Use of the inverse solution guidance algorithm method for RF ablation catheter guidance

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Running title: Catheter guidance to the ventricular arrhythmia origin

Keywords: Catheter guidance, Single equivalent moving dipole, Inverse solution guidance

algorithm, RF ablation

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This is the author manuscript accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.14965.

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ABSTRACT

We previously introduced the Inverse Solution Guidance Algorithm (ISGA) methodology using a Single Equivalent Moving Dipole model of cardiac electrical activity to localize both the exit site of a re-entrant circuit and the tip of a radiofrequency (RF) ablation catheter. The purpose of this study was to investigate the use of ISGA for ablation catheter guidance in an animal model.

Ventricular tachycardia (VT) was simulated by rapid ventricular pacing at a target site in eleven Yorkshire swine. The ablation target was established using three different techniques: a pacing lead placed into the ventricular wall at the mid-myocardial level (Type-1), an intracardiac mapping catheter (Type-2), and an RF ablation catheter placed at a random position on the endocardial surface (Type-3). In each experiment, one operator placed the catheter/pacing lead at the target location, while another used the ISGA system to manipulate the RF ablation catheter starting from a random ventricular location to locate the target.

The average localization error of the RF ablation catheter tip was 0.31 ± 0.08 cm. After analyzing ~35 cardiac cycles of simulated VT, the ISGA system's accuracy in locating the target was 0.4 cm after 4 catheter movements in the Type-1 experiment, 0.48 cm after 6 movements in the Type-2 experiment, and 0.67 cm after 7 movements in the Type-3 experiment.

We demonstrated the feasibility of using the ISGA method to guide an ablation catheter to the origin of a VT focus by analyzing a few beats of body surface potentials without electro-anatomic mapping.

INTRODUCTION

Radiofrequency (RF) ablation of the site of origin of ventricular tachycardia (VT) has been used to prevent the initiation of arrhythmia. In this procedure, an RF ablation catheter is introduced into the ventricle, and RF current is delivered to the site of origin of the VT to either disrupt the reentrant circuit or block the exit/entry point [1,2]. While catheter ablation of idiopathic or focal VT has been demonstrated to be a safe and curative procedure, catheter ablation of VT associated with structural heart disease has remained challenging and is associated with a high recurrence rate [3-10].

In order to maximize likelihood of a successful ablation outcome, the operator typically starts with a detailed electro-anatomical map of the ventricle, which can be a time-consuming procedure. Subsequently, activation and entrainment mapping define the reentrant circuit, including the exit and isthmus [11-13]. A caveat associated with this

level of VT mapping and definition, however, is that it requires that the VT is hemodynamically tolerated, as it has to be induced and maintained [9,10]. Alternate mapping techniques such as substrate mapping and pace mapping have limited utility in patients with advanced structural heart disease [14]. Other ablation strategies, such as substrate modification or use of hemodynamic support devices, are not associated with improved outcomes [15-19]. We propose that better techniques are required that would minimize the amount of time required to successfully map and ablate a VT, and ideally this would be feasible without the requirement of maintaining prolonged VT in a patient.

Recently, we introduced the Inverse Solution Guidance Algorithm (ISGA) methodology using a Single Equivalent Moving Dipole (SEMD) model of cardiac electrical activity to localize both the exit site of the re-entrant circuit and the tip of an RF ablation catheter [20-27]. By analyzing only a few beats of body surface potentials during ventricular arrhythmia, the ISGA method aims to guide an ablation catheter to the site of its origin. Although the SEMD model is a simplified representation of cardiac electrical activity, using multiple ventricular epicardial electrodes of known location in an *in vivo* swine model, we have shown that it is accurate when cardiac electrical activity is highly localized [25,26,28].

The purpose of this study was to investigate the feasibility of using the ISGA method to guide the ablation catheter, similar to a clinical setting. We simulated VT by means of rapid pacing at various rates using three different approaches (a pacing lead fixed in the

myocardium, an epicardial mapping catheter, and an intracardiac ablation catheter), at random positions in the swine's ventricle. We then applied the ISGA method to guide the ablation catheter to the vicinity of the origin of the simulated VT.

METHODS

Animal Preparation

The animal studies were approved by the MIT Committee on Animal Care. All experiments were performed in accordance with relevant guidelines and regulations. Eleven Yorkshire swine (40-50 kg) were used to evaluate the ISGA guidance system. The swine were pre-anesthetized with telazol (4 mg/kg), xylazine (2.2 mg/Kg), and atropine (0.04 mg/kg) prior to endotracheal intubation. The swine were maintained under anesthesia using positive pressure ventilation (~12 breaths/min and a tidal volume of ~500 ml) with Isoflurane 1 – 3 %. Once intubated, animals were positioned supine on the procedure table with circulating water heating pad underneath. An auricular vein was cannulated with an 18-22 G angio-catheter.

Sheath catheters were placed in the femoral artery, femoral veins, and jugular veins. A micromanometer-tipped pressure sensor (SPC350, Millar Instruments, Houston, TX) was introduced into the right femoral artery through a sheath catheter for blood pressure measurement. A sheath catheter in the right jugular vein was used for drug and fluid injection purposes. The animals were continually monitored using ECG, pulse oximetry, blood pressure, and body temperature, with all sensors connected to a data acquisition module (TSD104A, Biopac Systems, Santa Barbara, CA). The animal skin was

carefully shaved and scrubbed to allow attachment of body surface potential electrodes.

Inverse Solution Guidance Algorithm

ISGA can be used to localize both (i) the site of origin of an arrhythmia and (ii) the site of the ablation catheter tip when it is used to pace the ventricles. ISGA utilizes the SEMD model to analyze the body surface potentials. ISGA identifies the six dipole parameters (X, Y, and Z position coordinates and the three-dimensional components of the dipole moment) during a VT beat and calculates a sequence of dipole locations, representing the trajectory of the single equivalent dipole, over the cardiac cycle. Then, the dipole corresponding to the exit site of the re-entrant circuit is selected from the analysis of the trajectory.

In the ISGA, for a given dipole location, magnitude, and orientation, the estimated forward potential at the i^{th} body-surface electrode, φ_f^i, due to a single dipole is estimated using an infinite volume conductor model [20]:

$$\varphi_f^i = \frac{\mathbf{p}\cdot(\mathbf{r}-\mathbf{r}_i')}{4\pi g|\mathbf{r}-\mathbf{r}_i'|^3} - \frac{\mathbf{p}\cdot(\mathbf{r}-\mathbf{r}_{ref}')}{4\pi g|\mathbf{r}-\mathbf{r}_{ref}'|^3}$$

where, $\mathbf{r}_i'$ represents the i^{th} electrode location, $\mathbf{r}$ the dipole location, $\mathbf{p}$ the dipole moment, g the conductivity of the volume conductor, and $\mathbf{r}_{ref}'$ represents the location of the reference electrode.

An objective function, χ^2, describes how well the dipole reproduces the measured voltages:

where, φ_m^i is the measured $\chi^2 = \sum_{i=1}^{I}\left(\frac{\varphi_f^i - \varphi_m^i}{\sigma_m^i}\right)^2$ potential at the i^{th} electrode, $\sigma_m{}^i$ is the standard deviation of the measurement noise in lead *i*, and *I* is the number of electrodes.

Experimental Protocol (Figure 1)

Ventricular tachycardia was simulated by connecting a stimulus generator delivering pacing spikes (Model STG2008, Multi Channel Systems, Reutlingen, Germany) 1 ms in duration and 3 mA in amplitude to individual bipolar electrodes to pace the ventricles. Multiple pacing rates were applied, ranging from 120 bpm to 160 bpm.

An array of 64 Ag/AgCl body surface electrodes (A10040-60, Vermed Inc., Bellows Falls, VT) was placed on the animal's thorax in a symmetrical pattern (Figure 2A). We used a multi-channel bio-potential measurement system (ActiveTwo AD-box, BioSemi, Amsterdam, Netherlands) and a graphical user interface (Labview, National Instrument Corp., Austin, TX), to record body surface potentials at a sampling rate of 8192 Hz per channel. Body surface potentials were collected while pacing from the target site. The collected data segments included approximately 35 cardiac cycles.

Three different experiments were conducted, each using a different approach in simulating the target, as follows: ***Type-1 (N=3)***, an intracardiac pacing lead (Optim cardiac stimulation lead, St. Jude Medical, Little Canada, MN) fixed into the ventricular wall with the tip at the mid myocardial level; ***Type-2 (N=2),*** a 20-pole mapping catheter (Inquiry Luma-Cath diagnostic catheter, St. Jude Medical, Little Canada, MN) placed onto

the epicardial surface; ***Type-3 (N=5),*** an RF ablation catheter (EZ steer Bi-directional catheter, Biosense Webster Inc, Diamond Bar, CA) placed into the ventricle. In each case, the relevant target instrument was used to pace the *target* site. Through the ISGA system, the resulting ECG signals at the 64 body surface electrodes were collected and the *computational space* of the pacing electrode position was estimated. The position of the electrode used for pacing was defined as the "*target*" site for the catheter guidance procedure. The *real space* position of the *target* was determined using a biplanar fluoroscopic imaging system (OEC 9600 C-Arm, General Electric, Fairfield, CT).

In each experiment, after one operator completed the above procedure establishing the *real space* and *computational space* locations of the *target* site, an RF ablation catheter was introduced into the ventricle by a second operator not involved in the first procedure, and without prior knowledge of the target site. In the case of the Type-3 experiment, the same RF ablation catheter used for defining the *target* was moved to a random location within the ventricle prior to the arrival of the second operator. The ablation catheter tip was then initially placed at a random location on the ventricular endocardial or epicardial surface, and its *computational space* position was estimated by processing the corresponding 64 surface potentials using the ISGA generated by pacing the ventricle through the ablation catheter at the same rate as that of the simulated VT. The vector connecting the "*initial*" position to the "*target*" position in *computational space* was defined as the guidance vector. The second operator then moved the ablation catheter tip to a new location indicated by the guidance vector displayed on fluoroscopic images identifying the current *real space* location of the tip of the ablation catheter

(Figure 2B-C). The guidance procedure was repeated, and a new guidance vector was generated each time until the length of the guidance vector was less than 6 mm in *computational space*, i.e., the catheter tip was within 6 mm of the target in *computational space* (Figure 1).

In each animal, multiple guidance trials were conducted with a randomly chosen initial position of the ablation catheter tip. Also, multiple pacing rates were applied ranging from 120 bpm to 160 bpm. The *real space* position of the ablation catheter tip after each movement was measured under fluoroscopy. In one experiment, to determine reproducibility error, we performed five repetitions of *computational space* localization of the RF ablation catheter tip at heart rates of 120, 140, and 160 bpm in each ventricle.

To minimize the localization error resulting from chest movement, rocuronium (0.6 mg/kg IV initial dose plus a maintenance dosage of 0.1 to 0.2 mg/kg every 20 to 30 minutes) was injected and mechanical respiration was disabled at the end-expiration phase prior to each episode of ventricular pacing. At the conclusion of the experiment, animals were euthanized with an injection of sodium pentobarbital (100 mg/kg IV).

RESULTS

Reproducibility Error

In one experiment, we repeated five times the *computational space* localization of the tip of the RF ablation catheter at heart rates of 120, 140 and 160 bpm in each ventricle. The data were collected over a period of 30 minutes.

Table 1 shows reproducibility errors that are results of the *computational space* localization of the RF ablation catheter tip at three different heart rates. Averaged overall error was 0.31 ± 0.08 cm, with a maximum of 0.45 cm. There were no differences in errors due to different heart rates and different ventricle stimulations.

Catheter Guidance

Table 2 shows the results of the three types of experiments at each heart rate. The ISGA system guided the ablation catheter to the "*target*" electrodes with an accuracy of 0.4 cm after 4 catheter movements in Type-1 experiment, 0.48 cm after 6 catheter movements in Type-2 experiment, and 0.67 cm after 7 catheter movements in Type-3 experiment by analyzing brief a period of simulated VT after each movement.

Figure 3 shows examples of the final catheter tip locations after catheter movement using the ISGA system. Figure 4 shows an example of the result of the catheter guidance using the ISGA system displaying the proximity between the ablation site and the pacing electrode, in this case ~0.5 cm apart.

Correlation of *Computational Space* and *Real Space* Guidance Vector

In each experiment, for each pacing rate and guidance movement, the guidance vector in *real space* was calculated from the 3-D position of the catheter tip and the target measured under fluoroscopy. The correlation coefficients between *computational space* using the guidance vector and *real space* measured from the 3-D position of the catheter tip and target measured using the fluoroscopy at the pacing rate of 120, 140, and 160 bpm were 0.84, 0.86, and 0.80, respectively (Table 3).

DISCUSSION

RF catheter ablation has evolved as an effective treatment for clinical VT but requires extensive mapping technique(s) to identify the site(s) of the origin of the VT [4,9,10]. Mapping techniques have been improved and significantly contributed to improving the overall success rate of ablation procedures [1,29]. However, finding the site(s) of the VT origin by mapping of the electrical activity of the heart is still a painstaking and time-consuming procedure. In addition, some mapping techniques are not appropriate for patients who are hemodynamically unstable [30]. In this study, we evaluate a new technique using the ISGA to identify the site of origin of the arrhythmia, as well as a guidance technique to advance a RF ablation catheter to that site by analyzing a short segment of multichannel body surface ECG signals during a brief period of VT. We tested the validity of the ISGA method *in vivo* by simulating VT in swine. The data presented here demonstrate that the ISGA method could efficiently and accurately guide an ablation catheter to the "*target*" locations by analyzing only about 35 cardiac cycles and utilizing the *computational space* guiding vector information.

In this guidance method, an SEMD model was used to calculate both the locations of the simulated VT origin ("*target*") and the tip of the ablation catheter in the ventricle [20-27]. Although the SEMD model is a simplified representation of cardiac electrical activity, it is accurate when the cardiac electrical activity is highly localized, such as when an impulse emerges from the site of origin of VT or spreads from the tip of a pacing or ablation catheter. Even though the ISGA method does not take into account detailed anatomical information, variations in tissue conductivity or boundary effect, this method

enables accurate catheter guidance since any non-idealities similarly affect both the computed location of the site of origin of the arrhythmia and the ablation catheter tip. These distortions cancel out when the ablation catheter tip overlaps the arrhythmia origin. Recent studies have shown that the location of epicardial electrodes used for simulating arrhythmia could be identified accurately in *in-vivo* swine models [25,26,28].

In this study, three different types of pacing stimuli were utilized to simulate VT. In Type-1 experiments, an intracardiac pacing lead was fixed in the ventricular wall at the mid-myocardial level and an ablation catheter was moved from a random location to the "*target*" location using the ISGA system guidance. In Type-2 experiments, an intracardiac mapping catheter was placed on the epicardium and an ablation catheter was moved from a random location to the "*target*" electrodes using the ISGA system guidance. In Type-3 experiments, an ablation catheter was placed at a random location on the endocardium surface and defined as the "*target*" location. Once the ablation catheter was moved to a random location, a second operator then moved the ablation catheter tip to the "*target*" location using the ISGA system guidance.

In each experiment, the movement of the ablation catheter was performed by a second operator initially blinded to the location of the target. In Type-1 experiments, however, the second operator on the fluoroscopic image the operator could see the pacing lead and in Type-2 experiments the second operator could see on the fluoroscopic image the electrodes on the mapping catheter (but not know which electrode pair was chosen for pacing). The operator was instructed not to consider this

information in moving the catheter. In contrast, in Type-3 experiments the second operator had no "*target*" position information throughout the study. In this fully blinded experiment, the ablation catheter manipulator was able to guide the ablation catheter to the "*target*" location with an accuracy of 0.67 cm after 7 movements.

In the *computational space* localization of the catheter tip, the mean reproducibility error of the ISGA method was 0.31 cm, which is similar to the reproducibility error of the localization of the bipolar pacing electrode sutured to the epicardial surface (0.21 cm; [26]). This result indicates that the motion of the ablation catheter in the heart did not induce significant additional error to the ISGA guidance procedure. The reliable localization was due to the identification strategy of the earliest activation point (EAP) of the ISGA system [31]. The EAP was identified based on the medium beat (approximately 35 cardiac cycles) and the motion of the catheter tip on the ventricular surface was synchronized with the heartbeat.

The average number of guidance movements needed for the ablation catheter tip to reach the final position was 7.07, 77% higher than the previous phantom model experiments [25]. This increase in number of guidance movements might be the result of high amplitude of the measured noise, as well as inhomogeneities and anisotropies of the impedance distribution in an animal model, which may reduce the convergence of the iterative guidance procedure. In addition, due to the distortion between the *computational* and *real spaces*, the guidance vector may point towards a position located within or even outside of the ventricle wall in the *real space*. In this instance, the catheter was moved strictly by following directions specified by the guidance vector until

it reached the ventricular endocardial surface. The guidance procedure was then repeated, resulting in extra movements for the overall catheter guidance procedure. Although the above effects reduced the convergence of the iterative ISGA guidance procedure, the catheter was still guided to the target in only several steps. This indicates that catheter guidance using the ISGA method would be feasible and would only require a brief run of VT in a clinical setting.

The accuracy with which this method was able to guide the ablation catheter with respect to the target is important to note, especially in the context of current ablation technologies, which are able to create larger volume lesions than in the past. For example, Ilg et al. [32] studied ablation lesions from RF ablation of ventricular arrythmias in 35 patients using cardiac MRI and determined an endocardial lesion area of 3.5 ± 3.0 cm^2. Fenelon et al. demonstrated that epicardial RF ablation lesions in dogs measured as large as 9.3 ± 2.6 mm in length and 8.1 ± 1.9 mm in width using an open irrigated-tip catheter [33]. The creation of such large ablation lesions with current technologies gives more credence to the potential clinical application of guidance techniques such as that described here.

The CARTO™ (BiosenseWebster, Johnson and Johnson, Diamond Bar, CA, USA) system is an established method that provides an electro-anatomical map of the heart, under the assumption that the activation pattern and chamber geometry are constant on a beat to beat basis. While its success rate of a targeted VT reaches 82%, its procedural success rate in targeting all inducible monomorphic VTs is more modest [34]. This is of relevance when one considers that many patients with structural heart disease

will have multiple VT morphologies. The Ensite (St. Jude Medical, St. Paul, MN, USA) non-contact mapping system is an alternate available technology which utilizes a multi-electrode balloon catheter to allow high density mapping with each beat [35]. However, this system does not take into account cardiac motion during systole and may require repositioning in large cardiac chambers [36]. Novel and increasingly accessible imaging techniques, including cardiac MRI, CT, and ultrasound have been shown to provide complementary anatomical data that can be incorporated into a mapping system [37-40]. While these imaging technologies may address some of the shortcomings inherent to currently available electro-anatomic mapping systems, we propose that the addition of ISGA guidance would further supplement the currently available tools and improve success rate of ablation for VT.

Limitations

This study was designed to simulate VT using a pacing lead, a mapping catheter, and an ablation catheter at random locations. Several limitations are worth noting. A primary limitation inherent to this study is that the swine model has no structural heart disease, which is typically encountered in patients with VT. Although VT in the absence of structural heart disease, i.e., "idiopathic" VT, does occur, we concede that further work will be required to demonstrate the utilization of this method in the presence of both ischemic and non-ischemic cardiomyopathy. Second, we used a paralytic drug (rocuronium) and collected ECG data at end-expiration, while pacing the heart to minimize any localization error which may be attributed to chest movement. It might be possible that the presence of chest movement due to respiration could introduce error

into our results; however, we have developed techniques that can accurately estimate the respiratory cycle, thus allowing the timely ECG data acquisition and the delivery of ablative therapy [41]. Third, the pacing rates used in this study were sufficiently slow that an isoelectric baseline was still present. The method would need to be adapted to deal with rapid VT where no isoelectric baseline is present. Finally, in all our experiments, we have ensured that the initial catheter position co-localized with the cardiac chamber of the "target", i.e., in the RV. While VT in the setting of structural heart disease tends to have an RV exit, idiopathic VT may have an exit in either chamber. Further work will be required to ensure that our guidance algorithm can address the possibility of the initial position and target position being in different ventricular chambers.

The ISGA method used 64 body surface electrodes to localize both the origin of arrhythmia and an ablation tip. For the practical use in the clinical field, the number of body surface electrodes would have to be minimized. Further studies are required to improve algorithms for a reduced number of body surface electrodes.

CONCLUSION

In this study, the ISGA guidance method based on the SEMD model was tested to identify, in *computational space*, the locations of "*target*" electrodes and the ablation catheter. Three different type of "*target*" electrodes were used to simulate VT over a range of heart rates, and the ablation catheter was guided to the site of the "*target*" location by ISGA guidance method. We found a close correlation between the locations of the electrodes as measured in *computational space* and *real space*.

This study demonstrates the potential feasibility of using the ISGA method to guide

an ablation catheter to the origin of a pacing site by analyzing a few beats of body surface potentials without using electroanatomic or entrainment mapping. The present data demonstrate that the ISGA guidance method requires only a few seconds of pacing data to locate both the arrhythmic origin and the ablation catheter tip. Thus, we hypothesize that the ISGA method could be used to guide an ablation catheter to a VT focus without requiring the patient to be in VT for an extensive period. Importantly, when used in conjunction with currently available mapping technology, ISGA may present a promising technique to reduce ablation procedure time, especially in patients with hemodynamically unstable, poorly tolerated, VT.

Funding: None

Disclosures: RJC is a consultant for Medtronic, Inc. and for Sirona Medical Technologies, Inc. in which he also has an equity interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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FIGURES

Figure 1. Basic steps of the guidance procedure using Inverse Solution Guidance Algorithm method.

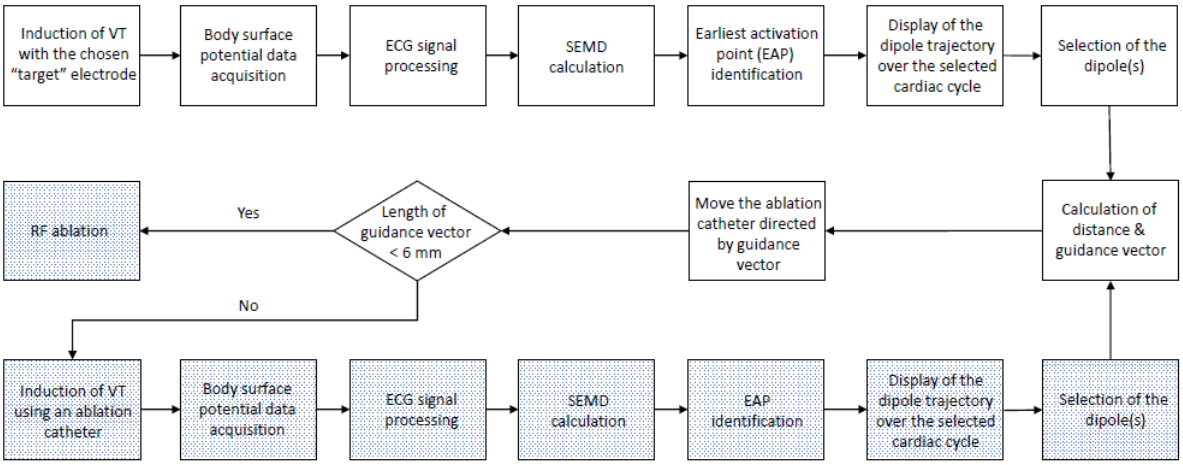


Figure 2. Typical swine experimental workflow. A) Example of distribution of 64 body surface electrodes on swine. B) Example of catheter (pink dot) trajectory, as guided by our algorithm, to final target position (green dot). C) Final fluoroscopic position in this particular example.

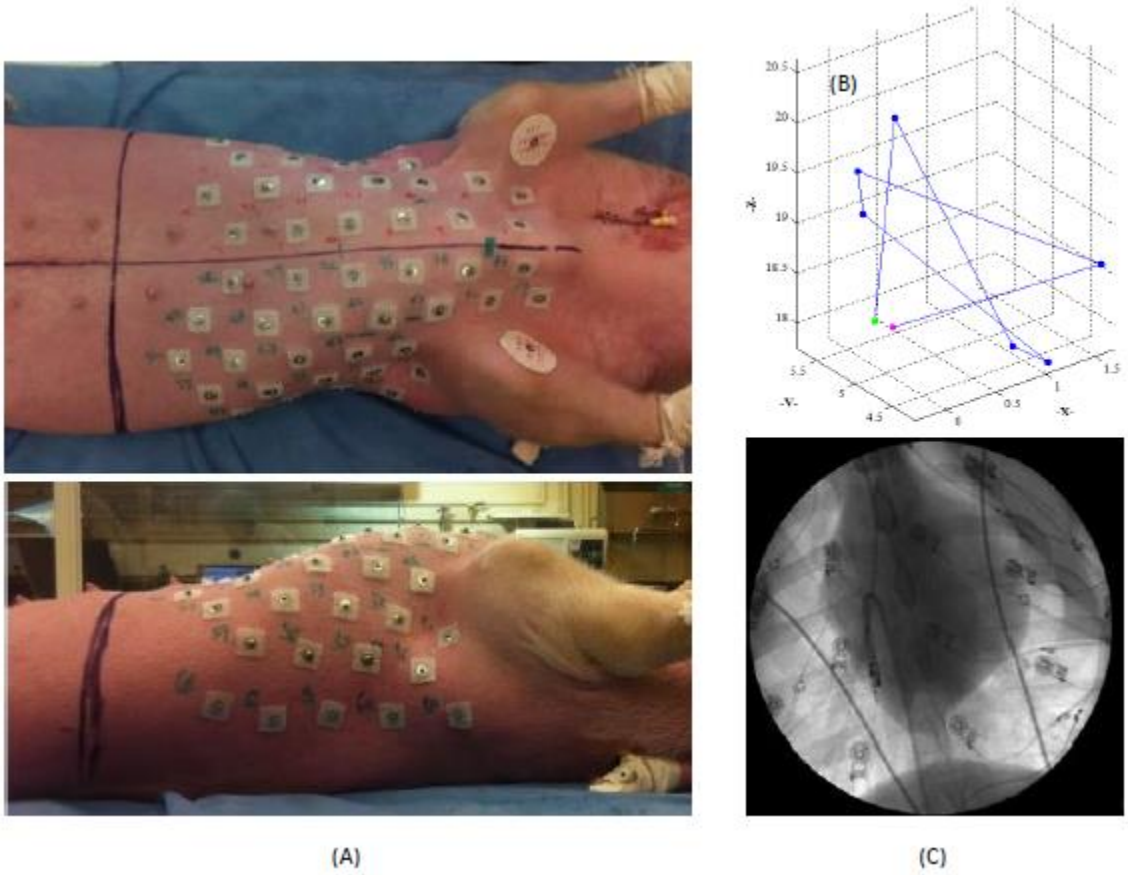
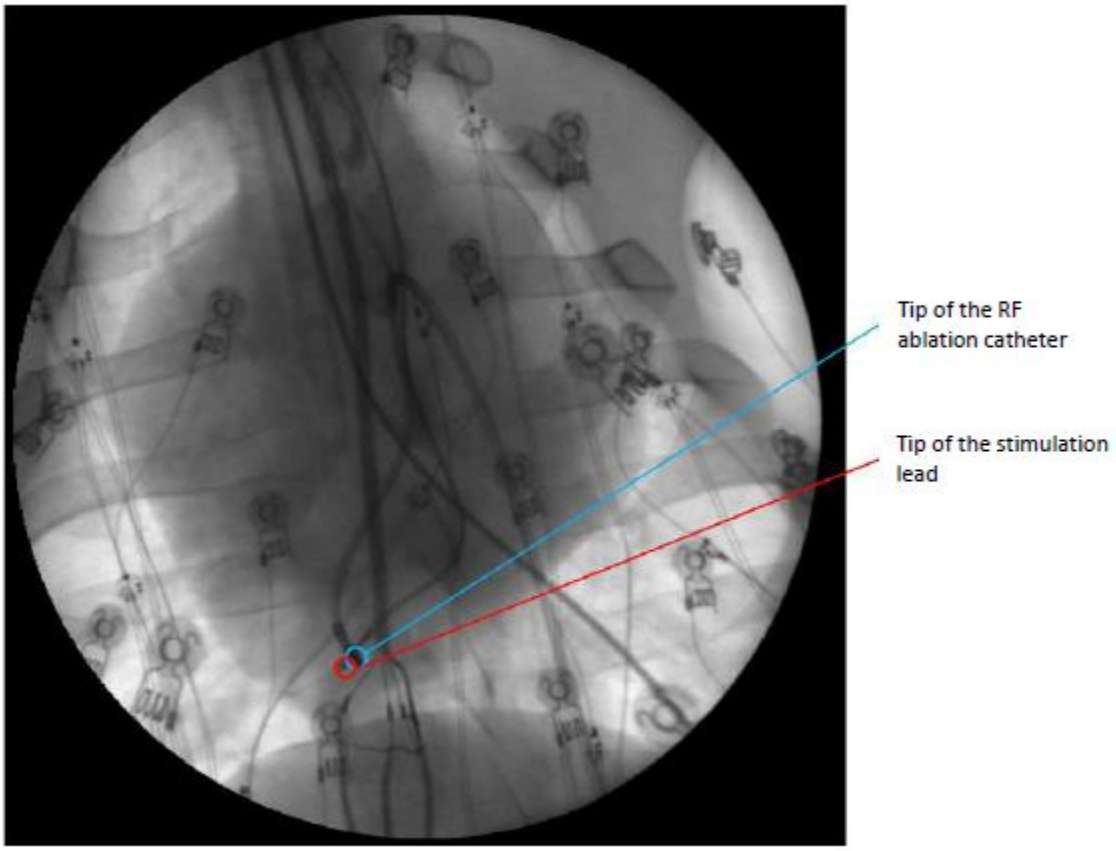
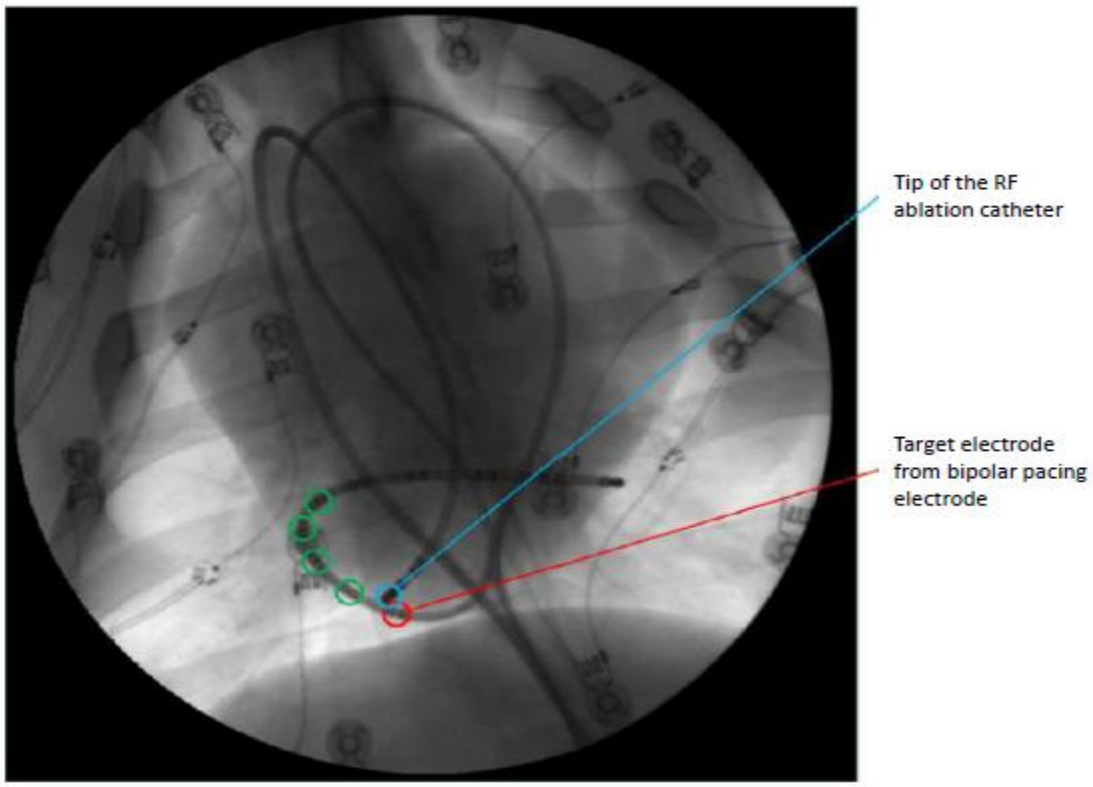


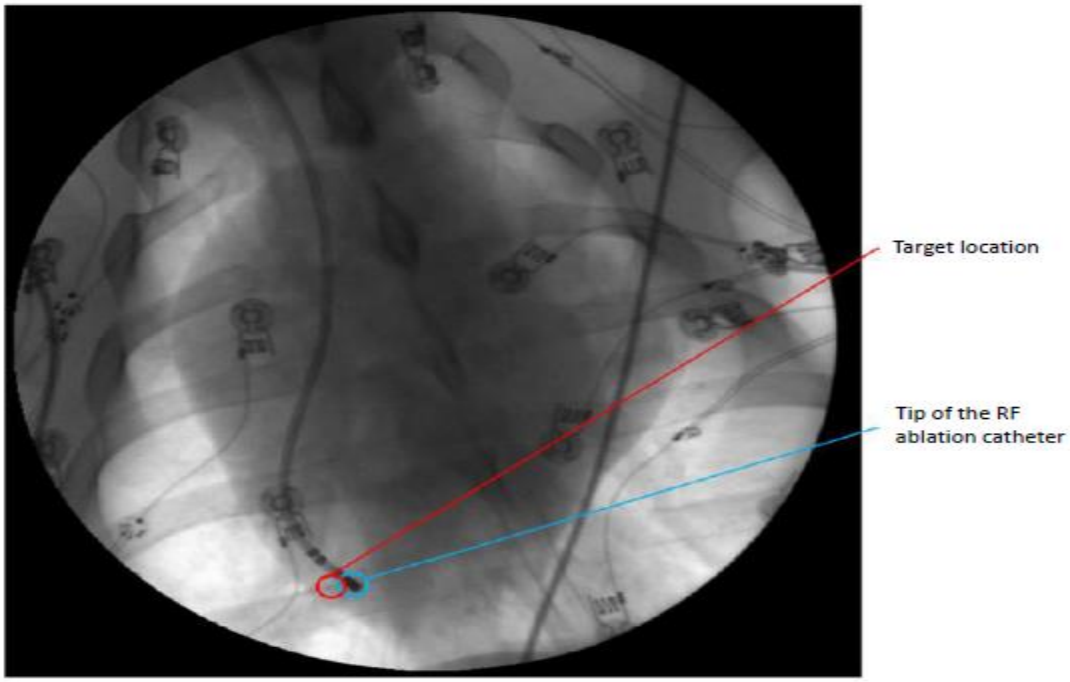
Figure 3. Sample fluoroscopic snapshots after moving the ablation catheter to the target location using the Inverse Solution Guidance Algorithm method for each experiment. A) The position of the pacing lead at the myocardium level was defined as the “target” site, B) A set of bipolar electrodes on the intracardiac mapping catheter on the epicardial surface was defined as the “target” site, and C) A random position of the ablation catheter tip on the endocardial surface was defined as the “target” site.



(A)

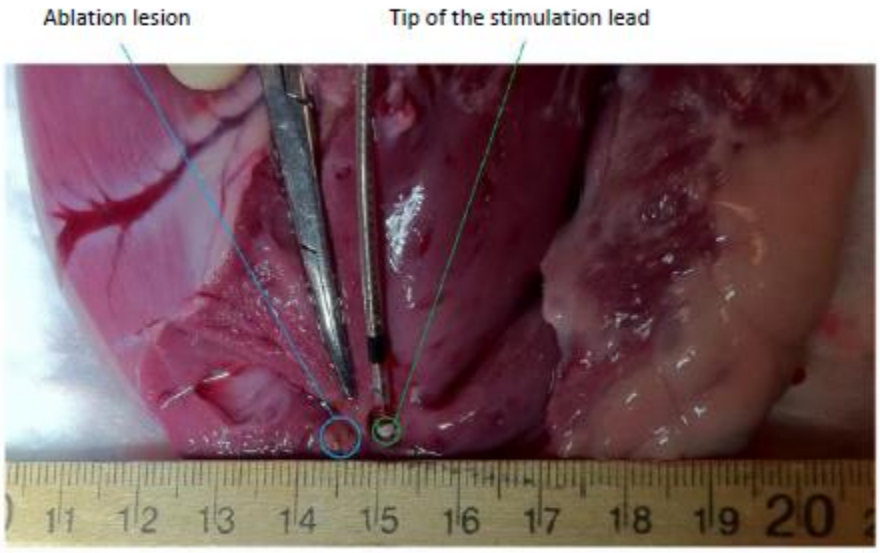


(B)



(C)

Figure 4. An example photo of a heart displaying the result of the catheter guidance. The blue circle represents the ablation lesion and the green circle represents the position of the pacing lead tip.



Tables

Table 1. Reproducibility error at the pacing rate of 120, 140, and 160 bpm (mean ± SD cm).

	Right ventricle	Left ventricle
120 bpm	0.27 ± 0.05	0.31 ± 0.12

140 bpm	0.30 ± 0.03	0.27 ± 0.06
160 bpm	0.35 ± 0.10	0.38 ± 0.08

Table 2. The catheter guidance results of three types of experiment.

Type of experiment	Pacing rate (bpm)	Number of trials	*Real space* "initial" distance (cm)	*Real space* "final" distance (cm)	Number of guidance movements
Type-1	120	3	6.46 ± 1.05	0.42 ± 0.03	3.67 ± 0.58
	140	2	5.45 ± 0.98	0.38 ± 0.04	4.50 ± 0.71
	160	2	6.24 ± 0.13	0.39 ± 0.05	4.00 ± 0.00
Type-2	120	0	-	-	-
	140	2	5.69 ± 1.27	0.48 ± 0.05	6.00 ± 0.00
	160	2	6.71 ± 0.86	0.47 ± 0.12	5.50 ± 2.12

Type-3	120	3	6.78 ± 0.32	0.67 ± 0.14	8.33 ± 0.58
	140	5	6.02 ± 1.04	0.67 ± 0.08	6.80 ± 0.84
	160	4	5.96 ± 1.08	0.67 ± 0.05	7.50 ± 1.29
	Total	12	6.04 ± 0.93	0.67 ± 0.08	7.07 ± 1.44

The initial distance is the distance between the target location and the initial RF ablation catheter location before catheter guidance. The final distance is the distance between the target location and the final RF ablation catheter location after ISGA guidance.

Table 3. The correlation coefficient between *computational space* and *real space* vector for each pacing rate.

	Correlation coefficient
120 bpm	0.84
140 bpm	0.86
160 bpm	0.80