REVISED MANUSCRIPT

Title: Non-randomised comparison of acute and long term outcomes of robotic versus manual ventricular tachycardia ablation in a single center ischemic cohort

Short title: Robotic vs. manual ischemic VT ablation

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ABSTRACT

INTRODUCTION: Robotically-guided radiofrequency (RF) ablation offers greater catheter stability that may improve lesion depth. We performed a non-randomised comparison of patients undergoing ventricular tachycardia (VT) ablation either manually or robotically using the Hansen Sensei system for recurrent implantable defibrillator (ICD) therapy.

METHODS: Patients with infarct-related scar underwent VT ablation using the Hansen system to assess feasibility compared with patients undergoing manual VT ablation during a similar time period. Power delivery during robotic ablation was restricted to 30W at 60 seconds. VT inducibility was checked at the end of the procedure. Pre-ablation ICD therapy burdens over 6mths were compared with post-ablation therapy averaged to a 6mth period.

RESULTS: 12 consecutive patients who underwent robotic VT ablation were compared to 12 consecutive patients undergoing a manual ablation. Patient demographics and comorbidities were similar in the two groups. A significantly higher proportion of robotic cases were urgent (9/12 (75%)) vs. manual (4/12 (33%)) (p=0.01). Post-ablation VT stimulation did not induce clinical VT in 11/12 (92%) in each group. There were no peri-procedural complications related to ablation delivery. Patients were followed up for approximately 2 years. Averaged over 6 months, robotic ICD therapy burdens fell from 32 (5-400) events to 2.5 (0-11) (p=0.015). Therapy burden fell from 14 (10-25) to 1 (0-5) (p=0.023) in the manual group. There was no difference in long-term outcome (p=0.60) and mortality ((4/12 (33%) p=1.0).

CONCLUSION: Robotically guided VT ablation is both feasible and safe when compared to manual ablation with good acute and long term outcomes.

Key Words:

Radiofrequency Catheter Ablation

Scar related Monomorphic Ventricular Tachycardia

Hansen Sensei Robotic System

Programmed ventricular stimulation

Internal cardioverter defibrillator therapies

INTRODUCTION

Ventricular Tachycardia (VT) remains a major cause of morbidity and mortality in patients with ischemic heart disease. Although implantable cardioverter-defibrillators (ICD) prevent sudden cardiac death, repeated device therapies have a major impact on quality of life [1]. Recurrent ICD therapies are associated with worse prognosis [2]. VT ablation has been used to both reduce and prevent ICD therapy. However, despite the introduction of cardiac mapping systems, irrigated tip catheters and substrate based ablation strategies, patients continue to experience on-going ICD therapies for VT recurrence in long term follow up [3-5]. Failure to achieve lesions with sufficient depth to target circuits near the epicardial surface is a potential cause for recurrent VT.

Robotically assisted ablation has been suggested as a method for increasing lesion depth and the Hansen Sensei® X Robotic Catheter system (Hansen Medical Inc., Mountain View, CA, USA) has been shown to be feasible for use in cardiac ablation [6]. In brief, it comprises the physician's workstation, remote catheter manipulator (RCM) and a steerable guide catheter (Artisan™ Control Catheter). The movements of a joystick within the physician's workstation are transferred into movements of the RCM, a robot that controls pull wires within the steerable sheath. The tensile strength of the pull-wires within the steerable sheath maintains its shape allowing improved catheter stability and increased lesion depth [7].

In animal studies, we demonstrated that at equivalent ablation settings, a more rapid and greater reduction in local electrogram amplitude during robotic ablation compared with manual. Macroscopic examination of robotic lesions was also associated with greater lesion transmurality [8].

The use of robotic catheter ablation in atrial based arrhythmias is well described [9-13]. Feasibility in VT ablation has also been proposed [14-17]. Robotic catheter ablation for scar related VT offers an attractive strategy in trying to target channels with deeper lesions. There is also the added benefit of reduced operator radiation exposure for these long procedures.

This study aimed to assess the feasibility and safety of using the Sensei Robotic System to guide VT ablation in a series of patients with post infarct related scar and be the first to compare acute and long-term outcome data to a cohort of patients who underwent manual ablation.

METHODS

Patients

The departmental procedural database was reviewed to identify all patients who underwent post infarct scar related VT ablation for recurrent ICD therapies using the Hansen Sensei Catheter Control System between January 2010 to January 2014. In the same time period that all robotic cases were identified, all manual ablations were also reviewed. These patients included those presenting acutely to our center either directly or from neighbouring local hospitals or electively following assessment in ICD clinic. Patients were excluded if they were involved in any other VT ablation study or if they were followed up outside of our institution. Patients were also excluded if they failed to undergo a programmed electrical ventricular stimulation to assess inducibility post ablation. Long term outcome data was gathered from the patients' clinical case notes, or their ICD device downloads from clinic or remote monitoring. All patients included in this study signed an informed consent before the ablation procedure.

End Points

The immediate ablation outcome was assessed with VT inducibility following programmed ventricular electrical stimulation. Patients were defined as non-inducible (group A), inducible for non-clinical VT (group B) and inducible for the clinical VT (group C).

Long-term outcomes were defined by the cumulative burden of appropriate ICD therapies (anti-tachycardia pacing (ATP) + shocks). This was assessed from 6 months pre-ablation and compared with the post ablation therapy burden till their most recent device interrogation or redo procedure. ICDs were interrogated whenever symptoms suggested delivery of device therapy in addition to routine follow-up in ICD clinic and by remote follow up. A 6 month proportion of each patient's total therapy burden during follow up was calculated for each patient ((6/follow-up duration (mths)) x total therapies post ablation)) allowing direct comparison with the 6 month pre-ablative burden.

Electrophysiology Study and Mapping

A conventional Electrophysiology Recording system (BARD, LabSystem™ PRO Review Workstation, Lowell, MA, USA) and the CARTO XP ™ electro-anatomical mapping system (Biosense Webster Inc., Diamond Bar, CA, USA) were used in all cases. Procedures were performed either under conscious sedation or general anaesthesia. Patients were continuously monitored throughout the procedure by invasive systemic arterial

pressure and non-invasive oxygen saturation. For systemic anticoagulation, repeat bolus injections of heparin based on the activated clotting time (ACT) measurements were given (target 300-350s). A trans-septal puncture was performed from a right femoral venous access and a J-wire placed in the left upper pulmonary vein before the sheath was withdrawn into the right atrium. The irrigated Hansen Artisan sheath was loaded with an open-irrigated radiofrequency ablation catheter (Navistar ThermocoolTM, Biosense Webster Inc.) and introduced through a long 14F sheath via the left femoral vein. The robotic catheter was steered along the J-wire to enter the left atrium. Intra-cardiac echocardiography was not used. The robotic sheath was steered into the left ventricle with the outer sheath of the Artisan positioned within the left atrium to support access to all parts of the left ventricle. A bipolar voltage map was created at standard scar settings. The Navistar Catheter was used for mapping the ventricle in all robotic cases. The Hansen system's integrated contact force feature, Intellisense™, was used for contact force feedback initially and latter cases used the Navistar SmartTouch™ catheter (Biosense Webster Inc) instead. VT was initiated using programmed electrical stimulation from two sites with a basic drive cycle of 600ms and/or 400ms and up to three extrastimuli. In patients with haemodynamically tolerated VT an activation map during VT was also created.

In the manual cases, access to the left ventricle was gained via a transeptal puncture or retrograde approach depending on the location of scar. The Navistar catheter was used for mapping the ventricle in all manual cases.

Ablation strategy and settings:

In stable VT cases the CARTO™ activation maps were combined with conventional entrainment manoeuvers to define the target ablation sites, ideally at sites with mid diastolic potentials. For poorly tolerated VT, the voltage map was used to perform substrate ablation using one or more of the following; local capture with a 12/12 pacemap of the clinical or induced VT [19], scar border location [20] , presence of a late potential [21] or completion of a linear lesion [22], as has been previously described. All patients undergoing robotic procedures in our unit using irrigated tip RF applications were limited to 30W at 60secs with a flow rate of 17mls/min and a temperature limit of and a temperature limit of 40^{o}C. In the manual group, power output and delivery time was at the discretion of the operator. ICD programming post procedure was left unchanged.

Statistical Analysis

Categorical variables were expressed as percentages. Continuous variables were expressed as mean ± 1 standard deviation for parametric data and/or median ± interquartile range for non-parametric data. Paired non

parametric data were analysed using the Wilcoxon Signed Ranks test for non-parametric data. Unpaired continuous variables were analysed using a student's t-test for parametric data and Mann-Whitney U-Test for non-parametric data. Fisher's Exact test was used for categorical data. A value of $p \leq 0.05$ was considered significant.

RESULTS

Patients

60 patients underwent scar related VT ablation during the study period. Figure 1 illustrates the number of patients within each exclusion criteria. This included 18 patients with non-ischemic cardiomyopathy and 9 patients involved in a concurrent VT ablation trial that commenced during this interval in our institution. 2 patients presented with VT below the device detection zone. 2 patients had their ICD implanted post ablation. The procedure was abandoned in 3 patients owing to transeptal puncture related complication. This included 1 patient who was a planned robotic procedure.

Of the remaining 26 patients, 12 underwent robotically guided post infarct VT ablation. The majority of patients were male (9/12, 75%) with a mean age of 70.8±5.5years at the time of the procedure. 42% (5/12) had diagnosed essential hypertension and 50% (6/12) type II diabetes mellitus. The mean body mass index (BMI) was 29.0±5.3 kg/m2. Patients had significantly impaired left ventricular function (28±14%) and 67% (8/12) had undergone coronary artery bypass grafting (CABG) with the remainder having undergone percutaneous coronary intervention (PCI). 42% (5/12) were biventricular paced prior to the procedure.

Of the 14 patients who underwent manually guided ablation, 2 were followed up externally and excluded from the study. There was no significant difference in baseline characteristics and comorbidities between the remaining 12 manually ablated patients and the robotic group (table 1).

Pre-procedural therapy burden

The Sensei robotic system was often considered for ablation in those who had failed manual procedures, and those presenting urgently with multiple ICD therapies/storm. In those who failed manual procedures, the coronary angiograms were also reviewed for consideration of intracoronary ethanol.

A total of 9/12 robotic ablations (75%) were undertaken in those presenting urgently, whereas only 4/12 (33%) were as such in the manual arm (p=0.01). 4/12 (33%) of the patients had undergone failed manual procedures compared 1/12 (8%) in the manual group undergoing a redo ablation (p=0.32). A numerically higher median

pre-ablation therapy burden was evident in the robotic arm (32 (5-400 IQR)) as compared to the manual arm (14 (10-25 IQR)) (p=0.49).

Procedural data

In the cohort that underwent robotic VT ablation, 2.4±1.9 different VT morphologies were induced in each patient. Mapping and ablation was performed in VT in 4 patients. 8 patients underwent substrate ablation only for unstable or non-sustained VT. Scar and ablation lesions were located around the anterior wall (including anterolateral and antero-septal walls) in 4 patients, around the inferior wall (including infero-septal and infero-lateral walls) in 4 patients, and apically (including 2 apical aneurysms) in 4 patients. All areas could be reached by robotic manipulation and procedures were all completed robotically. An average of 35±25 RF applications were delivered with a maximum temperature of 38.3±2.4ºC, power of 29.6±2.7 Watts and duration of 59.4±3.4 seconds.

The intra-procedural data for both robotic and manual groups are summarised in table 2. There was no significant difference in ventricular mapping times (51(±31) vs. 51(±34)mins, p=0.95) and number of CARTO points collected (168 (±97) vs. 209 (±107), p=0.54) between the robotic and manual approaches. Owing to the restriction in power output and ablation duration, RF delivery in patients undergoing robotically guided ablation was of significantly shorter duration (59.4±-3.4 vs. 71.9±19.1sec, p=0.05) with lower power output (29.6±2.7 vs. 44.6±10.0W, P<0.001) compared to those undergoing a manual ablation. A greater number of ablation lesions (35±25 vs. 23±9, p=0.15) were delivered over a significantly longer procedural duration (312±91 vs. 218±93mins, p=0.02) in the robotic cohort (defined as the time the patient arrived in the electrophysiology laboratory to subsequent exit). There was a trend towards an increased median fluoroscopic time (42.6±11.4 vs. 32.7±18.6mins, p=0.13) in the robotic group as compared to the manual.

Acute and long term Outcomes:

Robotic arm:

A comparison between the acute and long term procedural outcomes between the robotic and manual groups is detailed in table 3. Following programmed ventricular stimulation at the end of the procedure, 6/12 (50%) had no VT inducible (group A), 5/12 (42%) had non clinical VT only (group B), and 1/12 (8%) had clinical VT inducible (group C). 6/12 (50%) were maintained on amiodarone post procedure. Patients were followed up for a mean of 24.1±19.1 months. Data was available from patient attendances or ICD downloads from an average

of 6.8±3.9 device interrogations. The total therapy burden (ATP + shocks) fell to a median of 3.5 (1-11) events. The calculated averaged 6 month post procedural therapy burden fell significantly to a median of 2.5 (0-11) (p=0.015). This represented a 95% therapy burden reduction. 3/12 (25%) patients required a further ablation procedure during this follow up period. Figure 2 demonstrates pre and post ablation therapy burdens for each robotic patient averaged over 6 months.

Within Group A (non-inducible 1-6), 3/6 (50%) patients had already undergone at least 2 previous manual ablations. This included "patient-3", who was referred for robotic ablation owing to multiple ICD shocks despite 3 previous manual ablation procedures and maximal antiarrhythmic therapy (including amiodarone and mexilitine). Figures 3a&b show fluoroscopic views of the ablation catheter at the apical septum. Ablation at this site successfully terminated the clinical VT (figure 3c). Over more than 3 years of follow up, no ICD therapies have been detected. This also included "patient-4" who presented with ICD storm on a background of 1501 appropriate ICD therapies (majority ATP). Ablation targeted the anterolateral wall. The patient remained therapy free for 120 days, and has experienced only 10 therapies over more than a 4 year follow up period. This also included "patient-2" who presented with ICD storm. Following mexilitine administration, VT could not be induced in the lab, hence a substrate guided approach targeting the basal inferoseptum was performed. Having remained therapy free for 2 months, the patient represented in storm, and underwent a surgical ablation following which she remained therapy free for 2 years, till she eventually expired from end stage heart disease [18].

Within Group B (non-clinical VT only 8-12), "patient-7" experienced 11 appropriate ICD therapies (including 2 shocks) over the preceding 2 months. 7 VT morphologies were inducible in the lab – only 1 matched the documented pre-procedural VT, and was inducible from the start. 6 out of 7 VT's, including the clinical VT were successfully ablated to non-inducibility. Over more than 3 years of follow up, this patient has had only 1 appropriate ATP episode. Patient 10 was admitted with incessant tolerated VT that was non-pace-terminable and refractory to electrical cardioversion. The clinical VT was mapped towards the LV apex, including an aneurysmal component and terminated with ablation. A second VT was not eliminated, but was pace-terminable at the end of the procedure. Over a 29 month follow up, this patient has had only 1 appropriate ATP episode. Patient 11 presented with ICD storm refractory to amiodarone and mexilitine, on a background of 1557 appropriate ICD therapies. 5 VT's, including the clinical VT, were induced in the lab and ablation was targeted towards the apical inferior territory. 4 out of 5 VT's, including the presumed clinical VT, were successfully ablated to non-inducibility. The remaining VT was not haemodynamically tolerated requiring electrical

cardioversion. The patient however represented at month 11 and 13 with VT and underwent manual VT ablation procedures on each occasion. VT continued to occur, however owing to a post procedural dense stroke after the 3rd ablation, no further interventional approaches were considered. The patient expired at month 26 from end stage heart disease. Group C (Clinical VT inducible) included patient 12 alone, who presented with ICD storm on a background of 561 ICD therapies. 2 inducible VT morphologies were inducible in the lab, both of which were associated with haemodynamic instability. Ablation was performed by pace-mapping and substrate modification however despite multiple ablation lesions, VT 1 was still inducible. The procedure was terminated due to periods of haemodynamic instability and inability to find any further perfect pace-mapping sites in the region of interest. The patient experienced only 4 ATP's over 7 month follow up, and expired thereafter from end stage heart disease. The intra-procedural and long term outcomes for each patient have been categorised per group and summarised in table 4a.

Manual arm:

Following programmed ventricular stimulation at the end of the procedure, 8/12 (67%) had no VT inducible (group A), 3/12 (25%) had nonclinical VT only (group B), and 1/12 (8%) had clinical VT inducible (group C). 5/12 (42%) were maintained on amiodarone post procedure. Patients were followed up for a mean of 21.1±14.6 months. Data was available from patient attendances or ICD downloads from an average of 4.3±3.2 occasions. The total therapy burden (ATP + shocks) fell to a median of 1 (0-14) events. The averaged 6 month therapy burden fell significantly to median of 1 (0-5) (p=0.023). 4 patients required redo ablations, 3 for multiple recurrent therapies (30, 240, 660 days post ablation) and 1 for slow incessant VT unresponsive to medical therapy 90 days post ablation. Figure 2 demonstrates pre and post ablation therapy burdens for each manual patient averaged over 6 months. The intra-procedural and long term outcomes for each patient have been categorised per group and summarised in table 4b.

Procedure-Related Complications and Death

There were no peri-procedural complications related to ablation delivery in either of the groups in this study. The 30-day procedural mortality was nil in both arms. In the robotic group 4/12 (33%) patients died during this follow up interval an average 16.0±12.2 months remote of the procedure. 3 died from end stage heart failure and 1 died following a stroke. In the manual group, 4/12 (33%) patients died an average 15.5±7.0 months remote of the procedure. 3 died from end stage heart failure and 1 died from mitral valve endocarditis.

DISCUSSION

In this study, we have demonstrated both the feasibility and safety of using the Hansen Sensei® Robotic System in performing LV endocardial mapping and ablation in 12 patients who underwent post infarct scar-related VT ablation. The robotic system was often utilised in patients presenting urgently with multiple ICD events/storm, and those who had recurrence of VT despite a previous ablation procedure. Robotic VT ablation resulted in a 95% reduction in total ICD therapy burden (ATP + shocks) compared over a 6 month averaged interval ($p=0.015$).

We compared our acute and long-term robotic outcome data with manual cases over a similar time period. Despite a potentially more complex arrhythmic substrate in the robotic arm, the acute and long-term procedural outcomes between the two groups were similar. The clinical VT was non inducible in all but 1 patient in both arms at the end of the case and the total post procedural ICD therapy burden fell significantly in both arms, to a median of 2.5 (0-11) episodes in the robotic and 1 (0-5) in the manual ($p=0.60$).

We intentionally reduced the power delivery during robotic ablation to no more than 30W, and delivered each lesion for no more than 60 seconds. This was based on previous animal studies where, at 45W, charring, popping and perforation were seen [23]. As there was no restriction in the manual arm, both power output and duration were significantly higher for each ablation lesion delivered. The only other case series of robotic guided VT ablation allowed for a higher power output (50W) and also demonstrated a significant reduction in the frequency of patient VT episodes [17]. The absence of any acute procedural complications directly attributable to the robotic system or during ablation in both studies series is notable. The endpoint of non-inducibility of clinical VT is always sought but targeting non-clinical inducible VT is often a decision based on the risk-benefit decision made by the operator based on the clinical status of the patient and will also depend on the aggressiveness of the induction protocol. Therefore, outside a fully protocolized randomized study it is difficult to judge whether difference in procedure duration are due to the nature of the induction method or the endpoints that were sought.

The mean procedure duration and fluoroscopic times in the robotic arm were greater than in the manual arm. This was not the result of the mapping time which was similar. There are additional steps in a robotic procedure which include the introduction of a 14F femoral long sheath, advancing the Artisan sheath to the right atrium, navigation of the catheter and Artisan-sheath across the trans-septal puncture site and repositioning the outer sheath remotely during manipulation within the LV. Although non-significant, there were more VTs induced in the robotic arm implying more complex procedures in the robotic group.

We found movement of the ablation catheter within the left ventricle using the Hansen robotic sheath easier than manual manipulation of the ablation catheter within a deflectable sheath particularly for maintaining stability during RF delivery. Manoeuvrability around the papillary muscles was not more difficult with robotic ablation and there were no papillary muscle related complications. Reaching the outflow tract and mitral annulus required adjustment of the outer sheath and torque settings so that the inner sheath turned back on itself, but this was still easier to do robotically than manually, and, more importantly, with greater stability.

Several studies have reported only long term freedom from any VT recurrence post ablation as a marker of success [24]. VT ablation alters the existing substrate at the time of the procedure without influencing the progression of the underlying disease. Recurrence of VT during long term follow up may well be associated with disease progression through time, independent of the ablation procedure [25]. This outcome measure is particularly useful in studies of early ablation where many control patients do not receive any therapy. However, in this study our patients had advanced disease with a high burden of successful ATP and reduction of therapy burden was a primary goal. Other studies have also reported overall reduction in ICD therapy burdens as a reflection of long term success. Caution must be reserved in making comparisons with other studies owing to differences in ICD programming and use of antiarrhythmics post procedure. The Thermocool VT ablation Trial [26] and Euro VT study [27] both describe pre and post ICD therapy burdens in a cohort of patients with severe left ventricular impairment undergoing conventional VT ablation secondary to remote myocardial infarction. Both studies were large multicentre studies that described the effectiveness of saline irrigated catheter technology in VT ablation with electro-anatomic mapping systems, an approach we used in all cases. Ablation of all inducible VTs was accomplished in 49% of the 231 patients in the Thermocool trial. In our robotic cohort, complete non inducibility was seen in 50%. The Euro VT study witnessed 81% acute procedurally success in the 63 patients included, though some patients required 2 procedures. Of the 142 patients with ICD's that survived to 6 months in the Thermacool study, median VT episodes were reduced from 11.5 to 0, which was similar to our manual group. Although 47% of patients experienced VT recurrence within this interval, the frequency of VT was reduced by >75% in 67% of patients. VT recurrence in Euro VT was also high at 49% at 12 months, though mean ICD therapies fell from 60±70 pre-ablation to 14±15 six months post ablation ($P = 0.02$). Mortality rates at 1 year were 8% and 18% respectively. We witnessed 33% mortality at 2 year average follow up in both the robotic and manual arms. In summary, outcomes in both these large ablation studies were similar to our robotic cohort. Furthermore, power outputs in both studies averaged 45W. Fluoroscopy times and procedural durations in both studies were similar to our robotic cohort, however the operators using the

robotic approach had the benefit of being remote from the x-ray tube for the majority of the procedure with minimal radiation.

LIMITATIONS

The data presented is a small series from a single center where cases were performed by experienced operators. Larger, randomised studies will be required to further understand the clinical utility of this approach over manual ablation. A prospective, multicentre, randomised study (ERASE VT: NCT01182389) comparing robotic guided catheter ablation against medical therapy is on-going.

CONCLUSIONS

We have demonstrated that radiofrequency ablation of scar-related VT using the Hansen Sensei® X Robotic Catheter System is feasible with good long term outcomes, and this includes patients who have failed manual ablations and presented acutely with multiple ICD therapies/storm. Despite a higher pre-procedural therapy burden, when compared to a series of patients who underwent manual guided ablation, acute and long-term outcomes were similar.

Authors contributions:

VL: Data analysis/interpretation, Statistics, Drafting article

SJC: Data analysis/interpretation, Statistics, Drafting article & joint first author

MKW: Data analysis/interpretation, Drafting article,

MSS: Data analysis/interpretation, Statistics

IW: Data collection, Approval of article

NL: Data collection, Approval of article

PBL: Data collection, Approval of article

ZW: Data collection, Approval of article

SH: Data collection, Approval of article

DL: Data collection, Approval of article

NSP: Data collection, Approval of article

DWD: Data collection, Approval of article

PK: Concept/design, Critical revision of article, Approval of article

REFERENCES

1. Schron EB, Exner DV, Yao Q, Jenkins LS, Steinberg JS, Cook JR, Kutalek SP, Friedman PL, Bubien RS, Page RL, Powell J. Quality of life in the antiarrhythmics versus implantable defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. Circulation 2002; 105: 589–594

2. Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ, Raitt MH, Reddy RK, Marchlinski FE, Yee R, Guarnieri T, Talajic M, Wilber DJ, Fishbein DP, Packer DL, Mark DB, Lee KL, Bardy GH. Prognostic importance of defibrillator shocks in patients with heart failure. N. Engl. J. Med. 2008; 359, 1009–1017

3. Gonska D-B, Cao K, Schaumann A, Dorszewski A, von zur Muhlen F, Kreuzer H. Catheter ablation of ventricular tachycardia in 136 patients with coronary artery disease: results and long-term follow-up. *J Am Coll Cardiol*. 1994;24:1506–1514.

4. Dinov B, Fiedler L, Schönbauer R, Bollmann A, Rolf S, Piorkowski C, Hindricks G, Arya A. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: results from the Prospective Heart Centre of Leipzig VT (HELP-VT) Study. Circulation. 2014 Feb 18;129(7):728-36

5. Kuck KH1, Schaumann A, Eckardt L, Willems S, Ventura R, Delacrétaz E, Pitschner HF, Kautzner J, Schumacher B, Hansen PS; VTACH study group. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): A multicentre randomized controlled trial. Lancet 2010; 375: 31-40.

6. Kanagaratnam P, Koa-Wing M, Wallace DT, Goldenberg AS, Peters NS, Davies DW. Experience of robotic catheter ablation in humans using a novel remotely steerable catheter sheath. J Interv Card Electrophysiol. 2008 Jan;21(1):19-26

7. Okumura Y, Johnson SB, Bunch TJ, Henz BD, O'Brien CJ, Packer DL. A systematical analysis of in vivo contact forces on virtual catheter tip/tissue surface contact during cardiac mapping and intervention. J Cardiovasc Electrophysiol 2008; 19:632–640.

8. Koa-Wing M1, Kojodjojo P, Malcolme-Lawes LC, Salukhe TV, Linton NW, Grogan AP, Bergman D, Lim PB, Whinnett ZI, McCarthy K, Ho SY, O'Neill MD, Peters NS, Davies DW, Kanagaratnam P. Robotically assisted ablation produces more rapid and greater signal attenuation than manual ablation. J Cardiovasc Electrophysiol 2009; 20:1398– 1404.

9. Malcolme-Lawes LC, Lim PB, Koa-Wing M, Whinnett ZI, Jamil-Copley S, Hayat S, Francis DP, Kojodjojo P, Davies DW, Peters NS, Kanagaratnam P. Robotic assistance and general anaesthesia improve catheter stability and increase signal attenuation during atrial fibrillation ablation. Europace. 2013 Jan;15(1):41-7.

10. Wazni OM, Barrett C, Martin DO, Shaheen M, Tarakji K, Baranowski B, Hussein A, Callahan T, Dresing T, Bhargava M, Kanj M, Tchou P, Natale A, Saliba W. Experience with the Hansen robotic system for atrial fibrillation ablation – lessons learned and techniques modified: Hansen in the real world. J Cardiovasc Electrophysiol 2009; 20:1193–1196.

11. Di Biase L, Wang Y, Horton R, Gallinghouse GJ, Mohanty P, Sanchez J, Patel D, Dare M, Canby R, Price LD, Zagrodzky JD, Bailey S, Burkhardt JD, Natale A. Ablation of atrial fibrillation utilizing robotic catheter navigation in comparison to manual navigation and ablation: Single-centre experience. J Cardiovasc Electrophysiol 2009; 20(12):1328-1335

12. Hlivak P, Mlcochova H, Peichl P, Cihak R, Witchterle D, Kautzner J. Robotic Navigation in catheter ablation for paroxysmal atrial fibrillation: Midterm efficacy and predictors of postablation arrhythmia recurrence. Journal of Cardiovascular electrophysiology 2011; 22(5): 534-40.

13. Steven D, Rostock T, Servatius H, Hoffmann B, Drewitz I, Müllerleile K, Meinertz T, Willems S. Robotic versus conventional ablation for common-type atrial flutter: A prospective randomized trial to evaluate the effectiveness of remote catheter navigation. Heart Rhythm 2008; 5:1556–1560.

14. Lorgat F, Pudney E, van Deventer H. Robotically assisted ventricular tachycardia substrate modification ablation with the novel Lynx(TM) integrated sheath and RF ablation catheter. Cardiovasc J Afr. 2013 Apr 23;24(3):e9-e11.

15. Duncan E, Johns N, Schilling RJ, Sporton S. Robotic catheter navigation within the left ventricle. Pacing Clin Electrophysiol. 2011 Nov;34(11):102-4.

16. Koa-Wing M1, Linton NW, Kojodjojo P, O'Neill MD, Peters NS, Wyn Davies D, Kanagaratnam P. Robotic catheter ablation of ventricular tachycardia in a patient with congenital heart disease and Rastelli repair. J Cardiovasc Electrophysiol 2009; 20:1163–1166.

17. Valderrábano M, Dave AS, Báez-Escudero JL, Rami T. Robotic catheter ablation of ventricular tachycardia: initial experience. Heart Rhythm 2011; 8: 1837–1846.

18. Wright IJ, Kojodjojo P, Jamil-Copley S, Davies DW, Stanbridge RD, Kanagaratnam P. Sustained tachycardia in a cardiac resynchronization therapy recipient: what is the mechanism of tachycardia? Pacing Clin Electrophysiol. 2013 Nov;36(11):1427-30.

19. Tung R, Mathuria N, Michowitz Y, Yu R, Buch E, Bradfield J, Mandapati R, Wiener I, Boyle N, Shivkumar K. Functional pace-mapping responses for identification of targets for catheter ablation of scar-mediated ventricular tachycardia. Circ Arrhythm Electrophysiol. 2012 Apr;5(2):264-72

20. Tilz RR, Makimoto H, Lin T, Rillig A, Deiss S, Wissner E, Mathew S, Metzner A, Rausch P, Kuck KH, Ouyang F. Electrical isolation of substrate after myocardial infarction: a novel ablation strategy for unmappable ventricular tachycardias: feasibility and clinical outcome. Europace 2014;16: 1041–1053.

21. Vergara P1, Trevisi N, Ricco A, Petracca F, Baratto F, Cireddu M, Bisceglia C, Maccabelli G, Della Bella P.J Late potentials abolition as an additional technique for reduction of arrhythmia recurrence in scar related ventricular tachycardia ablation. Cardiovasc Electrophysiol. 2012 Jun;23(6):621-7.

22. Soejima K, Suzuki M, Maisel WH, Brunckhorst CB, Delacretaz E, Blier L, Tung S, Khan H, Stevenson WG: Catheter ablation in patients with multiple and unstable ventricular tachycardias after myocardial infarction: short ablation lines guided by reentry circuit isthmuses and sinus rhythm mapping. Circulation 104:664-669, 2001

23. Di Biase L, Natale A, Barrett C, Tan C, Elayi CS, Ching CK Wang P, Al-Ahmad A, Arruda M, Burkhardt JD, Wisnoskey BJ, Chowdhury P, De Marco S, Armaganijan L, Litwak KN, Schweikert RA, Cummings JE. Relationship between catheter forces, lesion characteristics, 'popping', and char formation: experience with robotic navigation system. J Cardiovasc Electrophysiol 2009;20:436–40.

24. El-Damaty A1, Sapp JL. The role of catheter ablation for ventricular tachycardia in patients with ischemic heart disease. Curr Opin Cardiol. 2011 Jan;26(1):30-9.

25. Yokokawa M1, Desjardins B, Crawford T, Good E, Morady F, Bogun F. Reasons for recurrent ventricular tachycardia after catheter ablation of post-infarction ventricular tachycardia. J Am Coll Cardiol. 2013 Jan 8;61(1):66-73.

26. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H; Multicenter Thermocool VT Ablation Trial Investigators. Irrigated Radiofrequency Catheter Ablation Guided by Electroanatomic Mapping for Recurrent Ventricular Tachycardia After Myocardial Infarction: The Multicenter Thermocool Ventricular Tachycardia Ablation Trial. Circulation. 2008;118:2773-2782

27. Tanner H, Hindricks G, Volkmer M, Furniss S, Kuhlkamp V, Lacroix D, DE Chillou C, Almendral J, Caponi D, Kuck KH, Kottkamp H. Catheter ablation of recurrent scar-related ventricular tachycardia using electroanatomical mapping and irrigated ablation technology: Results of the prospective multicenter Euro-VT-Study. J Cardiovasc Electrophysiol 2010; 21: 47-53.

Table 1. Baseline clinical characteristics

Clinical Characteristics	Robotic	Manual	p value
N	12	12	1*
Male	9/12 (75%)	12/12 (100%)	0.22*
Age/yrs (mean±SD)	70.8±5.5	73.8±6.7	0.24+
BMI (kg/m2)	29.0±5.3	26.2±4.8	0.18+
HTN	5/12 (42%)	5/12 (42%)	1*
DM	6/12 (50%)	6/12 (50%)	1*
CABG	8/12 (67%)	7/12 (58%)	1*
LVEF 2D echo: (mean±SD)	28.1±13.7%	31.2±10.7%	0.53+
AAD pre ablation			
Amiodarone	7/12 (58%)	8/12 (67%)	1*
Beta blocker	12/12 (100%)	12/12 (100%)	1*
Mexilitine	4/12 (33%)	1/12 (8%)	0.32*
Cardiac resynchronisation	5/12 (42%)	7/12 (58%)	0.68*

AAD – Antiarrhythmic drug. BMI - Body mass Index; CABG – Coronary artery bypass grafting; DM - Diabetes Mellitus; HTN – Hypertension; LVEF – left ventricular ejection fraction; *Fisher's exact test; +Students t-test.

Table 2: Intra-procedural data for both robotic and manual groups

Characteristics	Robotic	Manual	p value
No. of VT's induced (mean±SD)	2.4±1.9	1.7±1.0	0.31 +
VT CL of clinical tachycardia/ms, (mean±SD)	439±143	422±70	0.73 +
Scar location: Anterior Inferior Apical	 4 4 4	 3 7 2	 1 * 0.41 * 0.65 *
Number of CARTO points collected (mean±SD)	168 (±97)	209 (±107)	0.54+
Total LV mapping times/ mins (mean±SD)	51 (±31)	51 (±34)	0.95 +
Ablation strategy: During VT Substrate ablation	 4 8	 4 8	 1 * 1 *
RF ablation lesions (mean±SD)	35±25	23±9	0.15 +
Maximum temp/ ^{0}C (mean±SD)	38.3±2.4	38.9±4.2	0.66 +
Maximum power/ W (mean±SD)	29.6±2.7	44.6±10.0	<0.001 +
Duration of ablation lesion/sec (mean±SD)	59.4±3.4	71.9±19.1	0.05 +
Fluoroscopy time/mins (mean±SD)	42.6±11.4	32.7 ±18.6	0.13 +
Cumulative X ray dose/ cGycm2 (mean±SD)	4567±3601	2931+/-2329	0.20 +
Overall procedure duration/ min (mean±SD)	312±91	218±93	0.02 +

VT CL – Ventricular Tachycardia cycle length; *Fisher's exact test; +Students t-test.

Table 3: Comparison of robotic and manual ablation acute and long-term outcome data.

Characteristics	Robotic	Manual	p value
Total ATP's 6 mnths pre abl. (median (IQR))	19 (4-396)	11 (8-22)	0.56 +
Total shocks 6 mnths pre abl. (median (IQR))	1.5 (1-4)	1 (0-3)	0.73 +
Failed manual ablation	4/12 (33%)	1/12 (8%)	0.32 *
Urgent (multiple ICD therapies/ICD Storm)	9/12 (75%)	4/12 (33%)	0.01 *
Post proc VT non-ind: Post proc non-clinical VT ind: Post proc clinical VT ind:	6/12 (50%) 5/12 (42%) 1/12 (8%)	8/12 (67%) 3/12 (25%) 1/12 (8%)	0.68 * 0.67 * 1 *
Post proc complications	0/12	0/12	1 *
Post proc Amiodarone continued	6/12 (50%)	5/12 (42%)	1 *
Follow up (months): (mean±SD), (median (IQR))	24.1±19.1, 27 (5-40)	21.1±14.6, 22 (9-32)	0.77 +
Total ATP's post abl. (median (IQR))	3.5 (1-10)	0.5 (0-11)	0.38 +
Total Shocks post abl. (median (IQR))	0.6 (0-1)	0 (0-2)	0.52 +
Total ICD therapies post abl. (median (IQR))	3.5 (1-11)	1 (0-14)	0.38 +
Absolute therapy reduction (median (IQR))	22 (3-388)	12 (5-25)	0.51 +
6mth averaged ICD therapies (median (IQR))	Pre proc: 32 (5-400) Post proc: 2.5 (0-11) p=0.015 §	Pre proc: 14 (10-25) Post proc: 1 (0-5) p=0.023 §	0.49 + 0.60 +
Further ablation procedure	3/12 (21%)	4/12 (29%)	1 *
Mortality Months: mean±SD	4/12 (33%), 16±12.2	4/12 (33%), 15.5±7.0	1 *

abl – ablation, ATP – Anti-tachycardia Pacing, ICD – Implantable Cardioverter Defibrillator, ind – inducible, proc – procedural, *Fisher's exact test, +Mann-Whitney U-Test, §Wilcoxon signed rank test.

Table 4a: Pre, intra and post procedural data for each patient in the robotic group.

Pt	No. of prev Abl	ICD Rx 6 mnth	Elective/ urgent	VT Morph	VT CL	Ablation lesions	Scar Location	X-ray (cGycm 2)	skin dose (cGycm 2)	fluoro (min)	Duration (min)	Amio. Post Abl	Total F/u mnth	Total ATP Post Abl	Total Shock Post Abl	Total Rx Post Abl	Rx post 6 mnth	Rx fall 6 mnth	Redo Abl.	Death (mnth)
1	0	10	Elective	2	286	29	IS	2151	234	41	390	0	31	1	0	1	0	10	0	
2	2	346	Urgent	0	X	33	A	2318	252	40	240	1	2	5	0	5	15	331	1	27
3	3	5	Elective	1	538	31	A S	5117	675	40	420	1	41	0	0	0	0	5	0	
4	2	1501	Urgent	1	560	12	AL	2250	272	38	305	1	52	9	1	10	1	1500	0	
5	0	2	Elective	2	470	51	Ap A, AS, AL	2898	271	54	330	0	1	0	1	1	6	-4	1	
6	0	188	Urgent	1	406	29	IS	1272	152	33	228	0	25	3	0	3	0	188	0	
7	0	33	Urgent	7	536	30	AL	2258	231	36	266	1	40	1	0	1	0	33	0	
8	1	5	Urgent	3	364	12	IS	7944	100	24	196	0	49	73	0	73	9	-4	0	
9	0	30	Urgent	3	498	37	L	6855	759	67	397	0	2	12	1	13	39	-9	0	4
10	0	5	Urgent	2	636	50	Ap A Aneurysm	1992	209	37	236	0	29	1	0	1	0	5	0	
11	0	1557	Urgent	5	130	101	Ap I	6167	593	54	480	1	11	249	4	253	136	1421	2	26
12	0	561	Urgent	2	404	7	Ap A Aneurysm	13584	148	48	252	1	6	4	0	4	4	557	0	7

A=anterior; AL=anterolateral; Ap=Apical, IL=inferolateral; IS=inferoseptum; L=lateral; abl=ablations; Amio=Amiodarone; ICD=Implantable Cardioverter Defibrillator; Rx = Treatment (ATP (anti-tachycardia pacing) +shocks); VT CL=ventricular tachycardia cycle length.

Table 4b: Pre, intra and post procedural data for each patient in the manual group.

Pt	**No. of prev Abl**	**ICD Rx 6 mnth**	**Elective/ urgent**	VT 's Morph	VT CL/ Ms	Ablation lesions	Scar Location	X-ray (cGycm 2)	skin dose (cGycm 2)	fluoro time (min)	Duration (min)	Amio. post Abl	F/u mnth	Total ATP Post Abl	Total Shock Post Abl	Total Rx Post Abl	**Rx post 6 mnth**	**Rx fall 6 mnth**	Redo Abl.	Death (mnth)
1	0	15	Urgent	1	480	26	I	1394	151	20	206	0	39	1	0	1	0	15	0	
2	0	*17*	Elective	1	440	23	IL	540	62	10	174	0	43	0	0	0	0	17	0	
3	1	26	elective	2	420	29	IS	4156	403	53	346	0	34	0	0	0	0	26	0	
4	0	12	Elective	1	320	23	S	2806	389	42	242	0	32	15	2	17	3	9	0	
5	0	24	Urgent	1	398	4	I	175	18	6	36	0	10	0	0	0	0	24	0	
6	0	9	Elective	3	564	12	IL	4857	308	26	246	0	9	73	7	80	57	-48	0	9
7	0	514	Elective	0	X	26	S	1660	192	35	250	1	3	49	11	60	120	394	1	
8	0	11	Urgent	2	364	36	AS	2393	292	66	310	1	1	0	1	1	6	4	1	
9	0	6	Elective	2	400	21	IS	2238	201	22	160	0	30	5	0	*5*	1	5	0	
10	0	3	Elective	4	470	25	Ap, L, IS	1494	180	28	137	1	8	0	0	0	0	3	1	16
11	0	58	Urgent	2	364	32	Ap, AS	5072	384	57	353	1	22	0	0	0	0	54	0	12
12	0	10	Elective	2	423	23	S	8387	1154	27	153	1	22	10	3	13	4	6	1	25

A=anterior; AL=anterolateral; Ap=Apical, IL=inferolateral; IS=inferoseptum; L=lateral; abl=ablations; Amio=Amiodarone; ICD=Implantable Cardioverter Defibrillator; Rx = Treatment (ATP (anti-tachycardia pacing) +shocks); VT CL=ventricular tachycardia cycle length.

FIGURE LEGENDS

FIGURE 1: Patient inclusion flowchart

FIGURE 2: ICD therapies averaged over 6 months “pre” and “post” robotic and manual VT ablation.

FIGURE 3: (A) RAO view and (B) LAO view of the ablation catheter in the LV apical septum. (C) Ablation at this site lead to VT termination. This patient had undergone 3 previous manual VT ablations prior to a robotic approach - he has been therapy free for over 3 years of follow up.