp.2019.04.005>.
- [20] Harms J, Schreiber E, Mccall NS, Lloyd MS, Higgins KA, Castillo R. Cardiac motion and its dosimetric impact during radioablation for refractory ventricular tachycardia. *J Appl Clin Med Phys* 2023;21:1–9. <https://doi.org/10.1002/acm2.13925>.
- [21] Roujol S, Anter E, Josephson ME, Nezafat R. Characterization of respiratory and cardiac motion from electro-anatomical mapping data for improved fusion of MRI to left ventricular electrograms. *PLoS One* 2013;8. <https://doi.org/10.1371/journal.pone.0078852>.
- [22] Knybel L, Cvek J, Neuwirth R, Jiravsky O, Hecko J, Penhaker M, et al. Real-time measurement of ICD lead motion during stereotactic body radiotherapy of ventricular tachycardia. *Reports Pract Oncol Radiother* 2021;26:128–37. <https://doi.org/10.5603/RPOR.a2021.0020>.
- [23] Krug D, Blanck O, Demming T, Dottermusch M, Koch K, Hirt M, et al. Stereotactic body radiotherapy for ventricular tachycardia (cardiac radiosurgery): First-in-patient treatment in Germany. *Strahlentherapie Und Onkol* 2020;196:23–30. <https://doi.org/10.1007/s00066-019-01530-w>.
- [24] Gerard JJ, Bernier M, Hjal T, Kopeck N, Pater P, Stosky J, et al. Stereotactic arrhythmia radioablation for ventricular tachycardia: Single center first experiences. *Adv Radiat Oncol* 2021;6. <https://doi.org/10.1016/j.adro.2021.100702>.
- [25] Carubicchio C, Andreini D, Piperno G, Catto V, Conte E, Cattani F, et al. Stereotactic radioablation for the treatment of ventricular tachycardia: preliminary data and insights from the STRA-MI-VT phase Ib/II study. *J Interv Card Electrophysiol* 2021;62:427–39. <https://doi.org/10.1007/s10840-021-01060-5>.
- [26] Levis M, Dusi V, Magnano M, Cerrato M, Gallio E, Depaoli A, et al. A case report of long-term successful stereotactic arrhythmia radioablation in a cardiac contractility modulation device carrier with giant left atrium, including a detailed dosimetric analysis. *Front Cardiovasc Med* 2022;9. <https://doi.org/10.3389/fcvm.2022.934686>.
- [27] Nasu T, Toba M, Nekomiya N, Itasaka R, Mafune S, Nakata T, et al. Successful application of stereotactic body radiation therapy for ventricular tachycardia substrate in a patient with nonischemic cardiomyopathy. *Am J Cardiol* 2022;184:149–53. <https://doi.org/10.1016/j.amjcard.2022.08.017>.
- [28] Chang WL, Jo HH, Cha MJ, Chang JH, Choi CH, Kim HJ, et al. Short-term and long-term effects of noninvasive cardiac radioablation for ventricular tachycardia: A single-center case series. *Heart Rhythm* 2023;02:119–26. <https://doi.org/10.1016/j.hroop.2022.11.006>.
- [29] van der Ree MH, Dieleman EMT, Visser J, Planken RN, Boekholdt SM, de Bruin-Bon RHA, et al. Non-invasive stereotactic arrhythmia radiotherapy for

- ventricular tachycardia: results of the prospective STARNL-1 trial. EP Eur 2023;25:1015–24. <https://doi.org/10.1093/europace/ead020>.
- [30] Abdel-Kafi S, de Ridder M, de Riva M, van der Geest RJ, Rasch C, Zeppenfeld K. Integration of electroanatomical mapping with imaging to guide radiotherapy of VT substrates with high accuracy. JACC Clin Electrophysiol 2020;6:874–6. <https://doi.org/10.1016/j.jacep.2020.03.014>.
- [31] Widesott L, Dionisi F, Fracchiolla F, Tommasino F, Centonze M, Amichetti M, et al. Proton or photon radiosurgery for cardiac ablation of ventricular tachycardia? Breath and ECG gated robust optimization. Phys Medica 2020;78:15–31. <https://doi.org/10.1016/j.ejmp.2020.08.021>.
- [32] Amino M, Kabuki S, Kunieda E, Hashimoto J, Sugawara A, Sakai T, et al. Interim Report of a Japanese Phase II Trial for Cardiac Stereotactic Body Radiotherapy in Refractory Ventricular Tachycardia - Focus on Target Determination - Circ Reports 2023;5:CR-23-0003. <https://doi.org/10.1253/circrep.CR-23-0003>.
- [33] Scholz EP, Seidensaal K, Naumann P, André F, Katus HA, Debus J. Rescued from the dead: Cardiac stereotactic ablative radiotherapy as last rescue in a patient with refractory ventricular fibrillation storm. Hear Case Reports 2019;5:329–32. <https://doi.org/10.1016/j.hrcr.2019.03.004>.
- [34] Fuchs E, Müller MF, Oswald H, Thöny H, Mohacsi P, Hess OM. Cardiac rotation and relaxation in patients with chronic heart failure. Eur J Heart Fail 2004;6:715–22. <https://doi.org/10.1016/j.ejheart.2003.12.018>.
- [35] Tan W, Xu L, Wang X, Qiu D, Han G, Hu D. Estimation of the displacement of cardiac substructures and the motion of the coronary arteries using electrocardiographic gating. Onco Targets Ther 2013;6:1325. <https://doi.org/10.2147/OTT.S52101>.
- [36] Maurer CR, Fitzpatrick JM, Wang MY, Galloway RL, Maciunas RJ, Allen GS. Registration of head volume images using implantable fiducial markers. IEEE Trans Med Imaging 1997;16:447–62. <https://doi.org/10.1109/42.611354>.
- [37] Dou TH, Thomas DH, O'Connell D, Bradley JD, Lamb JM, Low DA. Technical note: Simulation of 4DCT tumor motion measurement errors. Med Phys 2015;42:6084–9. <https://doi.org/10.1118/1.4931416>.
- [38] Goo HW, Allmendinger T. Combined electrocardiography- and respiratory-triggered CT of the lung to reduce respiratory misregistration artifacts between imaging slabs in free-breathing children: Initial experience. Korean J Radiol 2017;18:860. <https://doi.org/10.3348/kjr.2017.18.5.860>.
- [39] Lydiard, PGDip S, Blanck O, Hugo G, O'Brien R, Keall P. A Review of Cardiac Radioablation (CR) for Arrhythmias: Procedures, Technology, and Future Opportunities. Int J Radiat Oncol 2021;109:783–800. <https://doi.org/10.1016/j.ijrobp.2020.10.036>.
- [40] Holland AE, Goldfarb JW, Edelman RR. Diaphragmatic and cardiac motion during suspended breathing: preliminary experience and implications for breath-hold MR imaging. Radiology 1998;209:483–9. <https://doi.org/10.1148/radiology.209.2.9807578>.
- [41] 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;111:178–85. <https://doi.org/10.1016/j.ijrobp.2021.03.051>.
- [42] Zhang DM, Navara R, Yin T, Szymanski J, Goldsztejn U, Kenkel C, et al. Cardiac radiotherapy induces electrical conduction reprogramming in the absence of transmural fibrosis. Nat Commun 2021;12. <https://doi.org/10.1038/s41467-021-25730-0>.
- [43] Blanck O, Boda-Heggemann J, Hohmann S, Mehrhof F, Krug D. Kardiale stereotaktische Strahlentherapie induziert eine Umprogrammierung des elektrischen Reizleitungssystems. Strahlenther Onkol 2022;198:209–11. <https://doi.org/10.1007/s00066-021-01891-1>.
- [44] Schmitt D, Blanck O, Gauer T, Fix MK, Brunner TB, Fleckenstein J, et al. Technological quality requirements for stereotactic radiotherapy. Strahlenther Onkol 2020;196:421–43. <https://doi.org/10.1007/s00066-020-01583-2>.
- [45] 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. EP Eur 2023. <https://doi.org/10.1093/europace/ead238>.
- [46] Blanck O, Buergy D, Vens M, Eidinger L, Zaman A, Krug D, et al. Radiosurgery for ventricular tachycardia: preclinical and clinical evidence and study design for a German multi-center multi-platform feasibility trial (RAVENTA). Clin Res Cardiol 2020;109:1319–32. <https://doi.org/10.1007/s00392-020-01650-9>.
- [47] Miszczyk M, Jadczyk T, Tomasik B, Latusek T, Bednarek J, Kurzelowski R, et al. Stereotactic management of arrhythmia - radiosurgery in treatment of ventricular tachycardia (SMART-VT) - clinical trial protocol and study rationale. OncoReview 2021;10:123–9. <https://doi.org/10.24292/or.420010221>.
- [48] Carbucicchio C, Jereczek-Fossa BA, Andreini D, Catto V, Piperno G, Conte E, et al. STRA-MI-VT (STereotactic RadioAblation by Multimodal Imaging for Ventricular Tachycardia): rationale and design of an Italian experimental prospective study. J Interv Card Electrophysiol 2021;61:583–93. <https://doi.org/10.1007/s10840-020-00855-2>.
- [49] Nehrke K, Börner P, Manke D, Böck JC. Free-breathing cardiac MR imaging: Study of implications of respiratory motion - Initial results. Radiology 2001;220:810–5. <https://doi.org/10.1148/radiol.2203010132>.
- [50] Ipsen S, Blanck O, Oborn B, Bode F, Liney G, Hunold P, et al. Radiotherapy beyond cancer: Target localization in real-time MRI and treatment planning for cardiac radiosurgery. Med Phys 2014;41:1–8. <https://doi.org/10.1118/1.4901414>.
- [51] Akdag O, Borman PTS, Woodhead P, Uijtewaal P, Mandija S, Van Asselen B, et al. First experimental exploration of real-time cardiorespiratory motion management for future stereotactic arrhythmia radioablation treatments on the MR-linac. Phys Med Biol 2022;67. <https://doi.org/10.1088/1361-6560/ac5717065003>.
- [52] Wang Z, Willett CG, Yin FF. Reduction of organ motion by combined cardiac gating and respiratory gating. Int J Radiat Oncol Biol Phys 2007;68:259–66. <https://doi.org/10.1016/j.ijrobp.2006.11.057>.
- [53] Ninni S, Gallot-Lavallée T, Klein C, Longère B, Brigadeau F, Potelle C, et al. Stereotactic radioablation for ventricular tachycardia in the setting of electrical storm. Circ Arrhythmia Electrophysiol 2022;15:E010955. <https://doi.org/10.1161/CIRCEP.122.010955>.
- [54] Huang LH, Gao ZZ, Li WY, Zhang HC, Zheng JW, Liu XP. Stereotactic body radiation therapy for refractory premature ventricular contractions that originate from the left ventricular summit: A case report. PACE - Pacing Clin Electrophysiol 2023;46:190–4. <https://doi.org/10.1111/pace.14590>.