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Publication Date

2023-12-01

DOI

10.1016/j.hroo.2023.12.006

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Running title: *Cardiac Contractile Motion in VT SBRT*

Keywords: stereotactic radioablation, ventricular arrhythmia, cardiac computed tomography, cardiac contractile motion, intracardiac fiducial

Word Count: 2320 words (subject to change based on final manuscript)

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Funding Sources

This work was supported by the American Heart Association (AHA 19CDA34760021), the National Institutes of Health (NIH 1KL2TR001444) and Muggleton Family via the Artificial Intelligence Arrhythmia Research Fund at UC San Diego Health.

Disclosures

Dr. Ho: grants from NIH (2KL2TR001444), AHA (19CDA34760021), and Muggleton Family via the Artificial Intelligence Arrhythmia Research Fund at UC San Diego Health, and equity in Vektor Medical Inc.

Dr. Han: research support from Abbott.

Dr. Hsu: honoraria from Medtronic, Boston Scientific, Abbott, Biotronik, Biosense-Webster, Pfizer, Bristol-Myers Squibb, Janssen Pharmaceuticals, research grants with Biotronik and Biosense-Webster, and equity interest in Acutus Medical and Vektor Medical.

Dr. Hoffmayer: grants from the NIH (F32 HL10472702 and LRP), consulting for Samsung Electronics, Inc. and Vektor Medical Inc.

Dr. Birgersdotter-Green: Honoraria from Medtronic, Boston Scientific, Abbott, Biotronik.

Dr. Feld: equity and consulting for Acutus Medical, Adagio, Medwaves, Varian, and co-founded and consulted for Perminova, received CCEP Fellowship Training program stipend support from Medtronic, Biotronik, Biosense Webster, Boston Scientific, and Abbott.

Dr Krummen: grant from the UCSD Galvanizing Engineering in Medicine Foundation and equity in Vektor Medical Inc.

Drs. Atwood, Raissi, and Mundt have no disclosures.

Abstract

Background:

Respiratory motion management strategies are used to minimize the effects of breathing on the precision of stereotactic ablative radiotherapy for ventricular tachycardia, but the extent of cardiac contractile motion of the human heart has not been systematically explored.

Objective:

We aim to assess the magnitude of cardiac contractile motion between different directions and locations in the heart.

Methods:

Patients with intracardiac leads or valves who underwent 4D cardiac computed tomography (4DCT) prior to a catheter ablation procedure for atrial or ventricular arrhythmias at 2 medical centers were studied retrospectively. The displacement of transvenous right atrial appendage (RA), right ventricle (RV) ICD, coronary sinus (CS) lead tips and prosthetic cardiac devices across the cardiac cycle were measured in orthogonal 3D views on a maximal-intensity projection CT reconstruction.

Results:

A total of 31 pre-ablation cardiac 4DCTs were analyzed. The LV lead tip had significantly greater motion compared to the RV lead in the anterior-posterior direction (6.0±2.2mm vs 3.8±1.7mm; p=0.01) and superior-inferior direction (4.4±2.9mm vs 3.5±2.0mm; p=0.049). The prosthetic aortic valves had the least movement of all fiducials, specifically compared to the RV lead tip in the left-right direction (3.2±1.2mm vs 6.1±3.8mm, p=0.04) and the LV lead tip in the antero-posterior direction (3.8±1.7mm vs 6.0±2.2mm, p=0.03).

Conclusion:

The degree of cardiac contractile motion varies significantly (1mm to 15.2 mm) across different locations in the heart. The effect of contractile motion on the precision of radiotherapy should be assessed on a patient-specific basis.

Manuscript

Introduction:

Stereotactic ablative radiotherapy (SAbR) is an emerging therapy for ventricular tachycardia (VT). Success rates vary in the literature, with recurrences of VT after SAbR ranging widely from 59-100% beyond the 6-week blanking period.[1,15] Factors such as cardiac and respiratory motion may affect the precision and safety of therapy, but the magnitude of motion in different locations and directions in the heart has not been well characterized. Motion management strategies have often focused on accounting for respiratory motion through the use of respiratory gating[6] or body immobilization equipment[4] due to known larger magnitude of respiratory motion, but the need to account for cardiac motion has not been as well addressed.

The aim of this study is to quantify the magnitude of cardiac contractile motion at different locations of the heart and orientations in patients with cardiac arrhythmias. We hypothesized that the magnitude of cardiac contractile motion may vary between different directions and locations in the heart.

Methods:

Patient Population

A total of 31 consecutive patients undergoing catheter or SAbR ablation procedures for ventricular tachycardia, premature ventricular tachycardia, atrial fibrillation and atrial flutter were retrospectively enrolled from 2 centers (University of California San Diego and Veterans Affairs San Diego). These patients all had pre-procedural high resolution cardiac 4D computed tomography scans as part of a standard of care evaluation, and had radio-opaque implanted cardiac devices such as transvenous pacemakers, implantable cardioverter defibrillators (ICD), or prosthetic valves. There were no exclusion criteria for our study. This study was performed in accordance with an IRB-approved protocol and adhered to the Helsinki guidelines; all patients provided written informed consent.

4D Cardiac Computed Tomography Protocol

Patients in our study underwent high-resolution, dose modulated, retrospective cardiac-gated CT scans (Revolution, GE Healthcare, or Siemens Force) during expiratory breath hold. The cardiac CT images were obtained with extended intravenous contrast infusion and reconstructed with 0.5mm slice thickness in different phases of the cardiac cycle (0-95%).

Image Analysis

The displacement of transvenous right atrial appendage (RA), right ventricle (RV) ICD, coronary sinus (CS) lead tips and prosthetic cardiac devices across the cardiac cycle were measured in orthogonal 3D views on a maximal-intensity projection CT reconstruction using imaging analysis software (Horos Project). A representative 3D reconstruction is shown in Figure 1. The lead tips were used as the fiducial for all the study patients. The inferior aspect of the bioprosthetic aortic valve were used as a fiducial when available. The cardiac motion of individual fiducials was assessed on a maximum-intensity projection CT reconstruction using imaging analysis software (Horos Project). For each fiducial, we measured the displacements in the superior-inferior (SI), left-right (LR), and anterior-posterior directions (AP). The average displacement was calculated as a vector mean: $\sqrt{(SI)^2+(LR)^2+(AP)^2}$. (SI= motion in the superior-inferior direction; LR: motion in the left-right direction, AP: motion in the anterior-posterior direction)

Statistical Analysis

We used GraphPad Prism software to conduct our statistical analyses. For data samples with normal distributions (determined using the Kolmogorov-Smirnov normality test), paired student's t-test was used to compare intracardiac lead motion. For data samples without normal distribution, we used the non-parametric Wilcoxon signed-rank test. Unpaired student's t-test, Chi-square and linear regression were used to assess for predictors of increased magnitude of cardiac motion. For the data analysis, we reported the mean value ± standard deviation, and analyzed the maximum motion for each fiducial.

Results

Demographics

A total of 31 patients underwent pre-procedural cardiac contrast 4DCT scans prior to arrhythmia ablation and had a permanent pacemaker, ICD and/or a bioprosthetic valve. In this cohort, 25 patients had a RA lead, 29 had a RV lead, 11 had a LV coronary sinus lead, and 8 had a bioprosthetic aortic valve (AV). Baseline clinical characteristics (age, sex, arrhythmia profile, indication for cardiac CT, and cardiac comorbidities) are listed in Table 1.

Differences in the Magnitude of Motion between RV vs LV Lead Tips

In patients with a biventricular device, the LV lead had a significantly greater contractile motion compared to the RV lead in the anterior-posterior direction (6.0±2.2mm vs 3.8±1.7mm; p=0.01) and superior-inferior direction (4.4±2.9mm vs 3.5±2.0mm; p=0.049). There was a greater motion of the RV lead tip in the left-right direction (6.1±3.8mm vs 3.5±1.2mm, p=0.02). The maximal cardiac contractile ventricular motion of all patients was 15.2mm, occurring in the left-right direction of the RV lead tip. Figure 2 shows the mean magnitude and directions of cardiac contractile motion of the RV and LV lead tips. Table 2 shows the magnitude and directions of cardiac contractile motion of all intracardiac fiducials.

Differences in the Magnitude of Motion between Prosthetic Aortic Valve vs Ventricular Leads

The vector mean contractile motion of the prosthetic AVs (6.1±2.0mm) was less than both the LV lead tip (8.6±2.6mm; p=0.03) and RV lead tip (8.6±3.5mm; p=0.03).The prosthetic AVs had decreased movement than the RV lead tip in the left-right direction (3.2±1.2mm vs 6.1±3.8mm, p=0.02, figure 3) and the LV lead tip in the antero-posterior direction (3.8±1.7mm vs 6.0±2.2mm, p=0.03, figure 3). There were no differences between the prosthetic AV vs ventricular leads in the other orientations. The maximal cardiac contractile motion of the prosthetic AV was 7.2mm, occurring in the anterior-posterior direction. Table 2 shows the magnitude and directions of cardiac contractile motion of all intracardiac fiducials.

Greater Motion of the Right Atrial Appendage Lead Tip vs All Other Fiducials

The mean contractile motion of the RA lead was significantly greater than the RV lead in the anterior-posterior direction (9.0±5.4mm vs 3.8±1.8mm; p<0.01). The RA lead had greater motion than the LV lead in the left-right direction, (6.5±3.4mm vs 3.7±1.3mm; p=0.01).

Predictors of Increased Magnitude of Cardiac Contractile Motion

Clinical characteristics, including left ventricular systolic ejection fraction, left ventricular end-diastolic diameter in systole and diastole, and presence of coronary artery disease, were not found to be a predictor of magnitude of cardiac contractile motion (Table 3).

Discussion

There were three major significant findings from this study: 1) Cardiac contractile motion varied greatly across patients, ranging from 1mm to 15mm, 2) Cardiac contractile motion differed significantly across locations in the heart and was greatest in the RA appendage (vector mean 11.6mm) and LV lead (vector mean 8.6mm) while less at the aortic annulus (vector mean 6.1mm). 3) No single clinical characteristic predicted the magnitude of cardiac motion. To our knowledge, this is the largest study to assess cardiac contractile motion in a relevant human population with cardiac arrhythmias undergoing cardiac ablation therapy. These findings may provide rationale to consider incorporating patient and location-tailored cardiac contractile motion management to improve the precision of non-invasive stereotactic radioablative therapy of cardiac arrhythmias.

We noted differences in the magnitude of cardiac motion in different regions of the heart and in different directions. As expected, the RV and LV leads tended to exhibit greater motion than the aortic valve. This can be explained by the torsional movement of cardiac contraction, where the ventricles twist around the great vessels during systole[16]; this can be appreciated in representative 4D cardiac CT reconstruction videos in a patient with a normal ejection fraction (online video 1) and in a patient with severely reduced ejection fraction (online video 2).

This is the largest study to analyze the cardiac motion of intracardiac fiducials in patients with arrhythmias who already have undergone or may become candidates for stereotactic non-invasive radioablative therapy. In one recent study, Prusator et al evaluated the VT target displacement in 11 patients[17]. Our study included significantly more patients (31 vs 11 patients), which is powered to better capture a wider range of cardiac motion. We found a greater displacement of the RV lead tip in the L-R direction compared to Prusator et al (6.1cm vs 3.9cm), and this could be related to the greater heterogeneity of our larger patient sample. Secondly, our study was intentionally designed to only assess rigid radio-opaque structures affixed to the endocardium to ensure that the motion of the same exact point on the heart wall is tracked through time. This was important to maximize the precision and accuracy of our measurements and minimize any error introduced by estimating the location of the VT target on the myocardial wall which can be vague without a clear radio-opaque landmark and subject to estimation error. Finally, we systematically assessed the cardiac motion of LV lead tip, RA lead tip, and prosthetic aortic valve in addition to the ICD lead tip, which enabled sufficient power to compare the differences in motion between different locations of the heart.

While we chose to only evaluate clearly defined radio-opaque landmarks, such as lead tips, to precisely estimate the motion of specific myocardial locations, there are methods to help standardize targeting cardiac segments and track the motion of each segment[18]. However, the ability of this technique to track the precise motion of each segment is unknown, particularly as the ventricles move in a 3D torsion motion which may be difficult to track using a rigid circular 17 segment AHA model (arranged around a rigid circle). Without a radio-opaque fiducial, it is difficult to track the same point of the myocardium through time.

There was another recent study that analyzed manually contoured segmentations of structures on the cardiac CT to characterize cardiac motion in 10 patients undergoing transcatheter aortic valve replacement[14]. In that study, the ventricles and coronary artery ostia were contoured and the centroids of the chamber contours were tracked through the cardiac phases to measure the cardiac motion. In this study, the mean displacements were found to be mostly <5mm, with maximal displacement of 7mm by the RV centroid in the left-right direction. In comparison, the present study found slightly greater cardiac contractile motion (>5mm) by all the lead tips and prosthetic valve fiducials, with maximal displacement up to 15mm of the RV lead in the left-right direction. Potential reasons for this difference are 1) the coronary artery ostia that were tracked in the prior study are located at the valve annuli which would be expected to exhibit less motion compared to the ventricular apex, 2) the radiopaque lead tips imbedded in heart walls that were tracked in this study may reduce the potential error from manual contouring and chamber centroid estimation 3) a larger sample size of patients. Nevertheless, the mean magnitudes were still small (<1cm) overall and this study extends previous findings that there is a wide variation in the range of motion in different locations and orientations. Another study demonstrated a significant inter-observer variability among radiation oncologists in contouring cardiac substructures (e.g. valves, chambers, subsegments, coronary arteries)[19]. This finding further highlights the preference of utilizing ICD leads as fiducials as it involves a much more precise target.

Most published series of SAbR protocols have not been able to account for cardiac contractile motion of the VT target directly in a patient- or location-specific manner. A few centers have used an intracardiac fiducial-based radiotherapy delivery system that adjusts the beam based on the motion of an existing or temporarily implanted pacing lead in the RV apex, but usually is not directly located at the VT target (Cyberknife). To our knowledge, fiducial tracking is currently not done for other radiation delivery methods, such as volumetric modulated arc therapy. However, as our results suggest, the motion of the VT target could potentially be different from the motion of the cardiac fiducial, depending on their location in the heart. Further studies are needed to assess whether this difference will affect the precision of therapy delivery utilizing live fiducial tracking. At centers without this capability, most have empirically employed a general margin of error known as the internal target volume (ITV), in the ballpark of a 3-5mm expansion to account for both cardiac contractile motion and respiratory motion. Motion strategies such as body immobilization and respiratory gating have been employed at some centers, but do not address cardiac contractile motion. Nevertheless, the extent of cardiac contractile motion has not been quantified systematically in 3-dimensions.

Furthermore, respiratory and cardiac motion may be interconnected, and respiratory motion can potentially have physiologic changes on cardiac preload conditions. However, accounting for both cardiac and respiratory motion with gating methods can certainly lead to longer treatment times and is a limitation of considering cardiac motion gating as a motion management strategy. Further studies are needed to develop other cardiac motion management strategies and also to see which patients would benefit the most from cardiac gating.

The large variation in the magnitude of motion between patients and the differences in movement between locations of the heart may provide a rationale to consider tailoring cardiac contractile motion in order to improve precision of non-invasive therapy. For example, if a target near the RV apex exhibits greater cardiac contractile motion, more aggressive cardiac motion management strategies may need to be employed. These strategies may include increasing the PTV margin to account for the cardiac motion, utilizing cardiac ECG-gating LINACS

(Truebeam, Varian Medical Systems, Palo Alto, CA), or using fiducial tracking systems (Cyberknife, Accuray, Sunnyvale, CA). In the majority of published series, no cardiac contractile motion management is employed. On the other hand, if a target is near the aortic valve annulus and exhibits minimal motion, then a smaller PTV margin may be employed.

Our study has several limitations. First, our sample size is small, but was still sufficiently powered to detect statistically significant differences in motion. Second, we utilized ICD lead tips as fiducials to track cardiac contractile motion as a surrogate of the cardiac wall. In this study, we intentionally limited our analysis to include a radio-opaque marker touching the myocardium to clearly visualize motion of a specific location of the heart and limit any estimation errors. The fiducial motion may not correlate exactly with target motion, especially in circumstances where the target has regional wall motion abnormalities that would lead to less displacement than the fiducial. In the future, sophisticated myocardial tagging imaging protocols may potentially be used for any part of the heart to better track motion of the exact VT target. Further studies are also needed to assess whether ECG gating strategies (to treat only at the same part of the cardiac cycle) can potentially limit the effect of cardiac motion).

Conclusion

Cardiac contractile motion varies significantly across different locations in the heart and different patients, greatest in the LV and least at the aortic valve. Further studies are underway to develop optimal strategies to account for cardiac contractile motion, such as patient- and location-tailored planned target volume expansions and cardiac ECG-gated radiotherapy delivery.

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Figure 1. A representative 3D reconstruction of a patient's RV lead, which had a displacement of 1.4cm in the left-right direction.

Figure 2. Comparison of average displacements between RV and LV leads in different directions

Figure 3. Comparison of displacements between the aortic valve and ventricular lead tips

Table 1 Baseline Patient Demographics

Baseline Clinical Characteristics	
Age	68 ± 12
Male	29/31 (94%)
Hypertension	12/31 (39%)
Ventricular tachycardia	23/31 (74%)
Atrial fibrillation	16/31 (52%)
Congestive heart failure	27/31 (87%)
Obstructive CAD	15/31 (48%)
LV Ejection Fraction (%)	38% ± 18%
Indication for Cardiac CT:	
Ventricular Arrhythmia Ablation	22/31 (71%)
Atrial Arrhythmia Ablation	5/31 (16%)
Other	4/31 (13%)

Table 2. Summary of magnitude (mm) and directions of cardiac contractile motion of all intracardiac fiducials.

	RV L-R	LV L-R	AV L-R	RA L-R	RV S-I	LV S-I	AV S-I	RA S-I	RV A-P	LV A-P	AV A-P	RA A-P
Minimum	1.2	2.2	1.6	1.7	1.0	1.0	1.0	0.5	1.4	2.1	1.7	2.0
Maximum	15.2	6.0	5.6	15.4	9.3	9.3	5.2	9.7	8.5	8.6	7.2	23.0
Range	14.0	3.8	4.0	13.7	8.3	8.3	4.2	9.2	7.1	6.4	5.5	21.0
Mean	6.1	3.5	3.2	6.3	3.5	4.4	3.2	3.3	3.8	6.0	3.8	8.7
Std. Deviation	3.8	1.2	1.2	3.3	2.0	2.9	1.5	2.3	1.8	2.2	1.7	5.4
Std. Error of Mean	0.7	0.4	0.4	0.7	0.4	0.9	0.5	0.4	0.3	0.7	0.6	1.1

Table 3. Predictors of Increased Magnitude of Cardiac Contractile Motion

	RV mean (p-value)	LV mean (p-value)	AV mean (p-value)	RA mean (p-value)
LVEF	0.96	0.81	0.34	0.54
LVIDd	0.14	0.48	0.61	0.26
LVIDs	0.55	0.64	0.57	0.69
CAD	0.79	0.55	0.08	0.83

Abbreviations: LVEF= left ventricular ejection fraction, LVIDd= left ventricular internal dimension in diastole, LVIDs= left ventricular internal dimension in systole, CAD= history of coronary artery disease.