BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL

Dr. Kakarla Saikiran

PDF Cardiac Electrophysiology

THESIS

2023

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND

TECHNOLOGY, TRIVANDRUM

An Institution of National Importance established by an Act of the Indian Parliament
(Act No.52 of 1980)

Dept. of Science and Technology, Govt. of India
www.sctimst.ac.in

BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL

A THESIS SUBMITTED BY

Dr. Kakarla Saikiran

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

PDF Cardiac Electrophysiology

2023

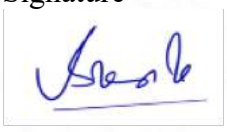
DECLARATION BY THE STUDENT

CERTIFICATE

I, Dr. Kakarla Saikiran, hereby certify that I had personally carried out the work depicted in the thesis titled, "BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL".

No part of this thesis has been submitted for the award of any other degree or diploma before this date.

Signature



Dr. Kakarla Saikiran

Name of the Candidate

Date: 30/12/2023

CERTIFICATE BY THE RESEARCH GUIDE

Name of the Guide: **Dr. Narayanan Namboodiri**

Division: **Cardiac Electrophysiology and Pacing**

Department: **Cardiology**

This is t,o certify that Dr. Saikiran Kakarla, Division of Cardiac Electrophysiology and Pacing, Department of Cardiology of this institute has fulfilled the requirements prescribed for the post-doctoral fellowship of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum. The thesis entitled, "**BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL**" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma before this date.

*Clearance was obtained from the Institutional Animal Ethics for carrying out the study.

Signature
Name of the Guide

Date

APPROVAL OF THE THESIS

The thesis entitled

BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL

Submitted by

Dr. Saikiran Kakarla

for post-doctoral fellowship in

Cardiac Electrophysiology and pacing

of

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

is evaluated and approved by

…..…… …….

(Name & Signature of the Guide) (Name & Signature of thesis examiner)

ACKNOWLEDGEMENTS

It has both been a pleasure and a privilege to undertake dissertation work for my post-doctoral fellowship course. The path was not easy, but it did not look tardy enough due to constant inspiration and well wishes from several people.

At the outset, I would like to thank my institute, Sree Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, for allowing us to nurture ourselves under its huge wings. This work has been made possible due to the efforts of many people who need to be acknowledged.

Firstly, I would like to thank my guide, Dr. Narayanan Namboodiri, for guiding me through the entire study and being a constant source of inspiration. His wisdom and in-depth understanding of the subject have made this work an enriching experience for me.

I would like to thank Dr. P.R. Uma Shankar, MVSc, PhD, Scientist G and SIC, Division of in-vivo models and training, Biomedical Technology Wing for his support during the preclinical studies which were conducted at the Biomedical Technology Wing.

I want to thank Mr. Sabari Saravanan, Abbott SJM, for his support during the animal experiments.

I extend my sincere thanks to Dr. Ramesh Babu, fabrication facility in charge, who helped in the fabrication and materialising of the 3D tissue fixing model for the bipolar ablation.

I want to thank Dr Abhilash SP, Professor, Department of Cardiology for the valuable support provided during the study.

I would thank Dr. Harikrishnan.S, Professor Senior grade, Head of the Department of Cardiology for his constant support during the fellowship period.

I would also like to thank all the other faculty members, and technical staff of the Department of Cardiology, SCTIMST, and Biomedical Technology Wing, SCTIMST, Trivandrum for their support and guidance.

I would like to thank all my seniors, colleagues and juniors for creating an optimal work environment where the study could be performed. I thank all of them for their constant support.

Above all, I thank my parents, Shri K. Bhaskar Naidu and Smt. Sridevi, for making me what I am today.

It is with profound humility that I express my gratitude to God, who, through his unwavering support, has made this academic achievement possible. I acknowledge his boundless grace which has been a cornerstone of my perseverance.

Last but not least, I want to thank my best friend and wife, Dr Manisha K, for her invaluable and continuous support throughout the process.

TABLE OF CONTENTS

DECLARATION BY THE STUDENT i

CERTIFICATE BY THE RESEARCH GUIDE ii

ACKNOWLEDGEMENTS iiv

TABLE OF CONTENTS vvi

LIST OF FIGURES vii

LIST OF TABLES viiiiii

LIST OF ABBREVIATIONS ixx

SYNOPSIS xi

1 INTRODUCTION 1

2 LITERATURE REVIEW 8

3 MATERIAL AND METHODS 16

4 RESULTS 28

5 DISCUSSION 44

6 SUMMARY AND IMPLICATIONS 54

7. CONCLUSION 56

8. BIBLIOGRAPHY 57

ANNEXURES

APPENDIX A: IAEC APPROVAL 62

APPENDIX B: PLAGIARISM CHECK REPORT 63

APPENDIX C: PROFORMA 64

APPENDIX D: CURRICULUM VITAE 66

LIST OF FIGURES

Figure No	*Figure Caption*	*Page No*
Fig 1	***Difference between Unipolar, Sequential unipolar and Bipolar RFA configurations***	*9*
Fig 2	***Different modes of Bipolar RFA connections***	*11*
Fig 3	***Custom-made 3D-printed tissue fixing model for Bipolar RFA.***	*18*
Fig.4	***Custom-made Bipolar RFA connections***	*18*
Fig.5	***Various catheter orientations studied.***	*19*
Fig.6	***Lesion measurements***	*22*
Fig.7	***Overall workflow of the bipolar ablation***	*25*
Fig.8	***Experimental setup of the Bipolar ablation***	*26*
Fig.9	***Analysis of steam pops in relation to the different power settings***	*30*
Fig.10	***Total lesional volumes in comparison with different configurations***	*39*
Fig.11	***Mean total lesional volumes in comparison with different power settings***	*40*
Fig.12	***Mean total lesional volumes in comparison with different duration***	*40*
Fig.13	***Configurations vs power vs volume vs time***	*42*
Fig.14	***Scatter plot between thickness of tissue and transmurality***	*46*
Fig.15	***Comparison of lesion depth and volume with various configurations.***	*47*
Fig.16	***Examples of lesional geometries in various configurations***	*51*

LIST OF TABLES

Table No	*Table Caption*	*Page No*
Table. 1	*Analysis of variance on lesion geometry*	*28*
Table. 2	*Distribution of steam pops*	*29*
Table. 3	*Comparison between lesion characteristics with and without steam pops*	*31*
Table.4	*Different configurations of the bipolar RFA and their volumes and incident steam pops*	*32*
Table.5	*Comparison of lesional parameters between 1,2 configurations*	*33*
Table.6	*Comparison of lesional parameters between 3,4 configurations*	*34*
Table.7	*Comparison of lesional parameters between 1,3 configurations*	*35*
Table.8	*Comparison of lesional parameters between 1,4 configurations*	*36, 37*
Table.9	*Comparison of lesional parameters between 2,3 configurations*	*37, 38*

LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1.	RFA	Radiofrequency ablation
2.	b-RF	Bipolar radio frequency ablation
3.	VT	Ventricular tachycardia
4.	VPC	Ventricular premature complexes
5.	ABL	Ablation catheter
6.	LV	Left ventricle
7.	LCC	Left coronary cusp

SYNOPSIS

BIOPHYSICAL EVALUATION OF VARIOUS BIPOLAR CONFIGURATIONS IN RF ABLATION OF VENTRICULAR MYOCARDIUM IN A BOVINE MODEL AND A PROTOTYPE DESIGN OF A CUSTOM-MADE BIPOLAR RF ABLATOR MODEL

SYNOPSIS

BY

Dr. Kakarla Saikiran

for PDF Cardiac Electrophysiology

of

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

SYNOPSIS

Background:

Bipolar radiofrequency ablation(B-RFA) strategy was increasingly used, mainly to target deep intramural re-entrant foci responsible for the arrhythmia that fails to be ablated by conventional unipolar RFA / sequential unipolar RFA. Lesion characteristics of various bipolar RFA configurations were largely unknown.

Aims and objectives:

1. To study the lesion geometry and variance between active and passive lesions
2. To assess the tissue temperatures at the indifferent electrode in bipolar mode,

Methods:

A custom-made validated ex-vivo bipolar ablation model was used to assess lesion formation. Two ablation catheters, one active and one ground, were placed with viable myocardium in between, in parallel or perpendicular orientation. Lesions were created with varying power (30 W, 40 W, 50 W, 60 W), and time (10,15, 20, 30, and 40 seconds). Tissue temperatures were measured with a custom-made thermocouple. Lesion dimensions and the incidence of steam pops were recorded and then analysed with binary logistic regression and multiple linear regression.

Results:

A total of 107 lesions were analysed with various powers and configurations. The average volume of the active catheter lesion significantly differed from that of the passive catheter Lesion volume active = 266 +/- 137 mm3 vs lesion volume

indifferent 130 +/- 91.8 mm 3 ($p < 0.001$). The return electrode temperature and tissue temperature at the passive end were lower than that of the active electrode (p 0.004). The frequency of steam pops was frequent with higher power long duration application ($p < 0.001$). True parallel configuration (both active and passive electrodes oriented parallelly) had fewer steam pops ($p<0.001$).

Conclusion:

1. This study demonstrated bipolar ablation with a single RF generator is technically feasible with modifications in connections in the pre-clinical study.

2. Additional temperature measurement at the passive electrode may not be necessary as the tissue temperatures and returning electrode temperatures never exceeded the active electrode.

3. The safest strategy in the case of bipolar ablation was with true parallel configuration with an inter-electrode distance of 15mm at a power of 30 W to 40 W generated lower steam pops and better transmurality and optimal lesions

1 INTRODUCTION

1.1 General Introduction

Bipolar ablation is a technique that involves the flow of radiofrequency current between two electrodes placed close to each other. When the distance between the tip electrode and the dispersive pad is reduced, the current density increases, resulting in more resistive heating and deeper lesion formation. Bipolar ablation creates narrower and deeper lesions that lead to the formation of a transmural scar in the tissue.

Previous research has indicated that bipolar radiofrequency ablation (RFA), which involves using two ablation catheters, can create larger and deeper lesions than unipolar RFA. Bipolar RFA may be useful in the treatment of refractory ventricular arrhythmias that have not responded to previous unipolar RF ablation. Some ventricular arrhythmias, both scar-related and idiopathic, can arise from deep within the myocardium, such as the inter-ventricular septum, mid-myocardium, or papillary muscle tissues. These areas may be inaccessible when using traditional unipolar ablation, which is why bipolar RFA could be particularly beneficial.

Apart from the type of catheter used as active or ground, catheter tip orientation of both active and ground were important determinants of lesion sizes during b-RFA in this study. Nguyen et al showed that when using externally irrigated catheters for b-RFA, maintaining a perpendicular orientation to the myocardium allowed for the largest and deepest lesions. The third factor that determined efficacy was the thickness of the target myocardium. If the myocardial tissue is too thick, b-

RFA is likely no better than sequential unipolar ablation. In their ex vivo studies, this threshold was 15 mm. If the tissue were above 15 mm, b-RFA could not achieve transmurality, and its combined depth and lesion volumes were no larger than with sequential unipolar ablation on either side of the myocardium.

To perform b-RF ablation efficiently, two catheters are needed, each connected to a separate RF generator. However, only a few centres have two separate RF generators, so custom-made solutions are required. Currently, commercially available tools or connectors for b-RF ablation are costly.

The lack of information received from a return electrode can be frequently a limitation of this technique. High RF current density near the catheter tip can cause steam pop or char formation. The incidence of steam-pop during b-RF ablation is conflicting as per previous studies. However, methods such as temperature control can help address these issues.

1. Irrigation of return electrode to provide effective cooling of return electrode.

2. Using a larger electrode tip (i.e. 8 mm) to reduce RF current density near the proximal end of a return catheter.

3. Receiving temperature signals from a return electrode using a second RF generator.

If the recorded temperature is convincingly shown to be within safer limits in experimental settings while using the first option – irrigated catheter as both active

and passive electrodes, the safety of b-RF ablation using similar settings can be inferred even in clinical settings.

PERTINENCE OF THIS STUDY

The relevance of this study in an Indian setting is two-fold. First, once answers to the above questions are properly identified, one can use the optimal ablation strategy in a clinical scenario and improve the ablative outcome. Two, if the temperature as recorded by a thermocouple temperature sensor display from the passive electrode is found to be within safe limits in multiple scenarios in our experimental settings, one can opt for the bipolar ablation with a single RF ablator (with an additional jumper cable) without the need of monitoring it in clinical settings. This will reduce the cost of the ablative procedures with great confidence in the safety of the procedure. On the contrary, if the temperature at the passive electrode is noted to reach unacceptably higher levels, the model must incorporate a mandatory temperature display too in the circuit due to safety concerns as being used in this experimental model.

HYPOTHESIS:

Bipolar RF (b-RF) lesions can complement conventional ablations strategies in creating deeper lesions if optimal settings are utilized. The temperature rise at the passive electrode is likely to be within safer limits and once it is proven ex vivo, a custom-made model that involves a single RF ablator with an additional jumper cable can be used to deliver bipolar RF energy in clinical settings, without compromising safety.

The importance and uniqueness of this project are the following. Bipolar ablation, a technique to achieve intramural lesions for ventricular arrhythmias arising from deeply located areas within the septum or intramural structures, using custom-made cables along with commercially available RF ablators is demonstrated in a few labs globally. However, the data available to validate these results is limited and the safety will be a major challenge in this configuration of ablation procedure. Proper application of this technique is likely to improve ablative outcome in deep foci of ventricular tachycardia especially in interventricular septum and at certain outflow tract VTs. The glaring lacuna in our knowledge regarding the nature of lesions can be summarized below.

How deep are the lesions formed with bipolar modes as compared to conventional configuration? (Bipolar/sequential bipolar mode vs. conventional unipolar mode)

A. What are the appropriate power settings required to achieve the desired lesions in bipolar mode?

B. What are the safe temperature settings to avoid coagulation and steam pops during RF delivery in bipolar mode?

C. In bipolar mode, currently the temperature will be sensed and displayed by the RF generator only from the active (+ve) electrode (ablation catheter -1 tip) as only a single RF generator with split cables is used in most of the centres. With this, the temperature at the passive electrode (-ve) electrode (ablation catheter-2 Tip) cannot be measured. It needs to be explored whether the heat generated by the passive electrode is within safe limits.

AIM:

- ***Primary objective:***

  To identify the optimal ablation strategy (RF settings, inter-catheter distance etc.) to produce an effective lesion at bipolar -RFA in an experimental bovine myocardial model.

- ***Secondary objective*** **:**

  1. To assess the safety concern related to temperature rise at the ground electrode during b-RFA by measuring the temperature in the ground electrode (this measurement is not possible in b-RFA using a single RF generator) by incorporating a thermocouple sensor display in the circuit.

  2. To validate the 'custom-made' cost-effective prototype b-RFA model that involves a single RF generator with commercially available jumper cable that can be potentially used in clinical settings

2 LITERATURE REVIEW

Bipolar RFA setup:

In the classic RF approach, alternating current flows between the distal tip of an ablation catheter and a dispersive patch located on the patient's skin. The discrepancy between the current density near the catheter tip (small electrode area = high RF current density) and the dispersive patch (large electrode area = low RF current density) results in lesion formation only near the ablation catheter. Nevertheless, even with perfect positioning of the ablation catheter close to the ablation target, current flow can be limited by nonuniform tissue resistivity(1,2). More specifically, tissue components of high resistivity, such as fat, collagen, or scar, will prevent effective lesion formation.

Alternative to the classic approach, RF ablation can be conducted in a bipolar fashion when two ablation catheters participate in the RF circuit (Fig. 4). This is achieved by connecting one of the ablation catheters to the indifferent port of the RF generator instead of the dispersive patch (Fig.4). When both catheters are positioned near the targeted site, such configuration results in increased RF current flow to the area of interest. Studies show that bipolar RF ablation can not only increase the likelihood of lesion transmurality but also result in lesions of more condensed structure (3,4).

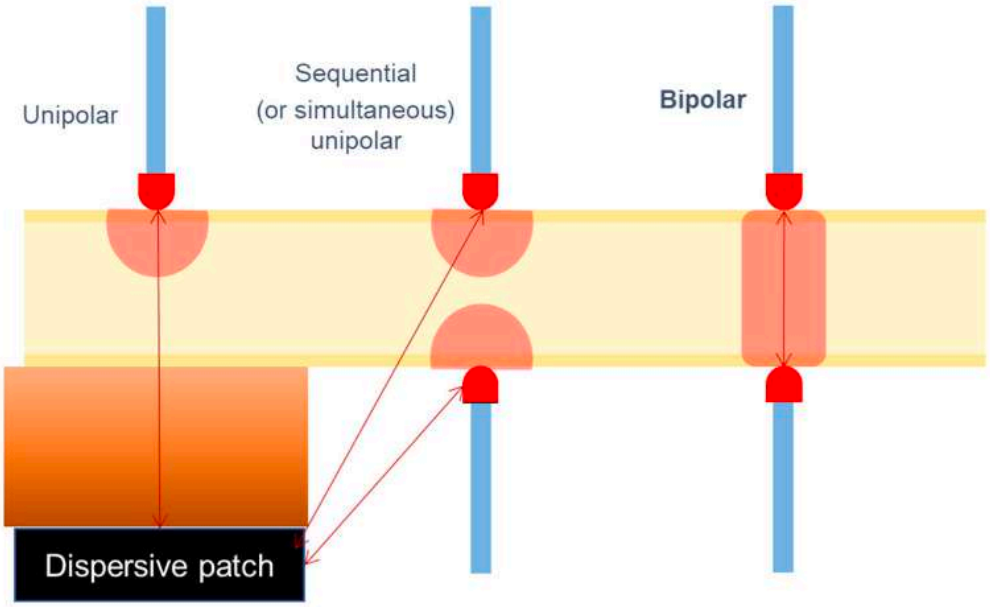


Fig.1: Difference between Unipolar, Sequential unipolar and Bipolar RFA configurations (2)

For the setting of bipolar RF ablation, either the dedicated bipolar ablation setting with temperature and power monitoring, or the unipolar modified/custom-made RF ablation setting can be used. A challenge faced by many electrophysiology centres is the lack of access to custom-made or dedicated adapters to perform bipolar ablation. This equipment should be readily available in case the need for bipolar ablation arises during a procedure, and the staff should be trained to handle and set up the bipolar ablation circuit in an expeditious manner.

Modes of bipolar connection:

1. Custom-made connection (Fig.5 A): Here in this method of connection, a custom cable is created from the ablation catheter connector and dispersive skin electrode cables. This connection allows the connection of a Carto system-compatible ablation catheter in the position of the return electrode. The disadvantage of this system is signals and temperature readings from that ground electrode were not available.
2. Using a T-jumper cable (Fig. 5B): The indifferent (ground) catheter cable was then plugged into the yellow female connection of the IBI T-Cable (Abbott). The distal pin of the quadripolar electrogram cable of the IBI T-Cable was then plugged into one of the pins in the black grounding patch ports on the front of the RF generator which was originally designed for an impedance-patch plug for unipolar radiofrequency ablation. (2,5–7)
3. Using a dedicated adapter system from the Core system (Rzeszow, Poland) (Fig. 5 C): A dedicated adapter which, apart from the possibility of connecting the second ablation catheter into the return port of the radiofrequency generator, allows the transfer of temperature data to the temperature monitor (Stockert EP Shuttle) and to connect all the electrodes from the tip of the catheter in order display signals, reconstruct the second ablation catheter using the impedance data(2).

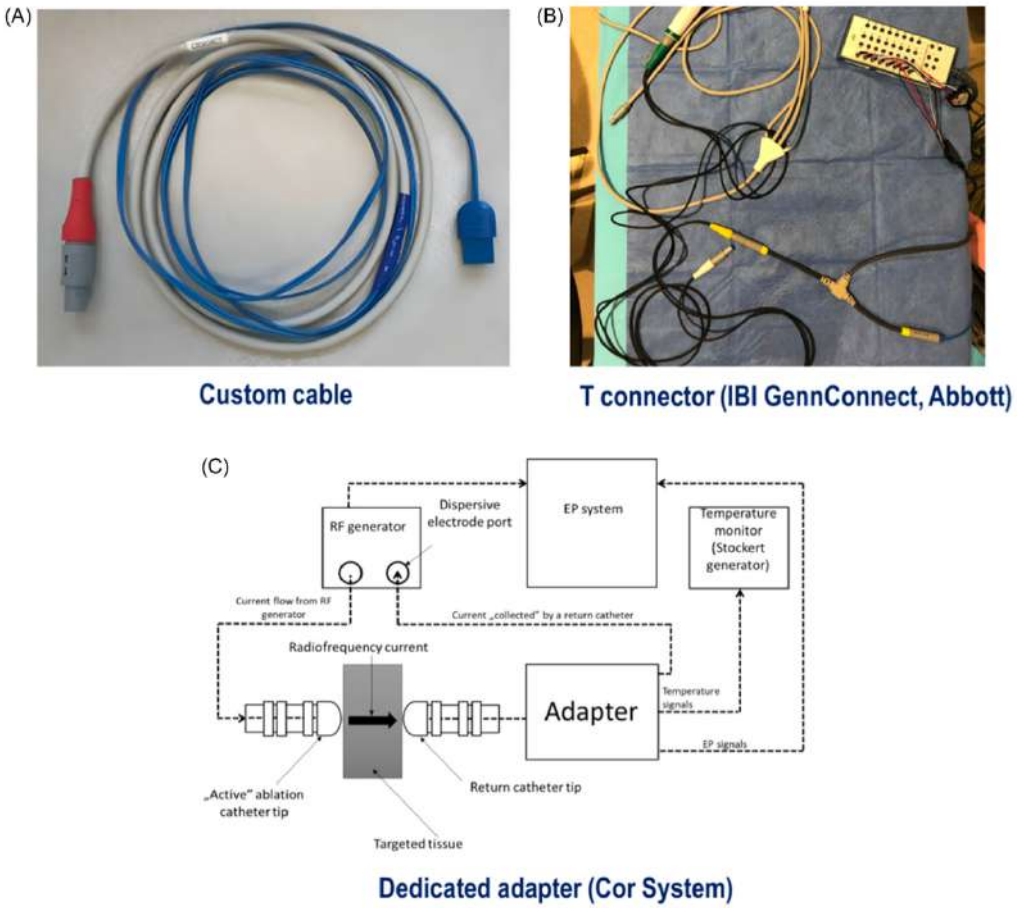


Fig.2: Different modes of Bipolar RFA connections (2)

With the introduction of irrigated ablation mediated radiofrequency ablation (RFA) of various cardiac arrhythmias has increased in efficacy and frequently has become a first-line therapy(8). The creation of durable lesions to treat ventricular arrhythmias remains a complex undertaking due to various challenges encountered during the procedure. Ventricular arrhythmias, which can be either scar-related or idiopathic, can arise from deep regions of the myocardium, including the interventricular septum, mid-myocardium, or papillary muscle tissues. Unfortunately, these sites may prove difficult to reach when using traditional unipolar ablation techniques, which can further exacerbate the complexity of the procedure.

Standard RFA is performed in a unipolar configuration between the ablation catheter tip (active pole) and a ground patch placed on the body surface. Recent studies have demonstrated that bipolar radiofrequency ablation (bRFA), using 2 ablation catheter tips as the active and ground poles, may potentially create larger and deeper lesions and more effectively target ventricular arrhythmias using deeper mid-myocardial circuits(9–11). Previous studies(12) demonstrated in ex vivo studies that bRFA applied between 2 irrigated-tip catheters can better achieve transmural lesions, compared to sequential unipolar ablations. They further showed that bRFA applied to an ex vivo epicardial preparation using an irrigated catheter and a 10-mm non-irrigated catheter can create deeper lesions(13) . In addition, in a small case series, Koruth et al(14) reported on their experience with bRFA using 2 irrigated catheters for septal atrial arrhythmias and deep ventricular tachycardia (VT) circuits.

Nevertheless, there remains a paucity of data regarding optimal conditions for bRFA, including catheter orientation of active and ground catheters. Therefore, we

sought to define optimal variables for bRFA, including catheter tip orientation, type of active and ground catheters, power delivery, and effect of catheter distance due to myocardial tissue thickness.

Previous studies have shown that bipolar RFA using 2 ablation catheters could create larger and deeper lesions than unipolar RFA(15,16). The refractory ventricular arrhythmias that have not responded to previous unipolar RF ablation could be treated effectively by using bipolar RFA to create a transmural lesion (15). Although the clinical utility of b-RFA has been reported, most of the studies were either small case series or case reports (14,17–19). Certain ventricular arrhythmias, both scar-related and idiopathic, can originate from deep within the myocardium, such as the inter-ventricular septum, the mid-myocardium, or papillary muscle tissues, and these sites may be inaccessible when using traditional unipolar ablation. Bipolar RFA could be particularly useful in them (9,15,18,19).

In previous studies, researchers have investigated certain biophysical characteristics of lesion formation with bipolar RF ablation and the factors affecting the safety and efficacy of this mode of application. Nguyen et al (3) showed that the largest and deepest lesions, without a higher incidence of steam pops, were achieved using 2 irrigated catheters. Using externally irrigated catheters as both active and ground electrodes produced larger and deeper lesions compared to using an irrigated tip active with a non-irrigated 4- -mm tip. Furthermore, although using an 8-mm catheter as the active catheter allowed for higher delivery of power beyond 50 W, this technique increased the risk of steam pops when used asymmetrically with a 4-mm or externally irrigated catheter assigned as the ground catheter.

Apart from the type of catheter used as active or ground, catheter tip orientation of both active and ground were important determinants of lesion sizes during b-RFA in this study. Nguyen et al (3)showed that when using externally irrigated catheters for b-RFA, maintaining a perpendicular orientation to the myocardium allowed for the largest and deepest lesions. The third factor that determined efficacy was the thickness of the target myocardium. If the myocardial tissue is too thick, b-RFA is likely no better than sequential unipolar ablation. In their ex vivo studies, this threshold was 15 mm. If the tissue were above 15 mm, b-RFA could not achieve transmurality, and its combined depth and lesion volumes were no larger than with sequential unipolar ablation on either side of the myocardium.

Bipolar ablation is when the RF current flows between two closely located rings(12). The decrease in the distance between the tip electrode and the dispersive pad will result in a bigger current density with more resistive heating, which leads to deeper lesion formation. Lesions created by bipolar ablation are narrower and deeper, resulting in a transmural scar in the tissue as thick as 25 mm(10). With good control of the impedance and contact pressure, the bipolar source of RF energy seems safe, and this has been confirmed by another study(11). Previous reports showed that unipolar RF ablation lesions can be 7 mm deep and B-RFA lesions can be 15 mm deep.

Small-tip catheters (4, 3, and 5 mm) in the b-RFA setting operate at higher impedance values(20). An experimental study reported that b-RFA has higher core lesion temperatures, corresponding to a denser and larger necrotic core, than

simultaneous unipolar RF (20). This is probably the reason why b-RFA is associated with denser lesion cores and possibly less collateral damage (4).

The optimal way to deliver b-RF ablation has been considered to be using two catheters (active or passive electrodes) connected to two separate RF generators. However, only a few centres in our country do have two separate RF generators in the lab. Many custom-made solutions have been made to tackle this but without any proper validation. There are no commercially available tools and connectors for b-RF ablation as of now, and connections during the procedure need to be custom-made.

Even the catheter irrigant is thought to affect the lesion size with b-RF ablation. Nguyen et al reported that the use of half-normal saline compared to normal saline as the catheter irrigant increased lesion depth and volume during b-RFA at 50 W for 60 seconds(3). The reduced salinity is hypothesized to decrease the loss of radiofrequency energy through dispersion to a lower impedance environment surrounding the ablation catheter, thus focusing more energy on the myocardium. However, in another study, no significant increase in lesion volume or depth was seen with the use of 0.45% saline during BA at 30 W for 120 seconds.

It is also shown that b-RFA creates larger lesions with significantly increased chances of transmurality but at lower risks of steam pops. The use of an irrigated catheter as the return electrode during BA and 30 W of radiofrequency energy delivered over 120 seconds provided the optimal balance between creating deep, transmural lesions, and avoiding steam pops at both the interventricular septum and left ventricular free wall in a recent study(21).

3 MATERIALS & METHODS

Design: Pre-clinical experimental study

Study Setting: Department of Cardiology – Electrophysiology lab and Biomedical Technology Wing, Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Trivandrum and Biomedical Technology Wing, Poojappura, Trivandrum.

Study period: from 01.06.2023 to 30.10.2023

Methods:

The Institutional Animal Care and Institutional Animal Ethics Committee approved experimental protocols.

Proposed sample size:

In an earlier ex-vivo ventricular model, transmurality was achieved in 82% of bipolar RF ablation compared with 33% of unipolar ablation (Koruth JS, Dukkipati S, Miller MA, Neuzil P, d'Avila A, Reddy VY. Bipolar irrigated radiofrequency ablation: a therapeutic option for refractory intramural atrial and ventricular tachycardia circuits. Heart Rhythm. 2012; 9:1932-1941).

Therefore, a sample of nine lesions per ablation configuration has 80% power to detect a 50% difference in lesion transmurality between different ablation configurations. For each configuration and power setting, a minimum of 10 lesions will be created in a random sequence.

A pilot study of 5 bovine hearts was performed for standardization of the experiment in the initial month. Later, we performed this experiment in at least 120 ventricular myocardial samples collected from 60 bovine hearts.

Experimental setup:

Fresh bovine hearts were used for this ex-vivo study. The bovine hearts will be transferred to 8-degree Celsius ice packs immediately after removal. Patches of the myocardium of a homogenous area (preferably septal and left ventricular free wall, approximately 4 x 4 cm in size) will be prepared for the study. For this, a section of viable bovine ventricular myocardium will be excised within 1 hour of experimentation. It will be placed on a custom 3-D printed apparatus (Figure 1) and immersed in a temperature-controlled circulating 15-litre 0.9 % saline bath. The saline bath was heated to 37.5 degrees C by a heating pump and circulator with a capacity to produce non-pulsatile uniform flow at around 5 litres/min, which was directed perpendicular to the myocardial surface. This circulator usage ensured constant temperature and flow circulation throughout the study. The impedance of the saline medium was maintained between 100 -140 Ohms. This ex vivo model is modified and prepared from the previously published validated models (22,3,23,5,24). The experimental setup is pictorially represented in Figure 2

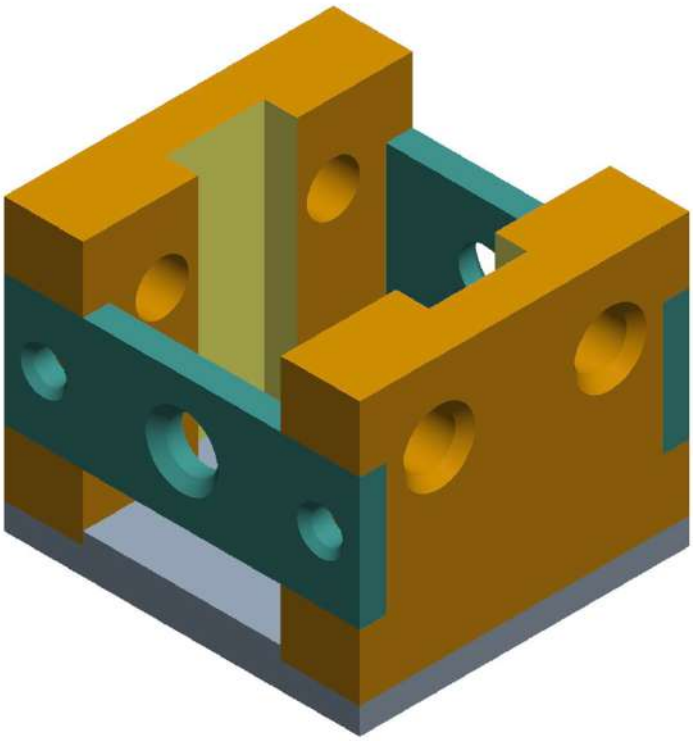


Fig.3: Custom-made 3D-printed tissue fixing model for Bipolar RFA

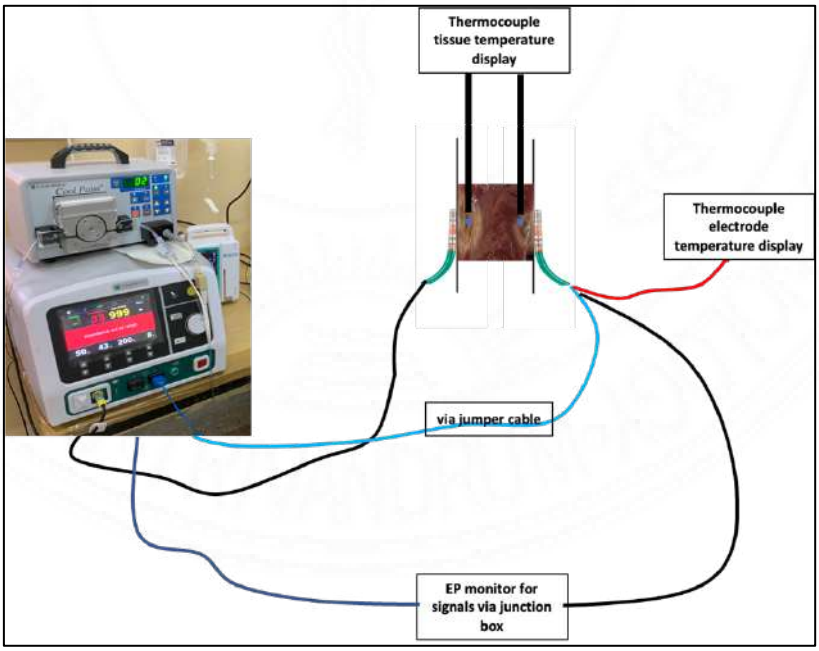


Fig.4: Custom-made Bipolar RFA connections

Catheter description:

Two open-irrigated ablation catheters (FlexAbility™, Abbott, St. Paul, MN) were used. This catheter has a 4mm flexible 8Fr tip, irrigated from the proximal to distal end through laser-cut kerfs and four holes on the distal end of the tip. Thermocouple embedded within the tip of the flexability catheter 0.3mm from the tip for temperature monitoring. Catheters were mechanically fixed using Tuohy-Borst valves and placed on opposite bath walls. These catheters were fed through these valves and oriented as per protocol. The valves were then closed to anchor the catheters in position throughout the study. A 2 ml/min irrigation rate with room-temperature normal saline solution was continuously maintained on a baseline basis. The catheter tips were placed in various combinations, perpendicular or parallel to the myocardium (Figure 3). Temperature, power, and impedance values were continuously monitored during RF delivery using the EnSite Precision cardiac mapping system.

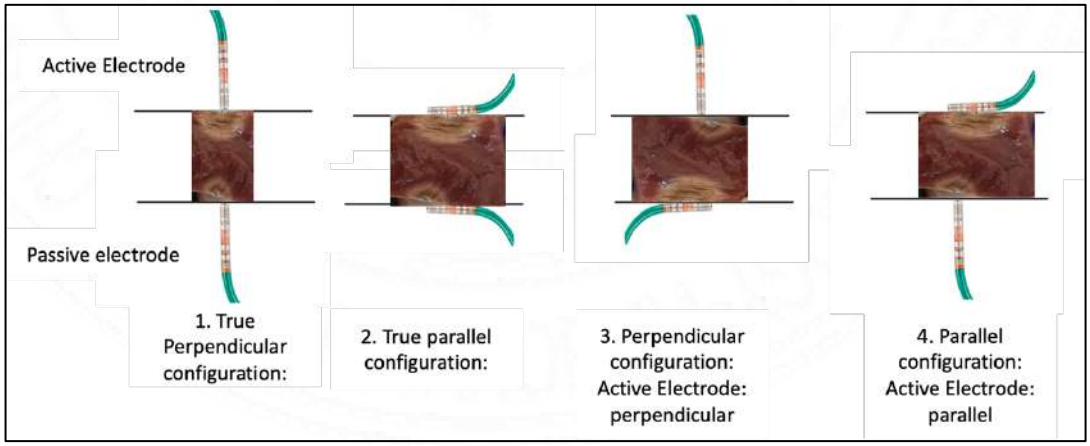


Fig.5: Various catheter orientations studied.

Bipolar RFA setup:

The circuitry of a true bipolar ablation circuit which we used is as follows:

- An open irrigated RFA catheter (Flexability^{TM}, Abbott, St. Paul, MN) (Active electrode/ ABL1) was connected to the anodal port of the commercially available RF ablator through an 85641-ablation cable RF cable.
- Another open irrigated ablation catheter (Flexability^{TM}, Abbott, St. Paul, MN) (passive electrode/indifferent electrode) will be connected with a custom-made cable.
- The connection from ABL2, the distal electrode will be split into two by using a jumper cable and one input will be given to the recording system junction box and another connected to the negative grounding port of the RF Generator; the remaining electrode cables from ABL 2 electrodes (2,3,4 electrodes) were plugged into recording system junction box directly.
- Each of the catheters was connected to a bag of normal saline for irrigation.
- The electrogram signals from the RF generator for ABL1 will be connected to the recording system junction box through an electrogram cable.

The connection described above helps in

- Delivering b-RF energy through distal electrodes of ABL 1 & ABL 2 catheters
- Monitoring temperature during RF delivery at the distal electrode of ABL1 in the RF Generator & distal electrode of ABL2 through Temperature display

- Recording electrograms from all the electrodes of ABL 1 & 2,

Delivery of RF energy:

The myocardial sample was fixed in a custom-designed tub which can complete a unipolar circuit with the help of an RF adhesive patch attached to it. Two ablation catheters, one active and one ground, were oriented across from each other, with the myocardium in between. The catheter tips were placed in 4 different configurations in bipolar ablation (fig.5).

Those are 1. True perpendicular configuration where active and ground catheters are oriented perpendicular to the myocardium.

2. True parallel configuration where active and ground catheters are oriented parallel to the myocardial surface,

3. Perpendicular configuration, where the active electrode is perpendicular, and the passive electrode is parallel to the myocardial surface.

4. Parallel configuration, where the active electrode is parallel, and the indifferent electrode is perpendicularly oriented. The active and ground catheters are 8Fr. 4mm tipped bidirectional irrigated ablation catheters. These catheters are held in position using Tuohy-Borst valves.

In each configuration, ablation was delivered at powers of 30, 40 and 50 W for time intervals of 30, and 40 seconds. Ablation was delivered similarly in other configurations as well and the lesions were done in triplicate for each set of

parameters. After each set of 3 ablations, the septal tissue was sliced to reveal the cross-section of the myocardium by a blinded experienced electrophysiologist.

After performing the ablation, lesions were sectioned and analysed. The thickness of the tissue and the depth and width of lesions were measured from the sections of the myocardium along their long axis and its blanched zone (Figure 3). The average transmurality values and their standard deviation are reported. Lesion transmurality was calculated by formula.

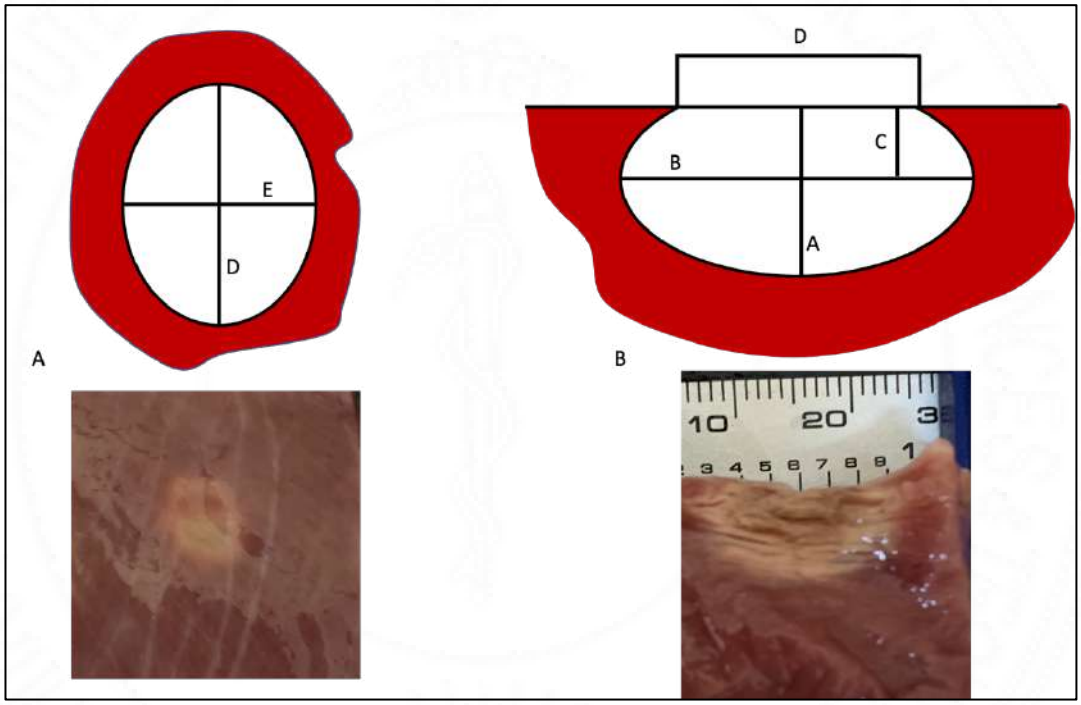


Fig.6: Lesion measurements

Lesion transmurality:

$$\left(\frac{depth\ of\ lesion(active\ electrode) + depth\ of lesion\ (passive\ electrode)}{Tissue\ thickness}\right) x\ 100\%$$

For each lesion, the maximum depth (A), maximum diameter(B), depth at the maximum diameter (C), and lesion surface diameter in two dimensions (longer being D and shorter being E) were measured using electronic micro callipers with 0.1mm resolution. In addition, the most effective configuration was then studied using a variable myocardium with a thickness of 15 or 20 mm and compared to sequential unipolar ablations applied to the myocardium of similar thickness.

Single lesion volumes will be calculated using the equation for an oblate ellipsoid. Lesion volumes were calculated using a previously validated formula for calculating volumes of lesions.(8,25,26) The shape of the lesion can be assumed as an oblate ellipsoid sphere with a missing superficial cap of the complete ellipse. The volume can be estimated by assuming the lesion as two different hemi-ellipses. The deeper part of the lesion approximates that of half an ellipsoid characterized by a long radius (B/2) and a short radius(A–C). The upper part of the lesion also approximates an ellipsoid but with a missed upper tissue cap. This volume is characterized by long axis B/2, a short axis that can be derived from the lesion surface diameter D, maximum diameter B, and depth at maximum lesion diameter C. This upper short radius is usually smaller than the lower short radius due to cooling at the tissue surface. Finally, the upper ellipsoid misses an upper cap (above tissue surface) whose height equals the difference between the upper ellipsoids' short

radius and C. Mathematically, the volume of both parts of the lesion can be finally summated as Volume of the lesion = $\frac{\pi}{6}(\frac{AB2+CD2}{2})$. The lesion surface area on the myocardial surface can be calculated by using the formula of $\left(\frac{\pi}{2}DE\right)$. This can avoid the limitation associated with the lesion created by parallel orientation. The total lesion volume will be calculated by the addition of the lesion volumes generated by the active and ground catheters. When opposing lesions coalesced, resulting in transmural lesions, the maximum depth was recorded as 50% of the myocardial thickness. Transmurality and the occurrence of audible steam pops will be recorded. Energy delivery will be completed despite steam pops midway during ablation. Lesions with steam pops, too, will be included in lesion measurement and analysis.

Figure: 7 : Overall workflow of the bipolar ablation

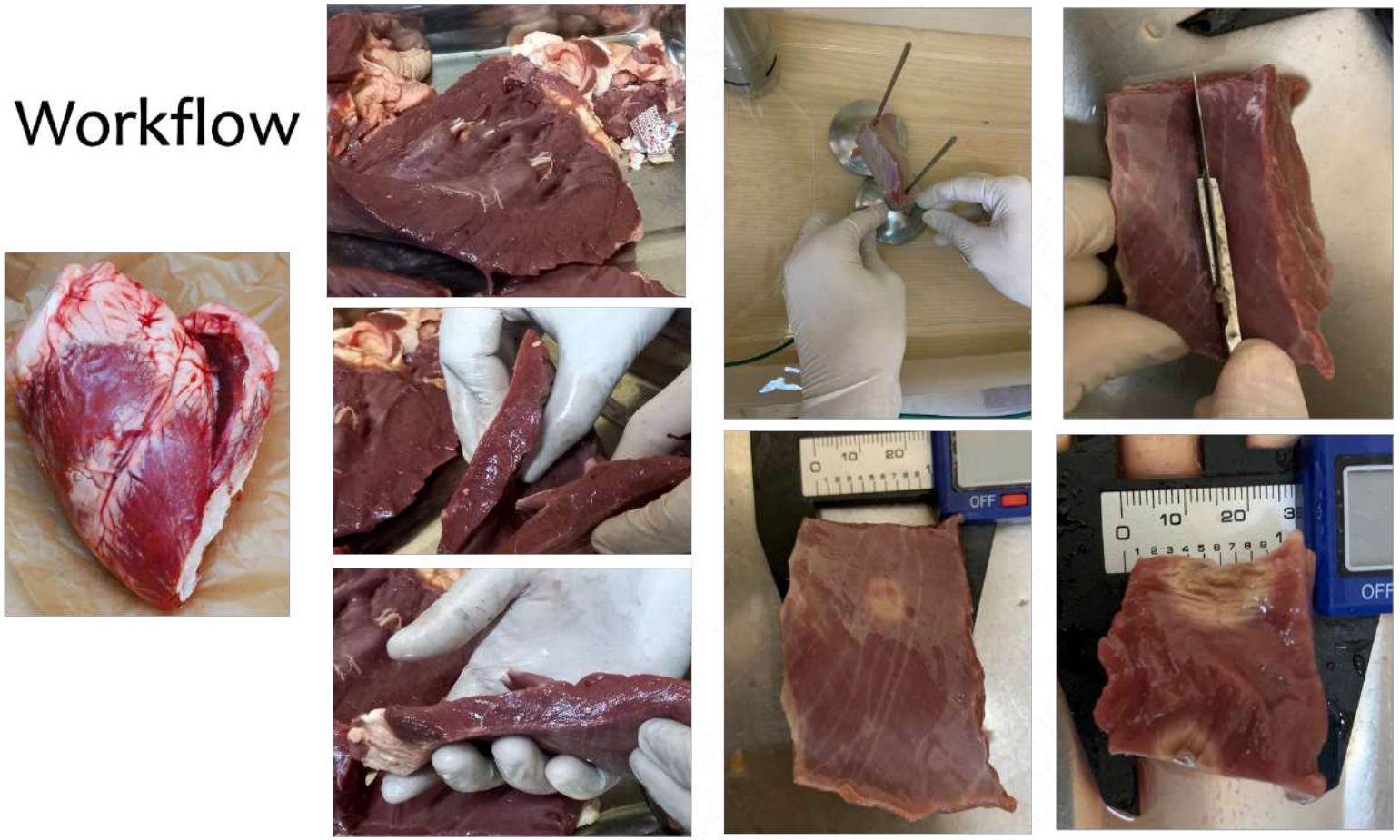




Figure:8 : Experimental setup of the Bipolar ablation

STATISTICAL ANALYSIS

- Statistical analysis was done using IBM SPSS version 28.0.1.1.
- The results are presented as mean ± standard deviation or numbers and percentages. the Kolmogorov–Smirnov test was previously used to assess normality.
- Continuous variables were compared using the two-tailed Student t-test. Categorical variables were compared using the $\chi 2$ test with Yates correction or Fisher exact test where appropriate.
- Parameters (IRE temperature, impedance, mean, and maximal powers) from bipolar applications conducted with irrigated small and large-tip IRE were used for calculations.
- Analysis of variance was carried out to compare tissue temperature, displayed thermocouple temperature and lesion geometry on the active side to that on the indifferent side.
- A P value < 0.05 was considered to be significant. Binary logistic regression was performed to determine the effects of power, time, and catheter configuration on the incidence of steam pops and transmurality.
- Similarly, multiple regression was performed to determine these variables' effects on per cent transmurality.

4 RESULTS

A total of 107 lesions were given in various configurations and settings and results were analyzed.

Analysis of variance on lesion geometry:

The average thickness and width of the active catheter lesion significantly differed from that of the passive catheter. Lesion depth $_{active}$ = 7.28 +/- 2.0 vs Lesion depth $_{indifferent}$ = 5.03 +/-1.66. Differences in the active and passive lesions were summarized in the table.1

Table: 1: Analysis of variance on lesion geometry

	Active electrode	Passive electrode	P value
Max depth	7.28 +/- 2.0	5.03 +/- 1.66	< 0.001
Maximum diameter	10.4 +/- 2.07	8.12 +/- 2.37	< 0.001
Depth at maximum diameter	2.82 +/- 0.679	2.33 +/- 0.859	< 0.001
Surface diameter (D)	6.71 +/- 2.09	5.74 +/- 1.62	< 0.001
Surface diameter (E)	4.35 +/- 1.12	4.21 +/- 1.25	< 0.001
Volume	266 +/- 137	130 +/- 91.8	< 0.001
Surface area	24 +/- 12.6	20.2 +/- 10.5	< 0.001

Temperature:

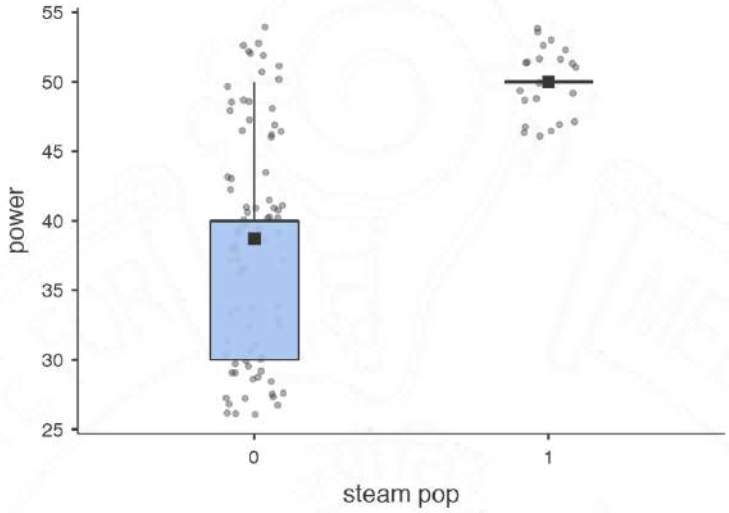
Mean tissue temperature at active catheter lesion 43.6 +/- 7 degrees C Vs passive catheter 40.5 +/-3.92 degrees C (p-value 0.004).

Stream pops:

- The frequency of steam pops is higher with a longer duration of application 30 seconds vs 60 seconds (16.7% vs 83.3% p-value. <0.001), higher power 30W vs 50 W (0 vs 51.2% p-value <0.001)
- The parallel configuration had fewer steam pops than the other configurations (P value <0.01)
- The distribution of steam pops is summarised in Table 2, and their relation to configuration and power is shown in Fig. 1.

Table:2: Distribution of steam pops	
Configuration	**Number of Steam pops**
1. True perpendicular	2/26 (7.7%)
2. True parallel	0/26(0%)
3. Parallel	12/28 (42.9%)
4. Perpendicular	8/27(29.6%)

Figure: 9. Analysis of steam pops about the different power settings



A comparison was made between lesions with steam pops and those without, and the results were tabulated in Table 3.

Table:3: Comparison between lesion characteristics with and without steam pops			
Characteristics	**No steam pop(n=85)**	**Steam pop (n = 22)**	**P value**
Max depth $_{active}$	6.99+/-2.1	8.31 +/- 8.31	0.006
Maximum diameter $_{active}$	10.06 +/-2.09	11.75 +/- 1.2	<0.001
Depth at maximum diameter $_{active}$	2.62 +/-0.6	3.58+/- 0.29	<0.001
Surface diameter (D)$_{active}$	6.19 +/- 1.97	8.69 +/- 1.1	<0.001
Surface diameter (E)$_{active}$	4.09 +/- 0.9	5.35 +/- 1.2	<0.001
Volume $_{active}$	234.55 +/-134	377 +/- 68.9	<0.001
Surface area $_{active}$	20.44 +/- 10.8	37.17 +/- 11.1	<0.001
Max depth $_{passive}$	5.03 +/- 1.6	4.99 +/- 1.64	0.9
Maximum diameter $_{passive}$	7.74 +/- 2.23	9.46 +/- 2.45	0.002
Depth at maximum diameter $_{passive}$	2.19 +/- 0.739	2.79 +/- 1.09	0.003
Surface diameter (D)$_{passive}$	5.55 +/- 1.69	6.46 +/- 1.11	0.019
Surface diameter (E)$_{passive}$	4.05 +/- 1.32	4.8 +/- 0.7	0.011
Volume $_{passive}$	118.4 +/- 90.4	171.9 +/- 87.6	0.015
Surface area $_{passive}$	19.07 +/- 11.1	24.58 +/- 6.34	0.029
Inter electrode distance	23.31 +/-5.1	19.0 +/- 5.81	<0.001

Effect of catheter orientation on lesion characteristics:

When comparing all four configurations, catheter orientation was found to be an important determinant of the lesion. Table 5 summarizes the overall volume, depth, and incidence of steam pops.

Table: 4: Different configurations of the bipolar RFA and their volumes and incident steam pops

configuration	Active electrode	Passive electrode	Time	Power	Maximum depth	Volume active	Volume passive	Steam pops
1. True perpendicular	perpendicular	perpendicular	30	30	3.77+/-0.33	45.99+/-12.20	22.14+/-17.23	
				40	6.45 +/- 0.46	133.06+/-10.90	34.12+/-6.28	
				50	7 +/- 0.14	232.28+/-14.07	72.87+/-22.51	
			40	30	5.58+/-2.80	144.99+/-118.57	83.49+/-0.95	
				40	7.33+/-0.29	159.48+/-106.69	178.83+/-69.68	
				50	9.10+/-1.04	323.91+/-48.30	210.25+/-24.11	2/26
			60	50				
1. True parallel	parallel	Parallel	30	30	3.75+/-0.289	48.28+/-10.55	27.56+/-21.73	
				40	4.83+/-0.39	119.92+/-4.3	100.37+/-7.23	
				50	7.75+/-0.87	333.56+/-96.71	163.91+/-0.00	
			40	30	5.28+/-0.32	179.13+/-55.83	135.17+/-43.3	
				40	7.65+/-0.77	347.06+/-27.63	242.10+/-115.88	
				50	9.75+/2.6	427.24+/-64.81	136.85+/-25.29	
			60	50			373.36+/-0.00	0/26
1. Perpendicular	perpendicular	Parallel	30	30	8.05+/-0.058	222.45+/-2.15	69.47+/-2.16	
				40	7.65+/-0.17	192.72+/-6.9	121.8+/-2.01	
				50	7.65+/-0.17	365.27+/-1.09	190.93+/-22.16	
			40	30	5.50+/-0.081	113.17+/-10.04	100.06+/-5.39	
				40	6.53+/-0.05	196.18+/-5.68	309.14+/-5.12	
				50	7.10+/-0.116	306.96+/-16.37	180.19+/-2.88	
			60	50			211.79+/-11.28	12/28
1. Parallel	Parallel	perpendicular	30	30	5.15+/-0.173	138.11+/-5.245	18.64+/-1.44	
				40	9.03+/-0.05	354.81+/-12.07	66.30+/-1.45	
				50	10.10+/-0.081	483.86+/-4.12	176.45+/-7.75	
			40	30	6.05+/-0.058	269.82+/-14.55	27.25+/-1.08	
				40	11.78+/-0.19	526.13+/-14.62	78.39+/-3.71	
				50	8.85+/-0.24	454.34+/-27.5	177.06+/-2.38	
			60	50	8.0 +/-1.0	299.68 +/- 0.0	17.10+/-0	8/27

Comparison of all lesional parameters between different configurations:

Table. 5 : Comparison of lesional parameters between 1,2 configurations			
Variable	**Configuration 1 (n=25)**	**Configuration 2 (n=26)**	**P value**
Max depth $_{active}$	6.58 +/- 6.62	6.62 +/- 2.2	0.9
Maximum diameter $_{active}$	9.2 +/- 2.3	10.24 +/- 2.0	0.1
Depth at maximum diameter $_{active}$	2.61 +/- 0.75	2.56 +/- 0.68	0.8
Surface diameter (D)$_{active}$	6.36 +/- 2.11	7.05 +/- 2.24	0.2
Surface diameter (E)$_{active}$	4.38 +/- 1.36	4.05 +/- 0.95	0.32
Volume $_{active}$	192.01 +/- 122.3	243.79 +/- 140.5	0.16
Surface area $_{active}$	22.75 +/- 14.50	23.21 +/- 10.44	0.89
Max depth $_{passive}$	5.22 +/- 1.76	5.22 +/- 1.92	1.0
Maximum diameter $_{passive}$	7.46 +/- 2.35	8.94 +/- 2.15	0.022
Depth at maximum diameter $_{passive}$	2.22 +/- 0.798	2.03 +/- 0.46	0.3
Surface diameter (D)$_{passive}$	5.35 +/- 2.11	6.29 +/- 1.76	0.08
Surface diameter (E)$_{passive}$	3.92 +/- 1.94	4.10 +/- 1.24	0.7
Volume $_{passive}$	118.59 +/-98.49	152.71 +/-101.01	0.22
Surface area $_{passive}$	19.35 +/- 15.89	21.63 +/- 10.88	0.54
Inter electrode distance	22.81 +/- 3.02	26.92 +/- 3.74	<0.001
Transmurality	52.35 +/- 19.7	44.44 +/- 13.7	0.1
Total volume	310.60+/-208.183	396.5 +/- 206.06	0.14

There were no significant differences in lesion characteristics between configurations 1 and 2.

Table. 6 : Comparison of lesional parameters between 3,4 configurations			
Variable	**Configuration 3 (n=28)**	**Configuration 4 (n=28)**	**P value**
Max depth $_{active}$	7.37 +/-1.08	8.42 +/- 2.1	0.032
Maximum diameter $_{active}$	10.32 +/- 1.4	11.84 +/- 1.43	<0.001
Depth at maximum diameter $_{active}$	3.19 +/- 0.429	2.86 +/- 0.65	0.019
Surface diameter (D)$_{active}$	6.76 +/- 2.05	6.67 +/- 2.0	0.79
Surface diameter (E)$_{active}$	4.33 +/- 0.9	4.64 +/- 1.12	0.175
Volume $_{active}$	258.62 +/- 101.043	360.96 +/- 129.89	0.003
Surface area $_{active}$	24.2 +/- 12.03	25.63 +/- 13.6	0.98
Max depth $_{passive}$	5.63 +/- 0.986	4.09 +/- 1.48	<0.001
Maximum diameter $_{passive}$	9.25 +/- 1.89	6.84 +/- 2.22	<0.001
Depth at maximum diameter $_{passive}$	3.11 +/-0.48	1.94 +/- 1.0	<0.001
Surface diameter (D)$_{passive}$	6.19 +/- 1.14	5.15 +/- 1.03	<0.001
Surface diameter (E)$_{passive}$	4.81 +/- 0.74	3.98 +/- 0.32	<0.001
Volume $_{passive}$	169.05 +/- 76.4	80.17 +/- 66.08	<0.001
Surface area $_{passive}$	23.62 +/- 6.5	16.25 +/- 4.44	<0.001
Inter electrode distance	14.82 +/- 1.27	25.61 +/- 2.89	<0.001
Transmurality	88.37% +/- 11.07	48.77 +/- 10.9	<0.001
Total volume	428 +/-146	441 +/- 184	0.25

Although the overall volume created by the 3 and 4 configurations was the same, the lesion depths and other lesion metrics were significantly different between the two configurations.

Table. 7 : Comparison of lesional parameters between 1,3 configurations			
Variable	**Configuration 1 (n=25)**	**Configuration 3 (n=28)**	**P value**
Max depth $_{active}$	6.58+/-1.97	5.22+/-1.76	0.073
Maximum diameter $_{active}$	9.20+/-2.37	10.32+/-1.46	0.040
Depth at maximum diameter $_{active}$	2.61+/-0.76	3.19+/-0.43	<0.001
Surface diameter (D)$_{active}$	6.36+/-2.11	6.76+/-2.06	0.49
Surface diameter (E)$_{active}$	4.38+/-1.36	4.33+/-0.98	0.89
Volume $_{active}$	192.01+/-122.32	258.62+/-101.04	0.03
Surface area $_{active}$	22.75+/-14.50	24.02+/-12.04	0.69
Max depth $_{passive}$	5.22+/-1.76	5.63+/-0.99	0.29
Maximum diameter $_{passive}$	7.46+/-2.36	9.25+/-1.90	0.003
Depth at maximum diameter $_{passive}$	2.22+/-0.80	3.11+/-0.48	<0.001
Surface diameter (D)$_{passive}$	5.35+/-2.11	6.19+/-1.15	0.072
Surface diameter (E)$_{passive}$	3.92+/-1.95	4.81+/-0.74	0.029
Volume $_{passive}$	118.59+/-98.49	169.05+/-76.48	0.040
Surface area $_{passive}$	19.35+/-15.89	23.62+/-6.57	0.196
Inter electrode distance	22.8+/-3.02	14.8+/-1.28	<0.001
Transmurality	52.35+/-19.77	88.37+/-11.08	<0.001
Total volume	310.60+/-208.18	427.67+/-145.76	0.02

Total depth, volumes and transmurality % were significantly higher with perpendicular configuration (configuration.3: the active electrode is perpendicular, and the passive electrode is parallel) than with true perpendicular configuration (configuration.1).

Table. 8 : Comparison of lesional parameters between 1,4 configurations			
Variable	**Configuration 1 (n=25)**	**Configuration 4 (n=28)**	**P value**
Max depth $_{active}$	6.58+/-1.97	8.42+/-2.15	0.002
Maximum diameter $_{active}$	9.20+/-2.37	11.84+/-1.43	<0.001
Depth at maximum diameter $_{active}$	2.61+/-0.76	2.86+/-0.65	0.199
Surface diameter (D)$_{active}$	6.36+/-2.11	6.67+/-2.016	0.581
Surface diameter (E)$_{active}$	4.38+/-1.36	4.64+/-1.23	0.44
Volume $_{active}$	192.01+/-122.32	360.96+/-129.90	<0.001
Surface area $_{active}$	22.75+/-14.504	25.63+/-13.61	0.456
Max depth $_{passive}$	5.22+/-1.76	4.09+/-1.49	0.013
Maximum diameter $_{passive}$	7.46+/-2.36	6.84+/-2.82	0.328
Depth at maximum diameter $_{passive}$	2.22+/-0.80	1.94+/-1.00	0.266
Surface diameter (D)$_{passive}$	5.35+/-21.11	5.15+/-1.04	0.660
Surface diameter (E)$_{passive}$	3.92+/-1.95	3.98+/-0.33	0.874
Volume $_{passive}$	118.59+/-98.49	80.17+/-66.09	0.096
Surface area $_{passive}$	19.35+/-15.89	16.25+/-4.45	0.327

Inter electrode distance	22.81+/-3.02	25.61+/-2.89	0.001
Transmurality	52.35+/-19.77	48.77+/-10.90	0.409
Total volume	311+/-208	441+/-184	0.018

The total volume of the lesion created by the parallel configuration is statistically significantly higher than that of the true perpendicular configuration.

Table. 9 : Comparison of lesional parameters between 2,3 configurations

Variable	Configuration 2 (n=26)	Configuration 3 (n=28)	P value
Max depth $_{active}$	6.62+/-2.29	7.37+/-1.09	0.124
Maximum diameter $_{active}$	10.24+/-2.09	10.32+/-1.46	0.87
Depth at maximum diameter $_{active}$	2.56+/-0.69	3.19+/-0.43	<0.001
Surface diameter (D)$_{active}$	7.05+/-2.25	6.76+/-2.06	0.623
Surface diameter (E)$_{active}$	4.05+/-0.96	4.33+/-0.98	0.295
Volume $_{active}$	243.79+/-140.52	258.62+/-101.04	0.66
Surface area $_{active}$	23.21+/-10.44	24.2+/-12.04	0.75
Max depth $_{passive}$	5.22+/-1.93	5.63+/-0.99	0.33
Maximum diameter $_{passive}$	8.94+/-2.15	9.25+/-1.90	0.58
Depth at maximum diameter $_{passive}$	2.03+/-0.47	3.11+/-0.48	<0.001
Surface diameter (D)$_{passive}$	6.29+/-1.77	6.19+/-1.15	0.792
Surface diameter (E)$_{passive}$	4.10+/-1.29	4.81+/-0.74	0.02
Volume $_{passive}$	152.71+/-101.01	169.05+/-76.48	0.504

Surface area $_{passive}$	21.63+/-10.89	23.62+/-6.57	0.416
Inter electrode distance	26.92+/-3.74	14.82+/-1.28	<0.001
Transmurality	44.44+/-13.77	88.37+/-11.08	<0.001
Total volume	396.5+/-206.07	427.67+/-145.76	0.522

Though total volumes are not significantly different between both configurations, higher transmurality was noted with perpendicular configuration than true parallel configuration.

Total volume:

Among the different configurations, those that were true perpendicular generated lower volumes, while the others generated higher volumes. Though the volumes are higher in the other configurations the difference is not statistically significant.

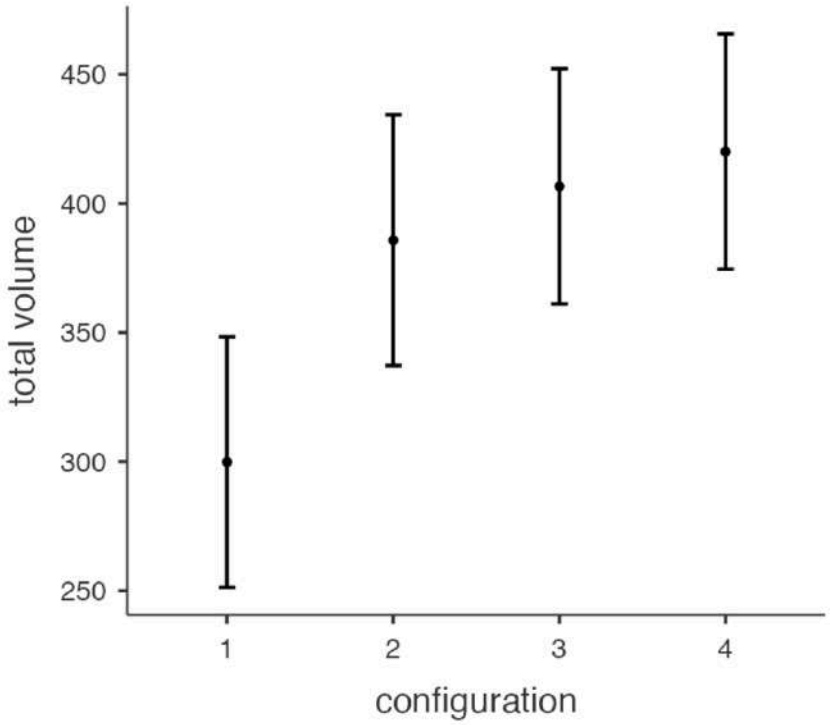


Figure:10. Total lesional volumes in comparison with different configurations

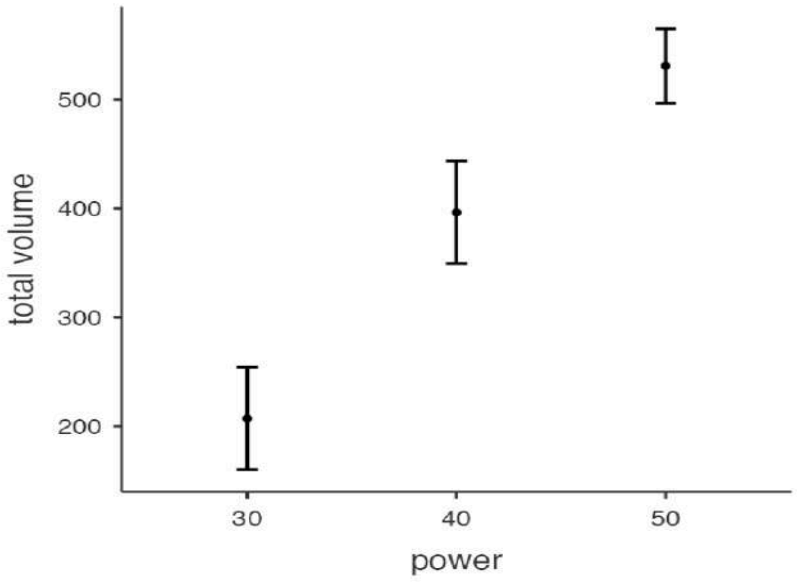


Figure:11 Mean total lesional volumes in comparison with different power settings

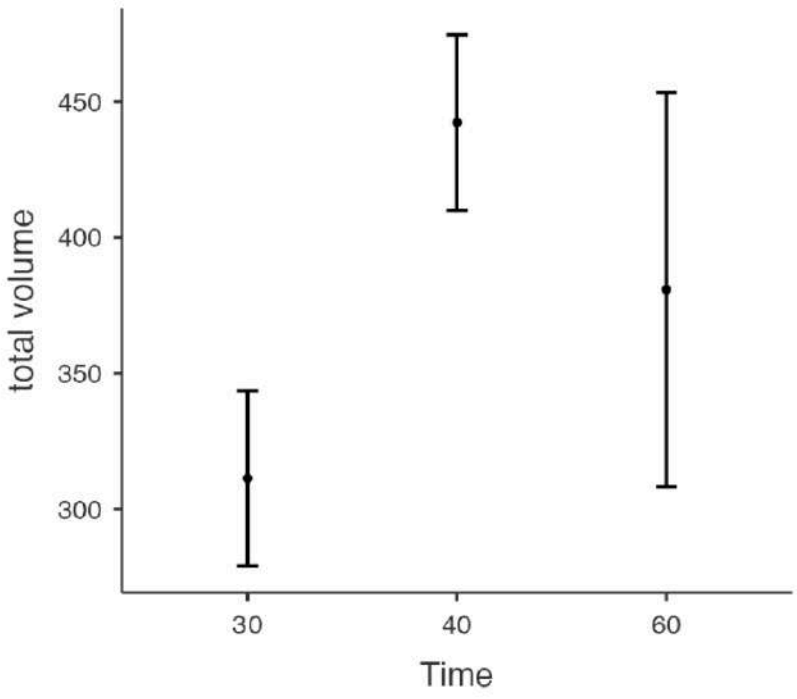


Figure: 12 Mean total lesional volumes in comparison with different duration

Application for 40 seconds produced higher volumes compared to 60 seconds. Steam pops are associated with higher times and powers. The relation with configurations, time, power and volume was depicted with this marginal mean estimation.

Power

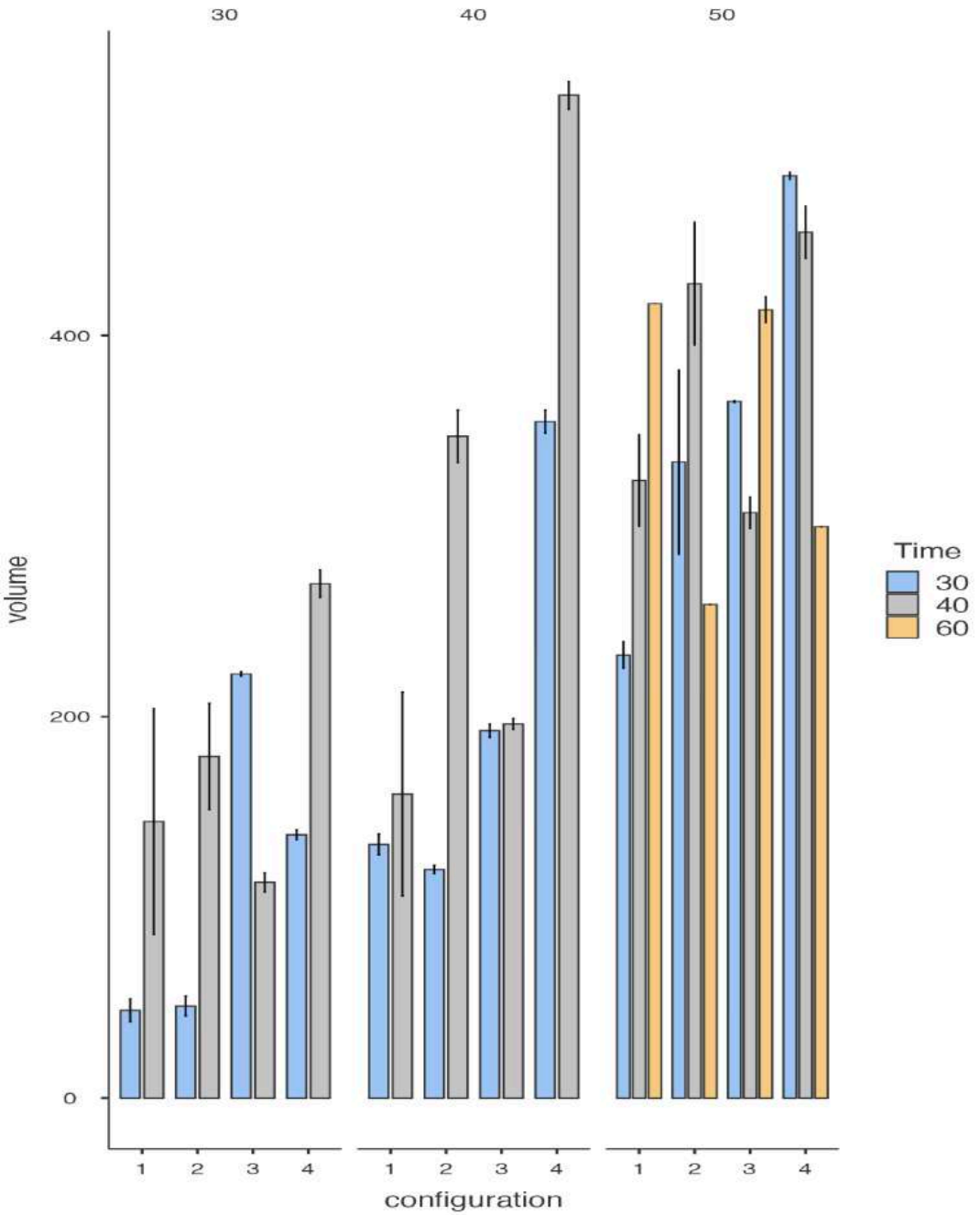


Fig.13 : Configurations vs power vs volume vs time

Multivariate analysis:

The independent association between the volume of the lesion and power, time and various configurations was assessed using linear regression analysis which showed, that parallel or perpendicular configuration, time of 40 sec and power of 50W were significantly associated with a higher total volume of lesion.

5 DISCUSSION

In this study, 107 ablations were carried out in an ex vivo setup to characterize the effects of power, time, relative catheter orientation, and tissue thick- ness on lesion geometry and risk of steam pops during bipolar ablation. Among these 107 lesions, 25 ablations were carried out in the true perpendicular configuration, 26 in the true parallel configuration, and 28 in perpendicular and parallel configurations each.

Lesion variance:

Analysis of lesional variance showed that lesions near the active catheter were deeper and wider with higher volumes and surface area than those near the indifferent catheter which were correlated with past studies by John et.al (5).

Steam pops:

Many previous studies also revealed that time contributed more to lesion depth whereas the combination of power, time, and tissue thickness contributed more to the risk of steam pops(2,3,5,27).

To determine the optimal ablation parameters, several testing conditions were examined. The results of the study indicated that ablation duration played a crucial role in the development of transmural lesions. Specifically, a 30-second ablation was found to be the least effective in terms of transmurality, resulting in the least transmural lesion compared to longer durations. Furthermore, the study also found that the amount of power used in ablation procedures was a critical factor in the occurrence of steam pops. It was observed that a 50-W ablation had a higher risk of steam pops than a 30-

W ablation irrespective of catheter configuration, which indicates that lower power levels are safer in ablation procedures. These findings are consistent with the results of previous studies. (3,5)

It is interesting to note that a lesser number of steam pops were observed with the true parallel configuration compared to the other configurations despite optimal cooling provided by the irrigated saline flow both from the laser cut kerfs and from four holes at the distal end of the catheter (27,28). These findings were not seen in previous studies. The majority of previous studies reported that unipolar parallel configurations have larger lesion volumes and greater incidence of steam pops given large tissue electrode contact(29,30). Very few studies reported that greater tissue heating with a perpendicular compared to parallel catheter placement is accompanied by an increased incidence of steam pops (27,31). According to a study by John et al, catheter orientation did not affect lesion transmurality or the risk of steam pops (5).

Degree of transmurality:

Previously, Nguyen and colleagues studied the effects of tissue thickness on lesion formation, using an optimal catheter configuration to produce deep lesions. The authors reported that thinner tissue was associated with greater transmurality. Our regression analysis also concurred with the previous findings and the thinner the tissue more transmurality which is shown in a scatter plot. Thicker tissues have a lower chance of transmurality and are not superior to sequential unipolar ablation(3,5,14). There is a negative correlation between tissue thickness and transmurality. (Fig.)

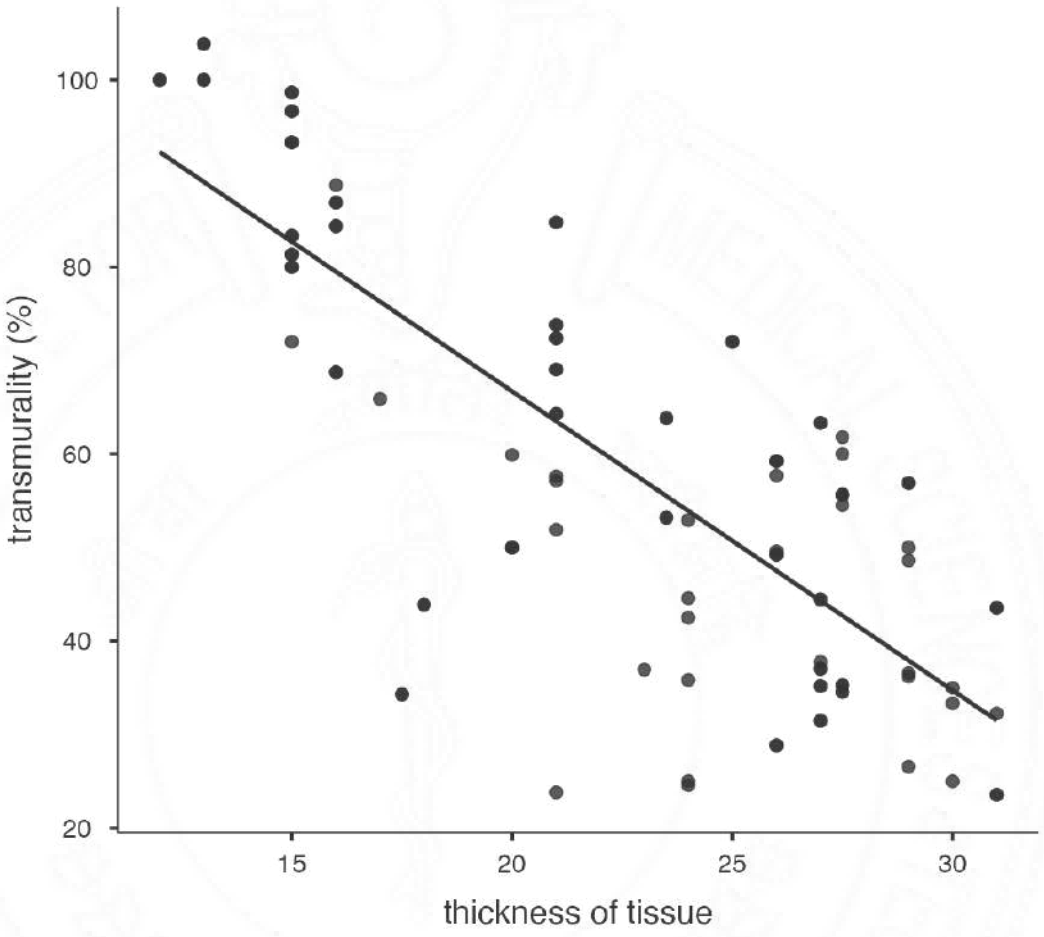


Fig. 14: Scatter plot between the thickness of tissue and transmurality

Of the 107 ablations studied, only 24.2% (n = 26) of lesions covered at least 75% of the total tissue thickness. The mean tissue thickness among the 26 lesions was 15.11mm +/- 5.95 mm.

Our findings correlated with the previous studies that bipolar ablation may not be much more effective than unipolar ablation when the 2 electrodes are sufficiently separated(3,14).

Effect of various configurations:

We chose to analyze lesion depth instead of transmurality to avoid confounding the multiple linear regression analysis. Which showed there is no significant association with catheter orientation in the production of deeper lesions.

Though the lesion depth may not be different with different catheter orientations, the overall lesional volumes are significantly different with different catheter configurations.

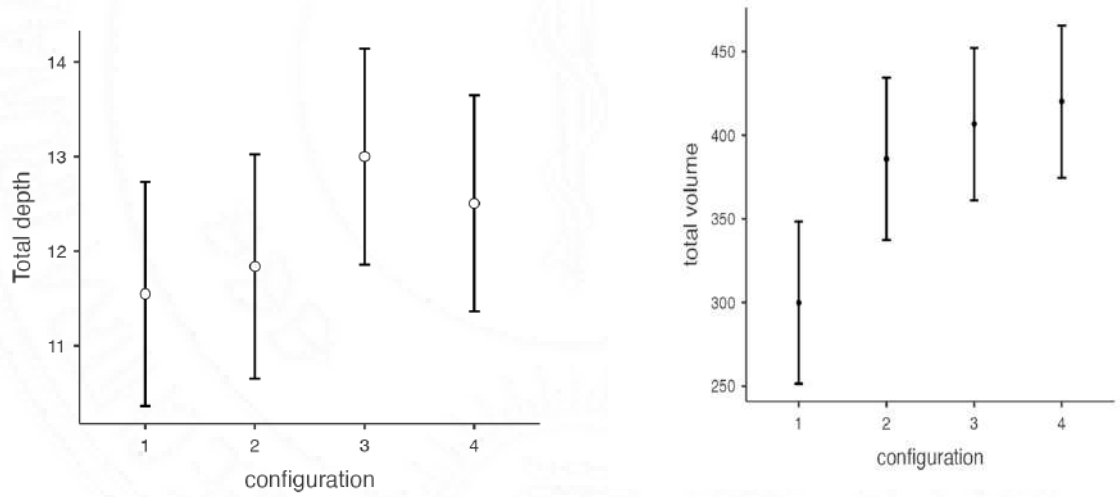


Fig.15 Comparison of lesion depth and volume with various configurations.

Our study did not align with the previous findings that configuration 1(true perpendicular) generated higher volumes than others (3).

Our research provided a comprehensive dataset for understanding the geometry of lesions and the formation of steam pops in bipolar ablation. Specifically, the ex vivo model uncovered the impact of power, time, and catheter configuration. The model presented in this study can be leveraged as a valuable tool for planning clinical ablation procedures, to avoid steam pop-related complications while ensuring complete lesion transmurality.

Based on our preclinical study, we have observed that a higher volume of the lesion is directly proportional to greater power, regardless of the configuration tested. However, this increase in power also comes with an increased risk of steam pops. Additionally, we found that the thickness of the tissue or inter-electrode distance significantly contributes to the risk of steam pops.

Though the number of steam pops is higher in configuration.3 (parallel configuration) but the important thing to note in those samples, the mean myocardial thickness was 15.11mm +/- 5.95 mm. only which may be a significant confounding variable.

All steam pop events are recorded at the active catheter following a significant drop in impedance(5,32).

The findings of this study have significant implications for the field of bipolar ablation. By identifying the key factors that contribute to steam pop formation, clinicians can now plan ablation procedures with greater confidence and precision.

Moreover, the dataset generated by this study can serve as a foundation for further research aimed at improving the safety and efficacy of bipolar ablation procedures.

Understanding the clinical relevance:

We selected the catheter configurations for analysis based on their clinical relevance.

Configuration: 1: True perpendicular configuration:

This configuration is rarely useful in Bipolar RFA due to anatomical limitations that make it unlikely for operators to manipulate catheters to be perpendicular to the ablation target during endocardial-epicardial ablation. Performing septal ablation using two catheters positioned perpendicular to each other is a highly challenging and unwieldy technique, which makes it unlikely to be used in real-world clinical scenarios. Sometimes, in cases where deep intramural LV summit VPCs are not accessible via the coronary venous route, a specific configuration can be helpful in their ablation. This involves placing a catheter in the left coronary cusp (LCC) and another through the anterior right ventricular outflow tract.

Our study failed to reproduce previous findings that deeper lesions can be formed when both catheters are perpendicular to the myocardium(3).

Configuration: 2: True parallel configuration:

This configuration can be easily practised in ventricular tachycardia ablations with an endocardial–epicardial approach or summit VT ablation with a trans coronary venous approach.

Configurations 3,4: (Parallel and perpendicular configurations):

During the procedure of epicardial ablation, one of the catheters is commonly introduced either into the pericardial space or via transvenous access into an epicardial vein. This catheter is positioned in proximity to the epicardial wall of the ventricle, while the other catheter is placed intracardially and may be directed in different orientations. This sort of catheter configuration henceforth possesses significant relevance in the realm of clinical applications.

Examples of Lesional geometries in various configurations

Limitations:

1. This study was conducted on bovine cardiac tissue outside of a living organism, which means that the experimental model may not precisely replicate the clinical conditions in the same way as an in vivo model would. Additionally, the model did not take into account the mechanical movement of a beating heart, which could potentially affect the stability of the catheter applied.
2. In the present un-perfused ex vivo model without cardiac and respiratory movement, steam-pop risks might be overestimated, and lesion characteristics might be different from those in a clinical setting.
3. This particular model employed a saline bath, which has roughly twice the electrical conductivity of blood(5,33). This means that RF energy could have been directed to the saline bath. It's important to note that the data presented here are not intended to predict how ablation would behave in a clinical model. However, we believe that the general trends observed in these experiments would still be relevant.
4. In addition, when performing bipolar ablation in clinical settings, likely, that some of the ventricular myocardium may already be scarred due to the disease state of the patient. It's important to note that this study does not simulate these conditions. Therefore, the depth of the lesion and the risk of steam pops may differ when scarred myocardium is present at the ablation site.

5. While the study's ex vivo nature is useful for certain research purposes, it may not fully capture the potential collateral injury to surrounding tissues during epicardial-endocardial bipolar ablation in vivo. It could be worthwhile to explore methods to account for this in future studies.
6. Contact force sensing catheters were not utilized directly in the study. This is a significant variable that can impact not only the lesion characteristics and geometry but also the transmurality and occurrence of steam pops.
7. Different irrigant solutions, flow rates and their effect on the lesion characters were not studied.

6 SUMMARY AND IMPLICATIONS

1. With modifications to the circuitry, it is technically feasible to perform Bipolar ablation using a single RF generator which has implications for cost-effectiveness.
2. Our findings indicate that increasing power and duration may not only fail to achieve deeper lesions but also lead to more steam pops.
3. Though the lesion depth may not be different with different catheter orientations, the overall lesional volumes are significantly different with different catheter configurations. From a clinical standpoint, it is beneficial to use the appropriate configuration based on the patient's specific needs.
4. Tissue thickness plays a major role in transmurality and steam pops. Thicker tissues have a lower chance of transmurality and are not superior to sequential unipolar ablation. Hence in those patients who had failed sequential unipolar ablations or septal thickness greater than 15mm, the degree of transmurality is lesser and bipolar ablation may not be useful.
5. Additional temperature measurement at the passive electrode may not be necessary as the tissue temperatures and returning electrode temperatures never exceeded the tissue temperatures of the active electrode. As the recorded temperature is convincingly shown to be within safer limits in experimental settings in all configurations of irrigated catheters as both active and passive electrodes, the safety of b-RF ablation using similar settings can be inferred even in clinical settings.

6. In bipolar ablation, lesions formed with 50 W power with a duration of 40 seconds generated the highest volumes. The safest strategy in the case of bipolar ablation was with true parallel configuration with an inter-electrode distance of 15mm at a power of 30 W to 40 W generating lower steam pops and better transmurality and optimal lesions.

7 CONCLUSIONS

1. This study demonstrated bipolar ablation with a single RF generator is technically feasible with modifications in connections in the pre-clinical study.

2. The safest strategy in the case of bipolar ablation was with true parallel configuration with an inter-electrode distance of at least 15mm at a power of 30 W to 40 W generating lower steam pops and better transmurality.

3. Additional temperature measurement at the passive electrode may not be necessary as the tissue temperatures and returning electrode temperatures never exceeded the active electrode.

8 REFERENCES

1. Barkagan M, Leshem E, Shapira-Daniels A, Sroubek J, Buxton AE, Saffitz JE, et al. Histopathological Characterization of Radiofrequency Ablation in Ventricular Scar Tissue. JACC Clin Electrophysiol. 2019 Aug;5(8):920–31.

2. Futyma P, Chen S, Enriquez A, Pürerfellner H, Santangeli P. Bipolar ablation of ventricular arrhythmias: Step-by-step. J Cardiovasc Electrophysiol. 2023 Nov 15;jce.16131.

3. Nguyen DT, Tzou WS, Brunnquell M, Zipse M, Schuller JL, Zheng L, et al. Clinical and biophysical evaluation of variable bipolar configurations during radiofrequency ablation for treatment of ventricular arrhythmias. Heart Rhythm. 2016 Nov;13(11):2161–71.

4. Nguyen DT, Zheng L, Zipse MM, Borne RT, Tzou WS, Fleeman B, et al. Bipolar radiofrequency ablation creates different lesion characteristics compared to simultaneous unipolar ablation. J Cardiovasc Electrophysiol. 2019 Dec;30(12):2960–7.

5. John M, Rook A, Post A, Mersman A, Allen W, Schramm C, et al. Bipolar ablation's unique paradigm: Duration and power as respectively distinct primary determinants of transmurality and steam pop formation. Heart Rhythm O2. 2020 Oct;1(4):290–6.

6. Sauer PJ, Kunkel MJ, Nguyen DT, Davies A, Lane C, Tzou WS. Successful ablation of ventricular tachycardia arising from a midmyocardial septal outflow tract site utilizing a simplified bipolar ablation setup. Hear Case Rep. 2019 Feb;5(2):105–8.

7. Kany S, Alken FA, Schleberger R, Baran J, Luik A, Haas A, et al. Bipolar ablation of therapy-refractory ventricular arrhythmias: application of a dedicated approach. EP Eur. 2022 Jul 15;24(6):959–69.

8. Nakagawa H, Yamanashi WS, Pitha JV, Arruda M, Wang X, Ohtomo K, et al. Comparison of In Vivo Tissue Temperature Profile and Lesion Geometry for Radiofrequency Ablation With a Saline-Irrigated Electrode Versus Temperature Control in a Canine Thigh Muscle Preparation. Circulation. 1995 Apr 15;91(8):2264–73.

9. Sivagangabalan G, Barry MA, Huang K, Lu J, Pouliopoulos J, Thomas SP, et al. Bipolar Ablation of the Interventricular Septum is More Efficient at Creating a Transmural Line than Sequential Unipolar Ablation. Pacing Clin Electrophysiol. 2010 Jan;33(1):16–26.

10. González-Suárez A, Trujillo M, Koruth J, d'Avila A, Berjano E. Radiofrequency cardiac ablation with catheters placed on opposing sides of the ventricular wall:

Computer modelling comparing bipolar and unipolar modes. Int J Hyperthermia. 2014 Sep;30(6):372–84.

11. Gizurarson S, Spears D, Sivagangabalan G, Farid T, Ha ACT, Masse S, et al. Bipolar ablation for deep intra-myocardial circuits: human ex vivo development and in vivo experience. Europace. 2014 Nov 1;16(11):1684–8.

12. Nagashima K, Watanabe I, Okumura Y, Ohkubo K, Kofune M, Ohya T, et al. Lesion Formation by Ventricular Septal Ablation With Irrigated Electrodes - Comparison of Bipolar and Sequential Unipolar Ablation -: – Comparison of Bipolar and Sequential Unipolar Ablation –. Circ J. 2011;75(3):565–70.

13. Nagashima K, Watanabe I, Okumura Y, Sonoda K, Kofune M, Mano H, et al. Epicardial Ablation With Irrigated Electrodes: – Effect of Bipolar vs. Unipolar Ablation on Lesion Formation – Circ J. 2012;76(2):322–7.

14. Koruth JS, Dukkipati S, Miller MA, Neuzil P, d'Avila A, Reddy VY. Bipolar irrigated radiofrequency ablation: A therapeutic option for refractory intramural atrial and ventricular tachycardia circuits. Heart Rhythm. 2012 Dec;9(12):1932–41.

15. Teh AW, Reddy VY, Koruth JS, Miller MA, Choudry S, D'Avila A, et al. Bipolar Radiofrequency Catheter Ablation for Refractory Ventricular Outflow Tract Arrhythmias. J Cardiovasc Electrophysiol. 2014 Oct;25(10):1093–9.

16. Al-Hadithi ABAK, Khakpour H, Cruz D, Boyle NG, Shivkumar K, Bradfield JS. Incessant intraseptal ventricular tachycardia ablated utilizing extracorporeal membrane oxygenation and bipolar ablation. Hear Case Rep. 2018 Dec;4(12):557–60.

17. Piers SRD, Dyrda K, Tao Q, Zeppenfeld K. Bipolar Ablation of Ventricular Tachycardia in a Patient After Atrial Switch Operation for Dextro-Transposition of the Great Arteries. Circ Arrhythm Electrophysiol [Internet]. 2012 Apr [cited 2024 Jan 1];5(2). Available from: https://www.ahajournals.org/doi/10.1161/CIRCEP.111.969345

18. Maury P, Duparc A, Capellino S, Mondoly P, Rollin A. High-Density Biventricular Activation Mapping During Intraseptal Ventricular Tachycardia. JACC Clin Electrophysiol. 2016 Aug;2(4):526–8.

19. Berte B, Sacher F, Mahida S, Yamashita S, Lim HS, Denis A, et al. Impact of Septal Radiofrequency Ventricular Tachycardia Ablation: Insights From Magnetic Resonance Imaging. Circulation. 2014 Aug 19;130(8):716–8.

20. Futyma P, Ciąpała K, Głuszczyk R, Sander J, Futyma M, Kułakowski P. Bipolar ablation of refractory atrial and ventricular arrhythmias: Importance of temperature values of intracardiac return electrodes. J Cardiovasc Electrophysiol. 2019 Sep;30(9):1718–26.

21. Liu X, Chen Q, Fan B, Zhu W, Zhao H, Zhu Y, et al. Bipolar catheter ablation in ventricular myocardium. Pacing Clin Electrophysiol. 2020 Jan;43(1):54–61.

22. Nguyen DT, Barham W, Zheng L, Shillinglaw B, Tzou WS, Neltner B, et al. Carbon Nanotube Facilitation of Myocardial Ablation with Radiofrequency Energy. J Cardiovasc Electrophysiol. 2014 Dec;25(12):1385–90.

23. Franco E, Rodríguez Muñoz D, Matía R, Hernández-Madrid A, Sánchez Pérez I, Zamorano JL, et al. Contact force-sensing catheters: performance in an ex vivo porcine heart model. J Interv Card Electrophysiol. 2018 Nov;53(2):141–50.

24. Lozano Granero C, Franco E, Matía Francés R, Hernández-Madrid A, Sánchez-Pérez I, Zamorano Gómez JL, et al. Impact of power and contact force on index-guided radiofrequency lesions in an ex vivo porcine heart model. J Interv Card Electrophysiol. 2022 Apr;63(3):687–97.

25. Wittkampf FHM, Nakagawa H, Foresti S, Aoyama H, Jackman WM. Saline-Irrigated Radiofrequency Ablation Electrode with External Cooling. J Cardiovasc Electrophysiol. 2005 Mar;16(3):323–8.

26. Stoffregen WC, Rousselle SD, Rippy MK. Pathology Approaches to Determine Safety and Efficacy of Cardiac Ablation Catheters. Toxicol Pathol. 2019 Apr;47(3):311–28.

27. Yamaguchi J, Takigawa M, Goya M, Martin C, Amemiya M, Yamamoto T, et al. Impact of tip design and thermocouple location on the efficacy and safety of radiofrequency application. J Interv Card Electrophysiol. 2022 Apr 22;66(4):885–96.

28. Winterfield JR, Jensen J, Gilbert T, Marchlinski F, Natale A, Packer D, et al. Lesion Size and Safety Comparison Between the Novel Flex Tip on the FlexAbility Ablation Catheter and the Solid Tips on the ThermoCool and ThermoCool SF Ablation Catheters. J Cardiovasc Electrophysiol. 2016 Jan;27(1):102–9.

29. Knecht S, Reichlin T, Pavlovic N, Schaer B, Osswald S, Sticherling C, et al. Contact force and impedance decrease during ablation depends on catheter location and orientation: insights from pulmonary vein isolation using a contact force-sensing catheter. J Interv Card Electrophysiol. 2015 Sep;43(3):297–306.

30. González-Suárez A, Berjano E, Guerra JM, Gerardo-Giorda L. Computational Modeling of Open-Irrigated Electrodes for Radiofrequency Cardiac Ablation Including Blood Motion-Saline Flow Interaction. PLOS ONE. 2016 Mar 3;11(3):e0150356.

31. Takigawa M, Yamaguchi J, Goya M, Iwakawa H, Yamamoto T, Iwakawa H, et al. How to enlarge lesion size in temperature control mode using an irrigation catheter with a flexible-tip of laser-cut kerfs [Internet]. Cardiovascular Medicine; 2023 Aug [cited 2024 Jan 2]. Available from: http://medrxiv.org/lookup/doi/10.1101/2023.08.08.23293854

32. Seiler J, Roberts-Thomson KC, Raymond JM, Vest J, Delacretaz E, Stevenson WG. Steam pops during irrigated radiofrequency ablation: feasibility of impedance monitoring for prevention. Heart Rhythm. 2008 Oct;5(10):1411–6.

33. Beving H, Eriksson LE, Davey CL, Kell DB. Dielectric properties of human blood and erythrocytes at radio frequencies (0.2-10 MHz); dependence on cell volume fraction and medium composition. Eur Biophys J EBJ. 1994;23(3):207–15.

ANNEXURES

Appendices

APPENDIX A – ETHICS COMMITTEE APPROVAL

APPENDIX B – PLAGIARISM CHECK REPORT

APPENDIX C – PROFORMA

APPENDIX D – CURRICULUM VITAE

APPENDIX E – PROJECT DETAILS

APPENDIX – A: ETHICS COMMITTEE APPROVAL LETTER

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY.
BIOMEDICAL TECHNOLOGY WING.

INSTITUTIONAL ANIMAL ETHICS COMMITTEE

To,

11/08/2021

Dr. Narayanan Namboodiri KK
Professor, Cardiology,
SCTIMST,Trivandrum

Dear Sir,

Your request to IAEC dated 16/06/2021 regarding the project entitled "Biophysical evaluation of various bipolar configurations in RF ablation of ventricular myocardium in a bovine model and a prototype design of a custom-made bipolar RF ablator model" has been considered on the IAEC meeting held on 26/07/2021 and it was decided to APPROVE your request to obtain 60 numbers of bovine hearts from slaughter house carcasses to complete the foresaid experiment.

Yours Sincerely

Dr Harikrishnan VS

Member secretary-IAEC

APPENDIX: B: PLAGIARISM REPORT

APPENDIX: C: PROFORMA

Mode	Active vs Indifferent	Time (sec)	Power (W)	Max depth (A)	Max diameter (B)	Depth at max distance (C)	Surface diameter (D)	Surface diameter (E)	Volume	Surface area	Thickness of tissue	transmurality (passive abln. cath. Temp)	Steam pop	Sample bottle No
True perpendicular configuration														
Bipolar	Active	30	30											
Bipolar	Indifferent	30	30											
Bipolar	Active	30	40											
Bipolar	Indifferent	30	40											
Bipolar	Active	30	50											
Bipolar	Indifferent	30	50											
Bipolar	Active	40	30											
Bipolar	Indifferent	40	30											
Bipolar	Active	40	40											
Bipolar	Indifferent	40	40											
Bipolar	Active	40	50											
Bipolar	Indifferent	40	50											
True parallel configuration														
Bipolar	Active	30	30											
Bipolar	Indifferent	30	30											
Bipolar	Active	30	40											
Bipolar	Indifferent	30	40											
Bipolar	Active	30	50											
Bipolar	Indifferent	30	50											
Bipolar	Active	40	30											
Bipolar	Indifferent	40	30											
Bipolar	Active	40	40											
Bipolar	Indifferent	40	40											
Bipolar	Active	40	50											
Bipolar	Indifferent	40	50											

Mode	Active vs Indifferent	Time (sec)	Power (W)	Max depth (A)	Max diameter (B)	Depth at max distance (C)	Surface diameter (D)	Surface diameter (E)	Volume	Surface area	Thickness of tissue	transmurality (passive abln. cath. Temp)	Steam pop	Sample bottle No
perpendicular configuration (active electrode is perpendicular)														
Bipolar	Active	30	30											
Bipolar	Indifferent	30	30											
Bipolar	Active	30	40											
Bipolar	Indifferent	30	40											
Bipolar	Active	30	50											
Bipolar	Indifferent	30	50											
Bipolar	Active	40	30											
Bipolar	Indifferent	40	30											
Bipolar	Active	40	40											
Bipolar	Indifferent	40	40											
Bipolar	Active	40	50											
Bipolar	Indifferent	40	50											
Parallel configuration (active electrode is parallel)														
Bipolar	Active	30	30											
Bipolar	Indifferent	30	30											
Bipolar	Active	30	40											
Bipolar	Indifferent	30	40											
Bipolar	Active	30	50											
Bipolar	Indifferent	30	50											
Bipolar	Active	40	30											
Bipolar	Indifferent	40	30											
Bipolar	Active	40	40											
Bipolar	Indifferent	40	40											
Bipolar	Active	40	50											
Bipolar	Indifferent	40	50											

APPENDIX : D :

Curriculum Vitaé

Name : Dr. Saikiran Kakarla
Permanent Address : 103, Anoop residency, Bhagya Nagar phase 3, opp to JNTU, Kukatpally, Hyderabad, 500072
Working address : Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India, 495011.
Mobile No : +91 8019672629
E-mail : doctorsaikirankakarla@gmail.com, doctorsaikirankakarla@sctimst.ac.in

Academic Qualifications:

Degree	Year of passing	Institute and University
PDF Cardiac electrophysiology	Jan 2023 to present	Sree Chitra Tirunal Institute for medical sciences and Technology, Thiruvananthapuram, Kerala, India
DM cardiology	Jan 2020 to Dec 2022	Sree Chitra Tirunal Institute for medical sciences and Technology, Thiruvananthapuram, Kerala, India
Senior residency	April 2019 to Nov 2019	Kurnool Medical college, Dr. NTRUHS
MD General Medicine	May 2016 to April 2019	Kurnool Medical college, Dr. NTRUHS
Internship	April 2015 to March 2016	Kurnool Medical college, Dr. NTRUHS
MBBS	April 2010 to March 2015	Kurnool Medical college, Dr. NTRUHS

Additional Qualification / Achievements / Certifications:

MBBS:

- ***Smt Annapurnamma Memorial Gold Medal in General Medicine, 2015***
- G.V. Rao Memorial Gold Medal in Biochemistry, 2010

Internship

- Best Intern of the Year Award 2015-2016 presented as a part of Republic Day Celebrations 2016
- Winner in Gastroenterology PG quiz conducted in 2015, Kurnool Medical College, Kurnool

MD. General Medicine:

- Best paper award in state APICON 2016 on "Predictors of recurrence in Gillian barre syndrome – a tertiary centre experience"
- Winner in APICON 2017 state-wide quiz competition
- Best outgoing junior resident in the department of general medicine of the year 2020
- **Dr. Sri Pada Pinakapani's Memorial Gold Medal award for the year 2020, Department of General Medicine, Kurnool Medical College**
- **The best Junior Resident award was given during Independence Day celebrations, in 2019**
- **University gold medal for the year 2020 in General Medicine (state-wide)**

DM Cardiology:

- ***1st in Epignosis Cardiology Quiz 2020 organised*** by The White Army
- ***Best Paper Award*** in *Cardiology Society of India Kerala (CSI Kerala) Annual National Conference 2021 (CSI Kerala 2021) held at Kochi, Kerala*
- ***Best Abstract in the oral free abstract category in the*** Indian Heart Rhythm Society annual National Conference, 2021 titled "Atrial cardiopathy – an etiology of recurrent stroke, a retrospective study."
- ***Best Challenging Case Presentation under device category "An elderly woman with CRT device at EOL" organised by CSI annual rhythm council conducted by the Department of Arrhythmia and Heart Failure, MMM, Chennai***
- ***Best case award in 2nd all India EP fellows' summit, conducted by MMM, Chennai 8/2022 "Approach to Bermuda triangle of heart."***
- ***ICMR funded study on Atrial cardiopathy and risk prediction in stroke retrospective study (PI: Dr. Sapna Erat Sreedharan)***
- ***ICMR funded study on Atrial cardiopathy and risk prediction in stroke prospective study (PI: Dr. Sapna Erat Sreedharan)***
- **APHRS travel award for the year 2022**

- **Gold medal award winner of IHJ-CSI thesis awards 2022 presented at 74th CSI national conference Chennai on Speckle tracking Echocardiography in postoperative ALCAPA patients.**
- Finalist in the Savitri Srivastava Imaging Award 2022, organized by PCSI-2022.
- Professional Member of Asia-Pacific Heart Rhythm Society
- ***Finalist in CSI National Quiz 2021,*** CSI Annual Conference 2021, Hyderabad
- ***2nd in National Heart Failure Quiz 2022***, HFAI Annual Conference, 2022
- ***Winner in Prodigy 2022 – The Echo Quiz,*** IAE Kerala Chapter Annual Conference, 2022
- ***Winner in Echo Quiz,*** IAE Kerala Chapter Annual Conference, 2021
- ***Winner in Cardiology Quiz, Cardiovascular Update 2022, organised*** by the Department of Cardiology, Medical College Trivandrum
- ***Winner at Rajneesh Juneja Memorial quiz PCSI 2022*** at Pediatric Cardiology Society of India, October 2022, Kolkata.
- ***Winner in Electrophysiology Quiz, TN Epic, (Tamil Nadu Electrophysiology Council) 2021*** organized by the Departments of Cardiology JIPMER, CMC Vellore.
- ***Winner in Physiological pacing quiz conducted as a part of 2nd annual national pacing symposium, conducted by Madras Medical Mission, Chennai***
- ***Winner of Cardiocon 2022, a cardiology update quiz conducted at Ahmedabad.***
- ***2nd prize in Nitish Kumar Memorial surgical quiz, held in PCSI-2022 at Kolkata.***
- ***Gold medal award winner for the*** **Heart Failure Association of India (HFAI) thesis awards 2023 "Speckle tracking Echocardiography in postoperative ALCAPA patients".**
- ***Finalist at APHRS Young Investigator Award session held in Singapore in 2022.***

PDF cardiac Electrophysiology:

- ***Certificate of Excellence:2022 from Sree Chitra Tirunal Institute for Medical Sciences and Technology***

- ***2nd prize in best case awards session at Indian Complex arrhythmia summit, Delhi***
- **Selected as one among 15 young scholars (post-doctoral fellows) amongst all ''BRICS'' nations for the Heart Sapling Visiting Scholar program at Xiamen, China, for the year 2024.**

Papers Published

1. Kakarla, S., Sasikumar, D., & Kurup, H. (2022). Left ventricular-infundibular apical septal defect: A rare entity revisited. Cardiology in the Young, 1-3. doi:10.1017/S1047951122000695
2. Lotlikar RS, Saikiran K, George J, Namboodiri N, Sylaja PN, Sreedharan SE. Predictors of Recurrence in Symptomatic Large Artery Atherosclerosis and Cryptogenic Strokes???A Comparative Study. Journal of str med.
3. Narayanan Namboodiri, Saikiran Kakarla, Krishna Kumar Mohanan Nair, Sreevilasam P Abhilash, Sabari Saravanan, Harsh Kumar Pandey, Jyothi Vijay, Deepa Sasikumar, Ajit Kumar Valaparambil, Three-dimensional electroanatomical mapping guided right bundle branch pacing in congenitally corrected transposition of great arteries, EP Europace, 2022;, euac239, https://doi.org/10.1093/europace/euac239
4. Kakarla S, Sasikumar D, Varma RP, Kurup HKN, Gopalakrishnan A, Nair KKM, Dharan BS, Krishnamoorthy KM. Influence of age at surgery on left ventricular strain in patients with anomalous origin of left coronary artery from pulmonary artery (ALCAPA). Eur J Cardiothorac Surg. 2022 Dec 13:ezac486. doi: 10.1093/ejcts/ezac486. Epub ahead of print. PMID: 36511627.
5. Kakarla, Saikiran1; Chopra, Vijay K2,; Oomman, Abraham3. Management of non-ischemic dilated cardiomyopathy. Heart Failure Journal of India 1(1):p 31-39, January-April 2023. | DOI: 10.4103/HFJI.HFJI_1_22
6. Kakarla, S., Sasikumar, D., & Dharan, B. (2022). Heart failure in a newborn with tetralogy of Fallot: Uncommon association of a common anomaly. Cardiology in the Young, 1-2. doi:10.1017/S104795112200364X
7. Kakarla S, Sasikumar,D, Kurup, HKN, Valakkada J, Normal pulmonary venous drainage in the setting of total anomalous pulmonary venous connection, Annals of ped cardiol, 2,2022

8. Kakarla S, Abhilash SP, Namboodiri N. Bump termination of an atriofascicular tachycardia. Where is the level of block? J Arrhythmia. 2023;00:1–2. https://doi.org/10.1002/joa3.12969
9. Kakarla S, Abhilash SP, Vijay J, Namboodiri N. Response to spontaneous and induced His refractory ventricular premature beats during long RP tachycardia: What is the mechanism? J Arrhythmia. 2023;00:1–2. https://doi.org/10.1002/joa3.12958

CHAPTERS AUTHORED

1. **Co-authored Chapter 16: Atrial fibrillation and flutter in Mariott practical electrocardiography, south Asian edition**
2. **Co-author of Hypertension in Heart failure, CSI 2022 Indian guidelines under publication**

Review articles published:

1. **Kakarla, Saikiran; Chopra, Vijay K, Oomman, Abraham. Management of non-ischemic dilated cardiomyopathy. Heart Failure Journal of India 1(1):p 31-39, January-April 2023. | DOI: 10.4103/HFJI.HFJI_1_22**

Ongoing projects:

1. **Biophysical evaluation of the various bipolar configurations in Rf ablation of ventricular myocardium in a bovine model as a prototype design of a custom-made bipolar RF ablation model.**
2. **Effect of left bundle branch area pacing on ventricular mechanical synchrony: a prospective observational study using 2d-speckle tracking echocardiography.**

Presentations:

30 national and 2 international presentations in award sessions/case series / free paper/poster presentations.