Clinical Investigational Plan

Jewel Electrophysiology (EP) Lab Study
(ES-1 and ES-2 models)

Protocol Number: PR-2038, Revision 6.0
NCT Number: NCT05490459

24 March 2021

Element Science, Inc.
200 Kansas Street, Suite 210
San Francisco, CA 94103

Title: Jewel Electrophysiology (EP) Lab Study	
Clinical Investigation Medical Device:	Jewel Electrophysiology (EP) Lab System
Device Classification:	IIb (European Union)
Version:	PR-2038, Rev. 6.0
Date:	24 March 2021
Principal Investigator:	Prof Petr Neužil Na Homolce Hospital Roentgenova 2 Prague, Czech Republic
Sponsor:	Element Science, Inc. 200 Kansas Street, Suite 210 San Francisco, CA 94103 USA
Sponsor's Representative:	High Tech Med Consult, .s. r. o. ID: 28443221, 155 00 Prague 5; Frimlova 1322/4e; Czech Republic Acting by: Štěpán Královec

1. SYNOPSIS OF THE CLINICAL INVESTIGATION

Sponsor	Element Science, Inc.
Name of Product	Jewel Electrophysiology (EP) Lab System
Title	Jewel Electrophysiology (EP) Lab Study
Study Design	This single center, prospective, single arm study will be conducted in the European Union. The sample size for the study is a maximum of 24 subjects. The study design will allow for continuous enrollment of eligible subjects until the sample size is met for the treatment analysis per the statistical analysis plan. The study will enroll subjects who are scheduled for a standard EP procedure where life-threatening VT or VF may spontaneously occur or may be induced.
Primary Objective	The primary objective of this study is to demonstrate safety and clinical effectiveness of the Jewel EP Lab System. The Jewel EP Lab System will be used to deliver a single transthoracic defibrillation shock to terminate life-threatening VT or VF.
Primary Endpoint	Primary Endpoint: The primary effectiveness endpoint will evaluate the percent of successful terminations of life-threatening VT or VF in subjects who are treated with the Jewel EP Lab System.
Safety Endpoint	Safety Endpoint: Descriptive statistics of safety outcomes will be reported to ensure that device safety performance is clinically meaningful. All adverse events (AEs) and serious adverse events (SAEs) during the acute procedure will be tabulated and presented along with the duration, severity, and relatedness to the Jewel EP Lab System. The proportion of subjects experiencing an AE or SAE will also be presented. No formal safety analyses will be performed due to the fact that the sample size does not allow for a powered safety endpoint.
Study Participants	Subjects must meet the following inclusion/exclusion criteria to be eligible for the study: Inclusion Criteria 1. Subjects of both genders of at least 18 years of age. 2. Subjects who are scheduled for a standard EP clinical procedure where fast VT or VF may spontaneously occur or may be induced. Exclusion Criteria 1. Subjects who may require sterile access to the right upper pectoral or lower left torso regions during the planned EP procedure. 2. Subjects who have taken amiodarone in the past 3 months. 3. Subjects with an existing unipolar pacemaker. 4. Subjects who exhibit a left ventricular ejection fraction (LVEF) less than 20% (as assessed by techniques such as echocardiography,

	magnetic resonance imaging, or radionuclide angiography) within the last 6 months. 5. Subjects who have been diagnosed with heart failure (Class IV) or experienced an acute heart failure exacerbation within the previous 30 days. 6. Subjects who exhibit unstable angina. 7. Subjects with atrial fibrillation with contraindication to anticoagulation or improper anticoagulation management. 8. Subjects who are participating in an investigational study of a drug, biologic, or device not currently approved for marketing. 9. Subjects who are allergic to or have had a known adverse reaction to medical adhesives. 10. Subjects who have active skin breakdown, erythema, or other signs of infection in the pectoral or torso regions where the study device is applied. 11. Subjects with a lower abdomen circumference of less than 68.5 cm or greater than 142 cm. 12. Females who are pregnant or breastfeeding, or planning to be pregnant in the next 12 months. 13. Subjects who cannot provide or have diminished capacity to provide informed consent. 14. Any condition that an Investigator believes would interfere with the intent of the study or is not in the best interest of the patient. 15. Any patient that according to the Declaration of Helsinki is unsuitable for enrollment. *Note: Subjects with an active implanted device, such as a pacemaker, ICD, or a subcutaneous-ICD, are not excluded in the eligibility criteria, but the Investigator may choose to screen out subjects where the active device or clinical procedure may interfere with the intent of the study.*
Study Device	The Jewel System is patch-wearable cardioverter defibrillator (P-WCD) applied directly to a patient's torso in an anterior-apical monitoring vector. The Jewel EP Lab System consists of a Jewel (ES-1, ES-2) System modified with the addition of a Controller Box to allow the operator to manually charge and manually administer a defibrillation shock. All other elements of the Adhesive Electrode Patches are identical to the Jewel (ES-1, ES-2) System.
Procedure	The study device is intended to be used in conjunction with a standard EP clinical procedure. The Jewel EP Lab System will be used to terminate the first spontaneous or induced life-threatening episode of VT or VF. As an added safety precaution, rescue defibrillator pads will be placed on the subject in the anterior-posterior position and connected to a rescue defibrillator.

TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
AED	Automated External Defibrillator
CABG	Coronary Artery Bypass Graft
CMS	Centers for Medicare and Medicaid Services
CRF	Case Report Form
DD	Device Deficiency
DME	Durable Medical Equipment
ECG	Electrocardiogram
EP	Electrophysiology
EU	European Union
FDA	Food and Drug Administration
ICD	Implantable Cardioverter Defibrillator
IEC	Independent Ethics Committee
ISO	International Organization for Standardization
ITT	Intent to Treat
LVEF	Left Ventricular Ejection Fraction
MI	Myocardial Infarction
NYHA	New York Heart Association
PCI	Percutaneous Coronary Intervention
PIC	Patient Informed Consent
P-WCD	Patch-Wearable Cardioverter Defibrillator
RCT	Randomized Controlled Trial
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SCD	Sudden Cardiac Death
S-ICD	Subcutaneous Implantable Cardioverter Defibrillator
SOP	Standard Operating Procedure
TTI	Transthoracic Impedance
UADE	Unanticipated Adverse Device Effect
US	United States
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
WCD	Wearable Cardioverter Defibrillator

3. INTRODUCTION

3.1. SUDDEN CARDIAC DEATH

Sudden Cardiac Death (SCD) is sudden, unexpected death caused by the abrupt loss of heart function, and is one of the largest causes of natural death in Europe, leading to 275,000 adult deaths each year.[1] SCD is most often caused by abnormal heart rhythms, called arrhythmias, which prevent the heart from adequately pumping blood to the body. Ventricular Fibrillation (VF) is an erratic, disorganized firing of impulses from the ventricles and is the most common life-threatening arrhythmia.[2] Ventricular Tachycardia (VT) occurs when the heart's ventricles rapidly contract due to improper electrical activity and can also be potentially life threatening.

While the Implantable Cardioverter Defibrillator (ICD) is typically implanted for long-term prevention of SCD in high-risk populations, there are temporary periods of time when ICD implantation is commonly deferred. Examples include the initial 40 days after myocardial infarction (MI), the initial 90 days after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), or after ICD explantation. The Wearable Cardioverter Defibrillator (WCD) has become a viable option to treat temporary periods of elevated risk for SCD. Patients are typically prescribed to wear a WCD 24 hours a day, 7 days a week, for 40 to 90 days or longer, until a medical decision is made on whether to implant an ICD.[3]

3.2. DEVICE DESCRIPTION: JEWEL SYSTEM

Element Science, Inc. is developing the Jewel Patch Wearable Cardioverter Defibrillator (P-WCD) System ("Jewel System") for patients who are at risk of SCD to improve the comfort and convenience of a WCD by focusing on developing a patient-centric design. The Jewel System continuously monitors a patient's cardiac rhythm and, in the event that a patient experiences a life-threatening episode of VT (greater than ~200 beats per minute) or VF, delivers a therapeutic shock to convert a patient's rhythm out of the detected VT or VF. The device used in this study is a modified version of the Jewel System.

The study includes both the ES-1 model and the ES-2 model of the Jewel System. ***The ES-1 and ES-2 models, together referred to as the Jewel family, have identical functionality while incorporating device improvements and meeting Durable Medical Equipment (DME) requirements specified by the United States Centers for Medicare and Medicaid Services for reimbursement (Defibrillator Unit of the ES-2 model is now reusable)***. The Jewel EP Lab System utilized in this study consists of a Jewel (ES-1, ES-2) modified with the addition of a Controller Box to allow the operator to manually administer a defibrillation shock. All other elements of the Adhesive Electrode Patches are identical to the Jewel (ES-1, ES-2) System.

[1] European Resuscitation Council Guidelines for Resuscitation 2010 Section 10. Resuscitation. 2010; 81: 1445-1451.
[2] "Sudden Cardiac Death (Sudden Cardiac Arrest) | Cleveland Clinic." Sudden Cardiac Death (Sudden Cardiac Arrest) | Cleveland Clinic. Cleveland Clinic, 1 May 2015. Web. 08 Jan. 2016.
[3] Chung MK, Szymkiewicz SJ, et. al. "Aggregate national experience with the wearable cardioverter-defibrillator: event rates, compliance, and survival". J Am Coll Cardiol. 2010; 56: 194–203.

ES-1 Model of the Jewel EP Lab System ("Jewel")

The ES-1 model of the Jewel System includes the following three components: Upper Adhesive Electrode Patch, Monitoring and Defibrillation Unit with Lower Adhesive Electrode Patch, and Connection Cable. A schematic of the system is shown in Figure 3.1 and a brief description of each component is outlined in Table 3.1.

Figure 3.1: Schematic of Jewel (ES-1) System Components

Table 3.1: ES-1 Model of the Jewel System Component Descriptions

Jewel System Component	Description
Upper Adhesive Electrode Patch	Conformable adhesive patch containing ECG electrodes and a defibrillation electrode.
Monitoring and Defibrillation Unit with Lower Adhesive Electrode Patch	Conformable adhesive patch containing ECG electrodes and a defibrillation electrode. All electronics are contained within the Monitoring and Defibrillation Unit, which is integrated with the Lower Adhesive Electrode Patch. Control Buttons are located on the exterior of the Monitoring and Defibrillation Unit.
Connection Cable	Multi-conductor cable assembly connecting the Upper Adhesive Electrode Patch to the Monitoring and Defibrillation Unit with Lower Adhesive Electrode Patch.

ES-2 Model of the Jewel EP Lab System ("Jewel")

The ES-2 model of the Jewel System is composed of the following three components: disposable Upper Adhesive Electrode Patch, a reusable Monitoring and Defibrillation Unit (MDU) attached to a disposable Lower Adhesive Electrode Patch with permanently attached disposable Battery Unit, and the attached Connection Cable. A schematic of the ES-2 is shown in Figure 3.2 and a description is contained in Table 3.2.

Table 3.2: ES-2 Model of Jewel System Component Descriptions

Jewel System Component	Description
Upper Adhesive Electrode Patch	Conformable adhesive patch containing ECG electrodes and a defibrillation electrode.
Monitoring and Defibrillation Unit with Lower Adhesive Electrode Patch	Conformable adhesive patch containing ECG electrodes and a defibrillation electrode. All electronics are contained within the Monitoring and Defibrillation Unit, which is integrated with the Lower Adhesive Electrode Patch. Control Buttons are located on the exterior of the Monitoring and Defibrillation Unit.
Connection Cable	Multi-conductor cable assembly connecting the Upper Adhesive Electrode Patch to the Monitoring and Defibrillation Unit with Lower Adhesive Electrode Patch.

Figure 3.2: Schematic of the Jewel (ES-2) System Components

Jewel Accessories (ES-1, ES-2)

The Jewel System is packaged with accessories to aid in the application and removal of the Jewel System. The Skin Preparation Accessories aid in cleaning the torso area prior to application of the Adhesive Patches. A Placement Accessory ensures the Adhesive Electrode Patches are aligned correctly on the subject's torso. Removal Accessories are provided to aid in removing the Adhesive Electrode Patches and cleaning the skin area.

The Adhesive Electrode Patches are intended to be applied to an adult patient in an anterior-apical monitoring vector configuration. The Upper Adhesive Electrode Patch is applied to the skin above the right pectoral muscle, and the Lower Adhesive Electrode Patch is applied such that the defibrillation pad area is located along the left mid-axillary line. Figure 3.2 is a depiction of the Jewel System applied to a patient.

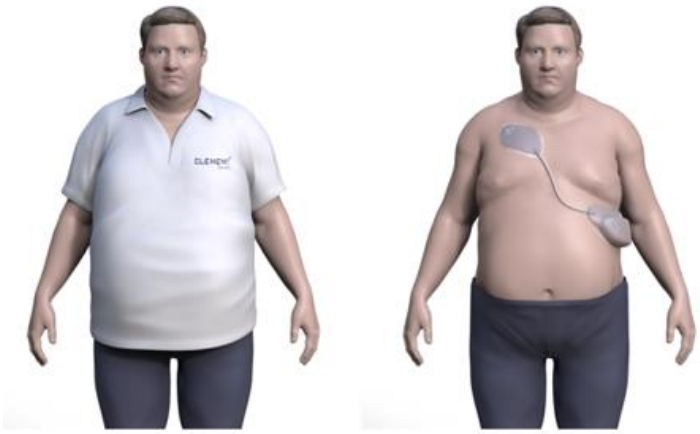


Figure 3.2: Jewel (ES-1, ES-2) System Applied to a Patient's Torso

The MADIT-RIT study results demonstrated a reduction in inappropriate therapy and all-cause mortality when ICDs were programmed to deliver therapy for tachyarrhythmias of 200 bpm and higher.[4] The Jewel System algorithm was designed with the MADIT-RIT rate cut-off as a guide for determining if a rhythm is life-threatening and requires therapy. The Jewel System does not allow the physician to program the device to alternate heart rate detection thresholds.

The Jewel System monitors a patient's ECG through five (5) electrodes located on the Adhesive Electrode Patches. The Jewel System employs a proprietary algorithm to detect and classify fast VT or VF that is deemed to be life-threatening ("shockable") versus cardiac rhythms that are non-life threatening ("non-shockable"). In the event of a shockable rhythm, the Jewel System firmware initiates the charge cycle of the capacitors, and in parallel, the Jewel System will initiate an alarm sequence to alert the patient that the device is preparing to deliver a shock. If the patient is conscious, the patient is instructed to press the Control Buttons to stop the alarms and prevent the delivery of the shock. If the patient does not respond, and the shockable rhythm continues, the Jewel System will continue to alarm the patient and also give a verbal warning to bystanders that a shock will be delivered. The Jewel System delivers the initial therapeutic shock with a fixed energy of approximately 150 joules using a biphasic truncated exponential defibrillation waveform using a constant energy pulse that is adjusted based on the transthoracic impedance (TTI) of the patient at the time of therapy delivery. Using a cardioversion algorithm, the Jewel System will attempt to cardiovert the rhythm and synchronize the shock with the R-peak of the QRS complex. This automatic synchronization delivers a cardioversion shock to a patient if R-peaks are detected, suggesting that the

[4] Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med 2012;367:2275-83. DOI: 10.1056/NEJMoa1211107

rhythm is a life-threatening VT. If the cardioversion algorithm is not able to identify a regular R-peak during the ventricular arrhythmia, the Jewel System will deliver an asynchronous defibrillation shock. After the initial shock of approximately 150 joules, if the Jewel System continues to detect a shockable rhythm, the Jewel System will re-initiate the alarm sequence and continue to deliver a salvo of up to four (4) additional shocks of approximately 162 joules, totaling five (5) consecutive shocks (150, 162, 162, 162, 162 joules).

The Jewel System is a Class III medical device in the United States and a Class IIb medical device in the European Union (EU).

3.3. DEVICE DESCRIPTION: JEWEL EP LAB SYSTEM

The Jewel EP Lab System delivers the same biphasic truncated exponential waveform as the Jewel System. The waveform parameters utilized by the Jewel EP Lab System are similar to other commercially-approved external defibrillators.

The Jewel EP Lab System consists of a Jewel System modified with the addition of a Controller Box. The Controller Box allows the operator to manually charge the Jewel System capacitors as well as manually administer a defibrillation shock. This minimizes the safety risk to the patient by limiting the VT or VF to a relatively short time period (less than 20-30 seconds).

The Control Buttons on the Controller Box which allow the clinicians to charge the capacitors and deliver the shock are unique to the Jewel EP Lab System. Since the user will control the timing of the shock delivery using the Controller Box, the shock will not be automatically synchronized to the R-peak of the ECG complex using the cardioversion algorithm that is integrated into the Jewel System. Since the shock is not controlled by the Jewel System, the TTI measurement used to determine the energy waveform is taken within 1 second of when the capacitors are fully charged.

Additionally, the Jewel EP Lab System contains a lower strength hydrocolloid adhesive in the Upper and Lower Adhesive Electrode Patches. The reduced peel strength of the hydrocolloid adhesive allows for easy peel-off of the Adhesive Electrode Patches after the short-term wear duration in the EP lab procedure. The regular strength hydrocolloid adhesive used in the Jewel System is only located in non-defibrillation areas to allow for an 8 day wear duration. Following the same geometry, the Jewel EP Lab System hydrocolloid does not cover any part of the ECG sensing or defibrillation electrodes, and therefore will not have any impact on the defibrillation area during the procedure.

The Jewel EP Lab System Instructions for Use contains a thorough description of the product's preparation and administration procedures.

The ES-2 model of the Jewel EP Lab System will be used as the study device for new subjects enrolled in the Jewel EP Lab Study.

3.4. PRIOR CLINICAL EXPERIENCE WITH THE JEWEL AND JEWEL EP LAB SYSTEMS

The Jewel System and the Jewel EP Lab System have both been investigated in animal models to characterize the safety of external defibrillation therapy. In addition, the full array of relevant biocompatibility tests were performed in accordance with ISO 10993. A complete summary of preclinical information regarding the Jewel EP Lab System is available in the Investigator's Brochure.

3.5. RISKS AND BENEFITS OF THE JEWEL EP LAB SYSTEM

The Jewel EP Lab System will be used for investigational purposes only. It is not intended for commercial use. The study device will be used for external defibrillation during a standard EP procedure. A detailed Risk Analysis has been completed and the risk to benefit ratio has been determined to be acceptable for use in a clinical investigational study.

4. STUDY OBJECTIVE

The primary objective of this study is to demonstrate safety and clinical effectiveness of the Jewel EP Lab System, utilizing either the ES-1 or the ES-2 model of the Jewel EP Lab System. The Jewel EP Lab System will be used to deliver a single transthoracic defibrillation shock to terminate life-threatening VT or VF to patients undergoing a cardiac EP procedure.

5. STUDY PURPOSE

The time to defibrillation is the single most critical determinant of survival in SCD. Survival rates after VF decrease approximately seven to ten percent with every minute that defibrillation is delayed.[5] While rapid defibrillation with an Automated External Defibrillator (AED) by nonmedical personnel can improve survival after out-of-hospital cardiac arrest, the time period between arrest and successful resuscitation must be short and the cardiac arrest must be witnessed. The development of a wearable cardioverter defibrillator has provided a new therapy option for patients who are at high risk of SCD and may require a defibrillation shock without the assistance from a bystander.

The Jewel System is an automatic external defibrillator which monitors patients at risk for SCD and provides a therapeutic shock if needed. The Jewel System is intended to be worn at home or in the hospital during temporary periods of time when ICD implantation is commonly deferred.

To date, ZOLL is the sole manufacturer of a commercial product approved as a wearable automated external defibrillator. The ZOLL LifeVest WCD is currently available in the United States, Europe, Australia, Israel, Japan, and Singapore.

The clinical efficacy of external defibrillation shock waveforms used in the ZOLL LifeVest WCD and other AEDs has been studied routinely in the controlled environment of the EP lab. For example, with the replacement of monophasic damped sine waveforms with lower energy biphasic truncated exponential waveforms, clinical efficacy was compared by measuring first shock success rate in patients undergoing electrophysiologic testing.[6] With the ZOLL LifeVest WCD, the clinical efficacy was also evaluated as part of a routine EP procedure in which ten (10) patients were induced into VF and the LifeVest was used to deliver a single defibrillation shock.[7] In this study, special WCD units were used that were manually charged and discharged by the physician to terminate the VF episode in a relatively short time period (mean duration of 32 seconds per episode).

Similar to the ZOLL LifeVest and AEDs, the Jewel System is designed to deliver a fixed energy of approximately 150 joules using a biphasic truncated exponential waveform that is adjusted based on the transthoracic impedance of the patient. The purpose of this clinical study is to demonstrate the safety and effectiveness of the Jewel EP Lab System to deliver a single transthoracic defibrillation shock to terminate life-threatening VT or VF.

The study is planned to be conducted in standard clinical cases, such as an EP study or an ablation case, in which life-threatening VT or VF may spontaneously occur or be induced. As with similar EP lab studies, the duration of life-threatening VT or VF will be limited to a relatively short time period (less than 20-30 seconds) to minimize the safety risk to the patient since the duration of life-threatening VT or VF has been shown to be inversely proportional to the success of defibrillation

[5] American Heart Association. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation, Supplement 2005.
[6] Bain et.al. Multicenter study if principles-based waveforms for external defibrillation. *Annals of Emergency Medicine*, Jan 2011: 37:1, 5-12.
[7] Auricchio, A. et.al. "Clinical Efficacy of the Wearable Cardioverter-Defibrillator in Acutely Terminating Episodes of Ventricular Fibrillation." Amer J Cardiol. 1998; 81: 1253-1256.

therapy.[8,9] Unlike the Jewel EP Lab System, the Jewel System is designed for ambulatory patients and therefore if the system detects a shockable rhythm, the firmware initiates the alarm sequence, allowing a conscious patient to have time to respond and press the Control Buttons to prevent delivery of a shock (approximately 50-60 seconds from the initial detection of the shockable rhythm). Although this is acceptable for an out-of-hospital event, the Jewel EP Lab System is a derivative of the Jewel System designed for the EP lab environment to allow the clinical user to manually charge the capacitors and trigger the delivery of the defibrillation shock at any time during the procedure. The Jewel EP Lab System does not require waiting for the algorithm to detect and classify a shockable rhythm. This ensures that the clinical user has full control of the delivery and timing of the therapeutic shock in order to avoid a prolongation of the response time during the acute EP lab procedure.

In this study, the EP lab procedure is a standard clinical procedure that follows the standard of care at the hospital facility. The clinical presentation of life-threatening VT or VF and the clinical guidelines for defibrillation do not differ between European or US clinical sites.

The results of the VEST trial, a randomized controlled trial (RCT) of over 2,300 subjects comparing the ZOLL LifeVest to Guideline Directed Medical Therapy, were reported at the American College of Cardiology Conference in March 2018, and in the New England Journal of Medicine on 27 September 2018.[10] In this RCT, there were a total of 21 appropriate shocks, of which 13 were converted with the first shock and 8 of which required ≥2 shocks (38%). This translates into a 62% first shock success rate.[11]

[8] Windecker, S et.al. The influence of ventricular fibrillation duration on defibrillation efficacy using biphasic waveforms in humans. *Journal of the American College of Cardiology*, Volume 33, Issue 1, January 1999, 33-38.
[9] Winkle, R et.al. Effect of duration of VF on defibrillation efficacy in humans. *Circulation*, Vol 81, No 5, May 1990, 1477-1481.
[10] Jeffrey E Olgin et al., "Wearable Cardioverter–Defibrillator after Myocardial Infarction," *N Engl j Med*, 2018, 11.

6. STUDY DESIGN

This study is a single center, prospective, single arm, non-randomized, non-blinded feasibility study that will be conducted in the European Union. The sample size for the study is a maximum of 24 subjects.

Eligible subjects will be those scheduled for a standard EP procedure where life-threatening VT or VF may spontaneously occur or may be induced. Subjects are excluded if they exhibit a left ventricular ejection fraction (LVEF) less than 20%, have been recently diagnosed with heart failure or have NYHA Class IV heart failure, have unstable angina or atrial fibrillation with a contra-indication to anticoagulation or improper anticoagulation management. The adaptive study design will allow for continuous enrollment of eligible subjects until the sample size is met for the treatment analysis per the statistical plan.

Patients undergoing a standard EP clinical procedure where life-threatening VT or VF may occur are eligible for enrollment in this study. The Jewel EP Lab System will be placed on the subject's torso in the anterior-apical monitoring vector and will be able to deliver an electric shock in the event the patient experiences spontaneous or induced VT or VF.

It is anticipated that the study will require 3 months for enrollment and completion as the study does not require follow-up after the completion of the EP Lab procedure except in the event of adverse events in which case the subject will be followed until resolution. The Sponsor and the Principal Investigator will continuously monitor the safety data (including all reported serious adverse events) throughout the trial.

6.1. PRIMARY EFFICACY ENDPOINT

The primary endpoint will evaluate the percent of successful terminations of life-threatening VT or VF in subjects who are enrolled in compliance with the protocol-defined entry criteria and are treated with either model of the Jewel EP Lab System. The endpoint will be achieved if the lower confidence limit exceeds the performance goal of 62% using a one-sided exact lower 97.4% confidence bound at one of three testing points. These conditions ensure that performance will be in line with previously published randomized controlled trial results on a relevant comparator, the ZOLL LifeVest, which is the only commercially approved WCD in Europe or the United States. A sequential method of testing will be used to evaluate conversion success. If the Jewel EP Lab System is NOT used to deliver a defibrillation shock during the EP procedure, the subject will not be included in the treatment analysis.

6.2. PRIMARY SAFETY ENDPOINT

Descriptive statistics of safety outcomes will be reported to ensure that device safety performance is clinically meaningful. All adverse events observed during the acute procedure will be tabulated and presented along with the duration, severity, and relatedness to the Jewel EP Lab System. The proportion of subjects experiencing an AE or SAE will also be presented. No formal safety analyses will be performed due to the fact that the sample size does not allow for a powered safety endpoint.

7. STUDY POPULATION

7.1. PATIENT INCLUSION/EXCLUSION CRITERIA

The study will only enroll up to 24 subjects that fulfill the eligibility criteria of the investigation. Subject participation is voluntary and the study will be conducted in accordance with the Declaration of Helsinki.

Inclusion Criteria:

Candidates for this study must meet all the following criteria:

1) Subjects of both genders of at least 18 years of age.
2) Subjects who are scheduled for a standard EP clinical procedure where life-threatening VT or VF may spontaneously occur or may be induced.

Exclusion Criteria:

Candidates will be ineligible for enrollment if any of the following conditions apply:

1) Subjects who may require sterile access to the right upper pectoral or lower left torso regions during the planned EP procedure.
2) Subjects who have taken amiodarone in the past 3 months.
3) Subjects with an existing unipolar pacemaker.
4) Subjects who exhibit a left ventricular ejection fraction (LVEF) less than 20% (as assessed by techniques such as echocardiography, magnetic resonance imaging, or radionuclide angiography within the last 6 months).
5) Subjects who have been diagnosed with heart failure (Class IV) or experienced an acute heart failure exacerbation within the previous 30 days.
6) Subjects who exhibit unstable angina.
7) Subjects with atrial fibrillation with contraindication to anticoagulation or improper anticoagulation management.
8) Subjects who are participating in an investigational study of a drug, biologic, or device not currently approved for marketing.
9) Subjects who are allergic to or have had a known adverse reaction to medical adhesives.
10) Subjects who have active skin breakdown, erythema, or other signs of infection in the pectoral or torso regions where the study device is applied.
11) Subjects with a lower abdomen circumference of less than 68.5 cm or greater than 142 cm.
12) Females who are pregnant or breastfeeding, or planning to be pregnant in the next 12 months.
13) Subjects who cannot provide or have diminished capacity to provide informed consent.
14) Any condition that an Investigator believes would interfere with the intent of the study or is not in the best interest of the patient.
15) Any patient that according to the Declaration of Helsinki is unsuitable for enrollment.

Note: Subjects with an active implanted device, such as a pacemaker, ICD, or a subcutaneous-ICD, are not excluded in the eligibility criteria, but the Investigator may choose to screen out subjects where the active device or clinical procedure may interfere with the intent of the study.

8. STUDY ACTIVITIES

The Study Activities are detailed in Table 8.1.

Table 8.1: Study Activities

Study Activity	Pre-Procedure	Intra-Procedure	Post-Procedure
Informed Consent	X		
Screening Visit	X		
Medical History/Clinical Status	X		
Skin Preparation & Device Placement (including photograph)		X	
Therapy Delivery		X (if applicable)	
Device Removal		X	
Adverse Events Assessment		X	X (if applicable)

8.1. SUBJECT ENROLLMENT

All patients admitted for an EP lab procedure will be screened for study eligibility. A member of the research team will review the patient's medical history for eligibility. A screening log will be maintained by each site and completed for all patients screened. The screening log will identify the reason(s) potential study subjects were not enrolled into the trial. If all inclusion criteria are met and no exclusion criteria are present, the patient will be presented with the Ethics Committee-approved Patient Informed Consent (PIC). This consent form will comply with all applicable local, state and federal regulations governing the protection of human patients. The Investigator must provide the Sponsor with a written copy of the PIC that the IEC reviewed, and the IEC approval of the PIC prior to enrollment of any subjects.

It is the responsibility of the Investigator to obtain written informed consent from each subject or the legally authorized representative of the subject prior to the initiation of any study-related procedures. Each prospective study subject must be informed of:

- The purpose, procedures, and expected duration of the subject's participation;
- Potential hazards/risks to the subject;
- Anticipated benefits to the subject or others;
- Disclosure of appropriate alternate procedures/treatments;
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and notes that the FDA and the Sponsor may inspect the records;
- An explanation of any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- An explanation of whom to contact for answers to questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
- A statement that participation is voluntary, that refusal to participate or withdrawal at any time will involve no penalty or loss of benefits;
- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
- Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent;
- Any additional costs to the subject that may result from participation in the study;
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; and
- The approximate number of subjects involved in the study.

Each subject will be given a signed copy of the Patient Informed Consent.

Signed PIC Forms must be retained in the study file by the Investigator, and be available for review by the Sponsor and/or regulatory agencies, as applicable. The time and date consent was rendered will be documented in the subject's medical record.

The PIC and any other written information provided to subjects will be revised whenever important new information becomes available, or if there is an amendment to the protocol which necessitates a change to the content of subject information and/or to the consent form. The Investigator will inform the subject of changes in a timely manner, and will ask the subject/patient to confirm his/her continuation in the study by signing a revised consent form. Any revised PIC Form and other written information provided to subjects must receive IEC, Sponsor, and regulatory agency approval, as applicable.

At the Screening visit the subject's baseline information will be collected, including demographics, medical history and cardiac-related test results, and will undergo a basic physical exam.

8.2. STUDY PROCEDURE

The study device is intended to be used in conjunction with a standard EP clinical procedure, such as an EP study or ablation procedure, where life-threatening VT or VF may spontaneously occur or may be induced. Although subjects will undergo a standard EP procedure, it is not anticipated that life-threatening VT or VF will occur or be induced in all subjects.

The Jewel EP Lab System will be set-up prior to initiation of the EP clinical procedure. The subject's torso will be prepared for the placement of the Jewel EP Lab System. If hair is present, it will be trimmed per the hospital's protocols. The areas where the Adhesive Electrode Patches will be cleaned with antiseptic, such as Isopropyl Alcohol prior to being placed on the subject.

The Adhesive Electrode Patches will be placed in the anterior-apical vector, with the upper patch located under the clavicle and lateral to the midline and the lower patch placed so that the 3rd/4th exterior housing junction is at or posterior to the mid-axillary line. The patches shall be placed by aligning the patch and pulling the release liners in order of their number, 1 through 4. After both patches have been placed, the time of device placement will be recorded on the Procedure Case Report Form (CRF). A photograph will be taken to document device location. The photograph will not include the subject's face. The device will be turned on and the time will be recorded on the Procedure CRF.

Hospital-supplied rescue defibrillator pads will be placed on the subject in an anterior-posterior position, ensuring a 1-2 centimeter margin between the defibrillation pads and the Adhesive Electrode Patches. A hospital-supplied ECG will be used per hospital procedure. The Investigator will continue with the planned EP clinical procedure and monitor the subject's heart rhythms per standard hospital protocol.

After the EP clinical procedure commences, the Jewel EP Lab System will be used to terminate the spontaneous or induced life-threatening VT or VF.

Prior to the onset of life-threatening VT or VF, the hospital staff will prepare the Jewel EP Lab System by initiating the device charge cycle. The user will depress the "CHARGE" button on the Controller Box to charge the capacitors for delivery of the defibrillation shock. Charging will take approximately 20 seconds during which the Controller Box will display a flashing green "CHARGE" light. The rescue defibrillator will also be prepared for use should the Jewel EP Lab System not deliver an electrical shock or fail to terminate VT/VF.

Upon completion of charging, the Jewel EP Lab System will display a solid green "CHARGE" light on the Controller Box. After the device is charged, the user will be able to manually deliver a

defibrillation shock through the Jewel EP Lab System by depressing the "SHOCK" buttons on the Controller Box.

Throughout the procedure, the Jewel EP Lab System will continuously monitor the ECG signal, and the Controller Box will illuminate the "DETECT" yellow light to notify the user when the algorithm has detected life-threatening VT or VF. The detection algorithm continuously analyzes the ECG signal in segments of eight seconds and determines whether a shockable rhythm is present in the majority of that segment after the entire segment has finished. Based on the timing of the onset of VT/VF relative to ECG segments, the algorithm may require up to 8-12 seconds of ECG signal to capture a full eight-second segment for determination of a shockable rhythm. If a shockable rhythm is detected, the light indicator on the Controller Box will flash a yellow light continuously. If the VT/VF is sustained through a second eight-second segment, the light indicator will change to a solid yellow light. At any time during this process, irrespective of algorithm determination, the defibrillation shock may be delivered using the "SHOCK" buttons on the Jewel EP Lab System. Although the performance of the detection algorithm is not a primary endpoint in this study, the status of the detection light will be recorded during the case.

In cases where the patient is stable, the VT/VF may be allowed to continue for 20-30 seconds to ensure the algorithm has sufficient ECG data to make a rhythm determination over multiple eight-second segments. The timing of the defibrillation shock is under the discretion of the physician to ensure patient safety. In the case where VT/VF is not sustained for the minimum of 8-12 seconds, the indicator light on the Controller Box will not illuminate. The ECG data recorded on the Jewel EP Lab System will also be analyzed post-procedure to assess the performance of the algorithm.

In the event that the defibrillation shock delivered through the Jewel EP Lab System does not successfully terminate the VT/VF, the rescue defibrillator will be used to deliver subsequent defibrillation shock(s).

Throughout the clinical procedure, the Jewel EP Lab System will only be used in appropriate cases based on physician judgment.

- In the case that a defibrillation shock is delivered through the Jewel EP Lab System, the clinical procedure will continue as planned. If a subsequent defibrillation shock is required during the procedure, the rescue defibrillator will be used. The Jewel EP Lab System will only be employed for a single shock during each procedure. In the case that the Jewel EP Lab System is used to deliver a defibrillation shock and the subject meets all enrollment criteria, the subject will be included in the treatment analysis for the primary endpoint.

- In the case that the Jewel EP Lab System is not used to deliver a defibrillation shock during the procedure, the subject will not be included in the treatment analysis to meet the sample size requirements per the statistical plan. In approximately 30 percent of cases, life-threatening VT or VF may not occur or be inducible and therefore an external defibrillation shock would not be required.[11] In addition, based on physician judgment, the Jewel EP Lab System may not be used to provide a defibrillation shock during the procedure. In these cases, the subject will not be included in the treatment analysis for the primary endpoint, however, an Intent-to-Treat (ITT) analysis will be performed for informational purpose.

At the conclusion of the acute procedure, the Jewel EP Lab System will be removed from the subject and the Controller Box will be disconnected from the Adhesive Electrode Patches. The subject will exit the study immediately after completion of the EP clinical procedure.

[11] Krummen, D. et.al. "Rotor Stability Separates Sustained Ventricular Fibrillation from Self-Terminating Episodes in Humans." J Am Coll Cardiol. 2014; 63: 2712–21.

8.3. FOLLOW-UP

No clinical follow-up is required following the acute procedure, and subjects will exit the study immediately after completion of the procedure unless an adverse event (AE) is observed during the Jewel EP Lab System treatment procedure in which case the subject will be followed until the AE has been resolved.

9. SUBJECT REMOVAL FROM STUDY

Only subjects that meet all enrollment criteria and have received a defibrillation shock will be included in the treatment analysis, however all subjects enrolled, whether or not receiving a defibrillation shock, will be included in the reporting of study results.

Overall, if a subject drops out of the study at any time due to an adverse event or for any other cause, the reason for discontinuation, the nature of the event, and its clinical course must be fully followed and documented. In the case of an adverse event, the Investigator must strive to follow the subject until the adverse event has either resolved, become clinically insignificant, the event is stabilized, or the subject is lost to follow-up.

If at any point during the study, the patient withdraws consent or the Investigator assesses that the risks to the subject outweigh the benefits of participation in the study, the subject will be discontinued. If, during the course of the study, the Investigator feels that, in his/her best clinical judgment, the study should be prematurely terminated, he/she will notify the Sponsor and give the reason(s) for this decision. If the Sponsor decides, based on data or internal information, that it would be prudent to discontinue temporarily or to terminate the study, the Sponsor will inform the Investigator of this decision and the reason(s) for the decision.

10. ASSESSMENT OF SAFETY

The Investigator will carefully monitor each subject throughout the study for possible adverse events. All adverse events must be documented on CRFs designed specifically for this purpose and followed until either completely resolved or until a stable chronic outcome is determined by the Investigator.

The definitions and procedures for reporting adverse events (AE), serious adverse events (SAE), adverse device effects (ADE)/serious adverse device effects (SADE), unanticipated adverse device effects (UADE), and device deficiencies (DD) are presented in the sections below. It is of the utmost importance that all staff involved in the investigation are familiar with the definitions and procedures.

10.1. SAFETY DEFINITIONS

Adverse Event (AE)
An Adverse Event is any unfavorable and unintended sign, symptom, or disease, temporally associated with the use of the Jewel EP Lab System, whether or not it is related to the Jewel EP Lab System.

No causal relationship with the clinical trial product is implied by the use of the term "Adverse Event." Exacerbations of a pre-existing condition/illness that are defined as a "more frequent occurrence" or as "an increase in the severity of the pre-existing conditions" are considered AEs.

Serious Adverse Event (SAE)
An adverse event is considered "serious" if, in the view of either the Investigator or Sponsor it:

- Results in death;
- Is considered life-threatening (meaning that its occurrence places the subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant incapacity or disability; or
- Results in a congenital anomaly/birth defect.

Adverse Device Effect /Serious Adverse Device Effect (ADE/SADE)
An adverse device effect/serious adverse device effect is any AE that is related to the Jewel EP Lab System. All ADEs/SADEs are further categorized as anticipated or unanticipated by the Sponsor.

Unanticipated Adverse Device Effect (UADE)
A UADE is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Device Deficiency
A device deficiency is an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as a malfunction, misuse or use error, and inadequate labeling.

10.2. REPORTING OF ADVERSE EVENTS

Reports of adverse events will be collected throughout the duration of the study for both the ES-1 and ES-2 models of the Jewel EP Lab System. Adverse events must be documented on the Adverse Event case report form by the Investigator or his/her designee; however, it is the responsibility of the Investigator to ensure that all information is correct.

When reporting AEs/SAEs, the Investigator should include the following information:

1. Description of event (diagnosis)
2. Onset of event
3. Duration of event
4. Severity
5. Relationship to device
6. Action taken
7. Patient outcome

Severity describes the intensity of an event and will be assessed as:
Mild – The AE does not interfere in a significant manner with the subject's normal functioning level and requires minimal or no treatment.
Moderate – The AE produces some impairment of function, but is not hazardous to health.
Severe – The AE produces significant impairment of function or incapacities and/or is a hazard to the subject. These events may require systemic therapy or other treatment.

All AEs will be assessed for relationship to the Jewel EP Lab by the Investigator who examines and evaluates the participant, based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below:
Definitely Related – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event occurs in a plausible time relationship to use of the study device and cannot be explained by concurrent disease or other drugs or chemicals.
Probably Related – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event occurs within a reasonable time after use of the study device, is unlikely to be attributed to concurrent disease or other drugs or chemicals.
Potentially Related – There is some evidence to suggest a causal relationship, however, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
Unlikely to be Related – A clinical event, including an abnormal laboratory test result, whose temporal relationship to use of the study device makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after use of the study device) and in which other drugs or chemicals or underlying disease provides plausible explanations.
Not Related – The AE is completely independent of use of the study device, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

All SAEs must be reported to the Sponsor within 24 hours of learning about the event, regardless of the time that may have elapsed from the time the event occurred. The Sponsor must also receive a completed Adverse Event CRF within three (3) working days of the Investigator being notified of the event and should include the Investigator's assessment of the event, action that is required, results of any diagnostic tests that were performed, a description of any treatment implemented, a statement of the subject's current clinical status, and the Investigator's signature and date. Investigators shall comply with all local reporting requirements.

All device deficiencies (ES-1, ES-2) shall be documented and reported to the Sponsor without unnecessary delay.

If required, the Sponsor should inform the Competent Authorities about all SAEs and device deficiencies that may have led to a SADE associated with the device, as per local requirements.

The Sponsor is responsible for relaying adequate information on all UADEs to all participating Investigators. Regulatory authorities will be informed of all UADEs by the Sponsor. The Sponsor is also responsible for assessing whether a UADE poses an unreasonable risk to patients if the study is continued.

10.3. FOLLOW-UP OF PATIENTS AFTER ADVERSE EVENTS / SERIOUS ADVERSE EVENTS

In the case that an AE is observed during the Jewel EP Lab System treatment procedure, the subject will be followed until the AE is resolved or the Investigator decides that the AE is stable and needs no further follow-up. The date when the Investigator considers one of these outcomes to have occurred for the AE will be considered the last visit for the subject, and the outcome should be recorded on the appropriate case report form.

11. STATISTICS

11.1. STATISTICAL ANALYSIS AND SAMPLE SIZE RATIONALE

A prospective Statistical Analysis Plan has been developed for this study. Specific information regarding the planned statistical analysis is presented below.

The VEST trial was a randomized controlled trial (RCT), the design of which controls for the bias inherently present in retrospective registries. VEST reported the real-world LifeVest performance in over 2,300 subjects. The results of the VEST trial were presented at the American College of Cardiology Conference in March 2018, and were published in the New England Journal of Medicine on 27 September 2018. In this RCT, there were a total of 21 appropriate shocks, of which 13 were converted with the first shock and 8 of which required ≥2 shocks (38%). This translates into a 62% first shock success rate.[10] Of the 21 subjects who received an appropriate shock, 15 subjects (71%) survived. There were 25 sudden deaths in the LifeVest arm, 9 of which were wearing the LifeVest at the time of death, suggesting that there were a fair number of deaths that likely should have been prevented through use of the LifeVest.[10] Taken together, these RCT data suggest that the true results when using the LifeVest are potentially much lower than typically reported in registries.

Prior to the start of the VEST trial, the VEST protocol estimated that WCD conversion success rate would be 79.7%. The VEST trial was powered for mortality, not conversion success, so there were no power calculations around this endpoint. As the results of the VEST RCT demonstrated a first shock conversion success rate of 62%, this first shock conversion success rate for LifeVest will be the performance goal for the EP Lab Study, meaning that when the confidence interval is calculated from the observed first shock conversion success rate for the Jewel, the Jewel lower confidence bound will be greater than 62%, which will mean that the Jewel results are better than LifeVest's point estimate.

Utilizing the observed 62% first shock conversion success rate seen with the LifeVest in the RCT as the EP Lab Study performance goal provides assurance that the performance of the Jewel is aligned to the real-world performance of LifeVest.

For the calculation of sample size, this study will use an anticipated first shock conversion success rate of 87.5% in the EP Lab Study with a performance goal of 62%, the same as the first shock success rate seen in VEST. The performance of the Jewel will be considered acceptable if the lower confidence limit exceeds the performance goal of 62% (green line in the graph on page 24).

The sample size for this study is a maximum of 24 subjects. Subjects can be treated with either the ES-1 or the ES-2 model of the Jewel EP Lab System, as the devices are representative of each other. This sample size is based on a group sequential design measuring the observed proportion of successful life-threatening VT or VF terminations. The group sequential design uses a Pocock alpha spending function and allows for testing after 12, 18, and 24 subjects are enrolled. The design controls the overall Type I error rate at 5%. In line with the Pocock alpha spending function, a one-sided lower 97.4% exact confidence bound will be calculated using the exact binomial (Clopper-Pearson) method at each testing point.

Primary Endpoint Analysis:

Upon completion of the Jewel EP Lab Study, all clinical data from both the ES-1 and ES-2 models of the Jewel EP Lab System will be pooled, as the devices are representative of each other. The primary endpoint will evaluate the percent of successful terminations of life-threatening VT or VF in subjects who are in subjects who are enrolled in compliance with the protocol-defined entry criteria and treated with the Jewel EP Lab System (either ES-1 or ES-2 model).

Using the VEST RCT results for the first shock success as a guide, the performance goal of 62% was established for the Jewel EP Lab Study. The endpoint will be achieved if the lower confidence limit exceeds the performance goal of 62% using a one-sided lower 94.5% exact confidence bound at one of the three testing points.

These conditions ensure that performance will be in line with previously published randomized controlled trial results on a relevant comparator, the ZOLL LifeVest which, is the only commercially approved WCD in Europe or the US. The method for testing the conversion success will follow these steps:

1. If after attempting to convert the first 12 subjects, all subjects have been successfully converted (100% conversion rate) the trial will be stopped and deemed a success. Otherwise, continue to Step 2.
2. If conversion is less than 100% after 12 total subjects, enroll six (6) additional subjects for a total of 18 subjects. If 17 out of the 18 are successfully converted (94.4% conversion rate), or if 16 out of the 18 are successfully converted (88.0% conversion rate), the trial will be stopped and deemed a success. Otherwise, continue to Step 3.
3. Enroll the final six (6) subjects for a total of 24 subjects. If after attempting to convert 24 subjects, 21 of the 24 are successful (87.5% conversion rate), the trial will be deemed a success.

A 100% conversion rate with 12 subjects results in a one-sided lower 97.4% exact confidence bound of approximately 73.7% which exceeds the 62% performance goal.

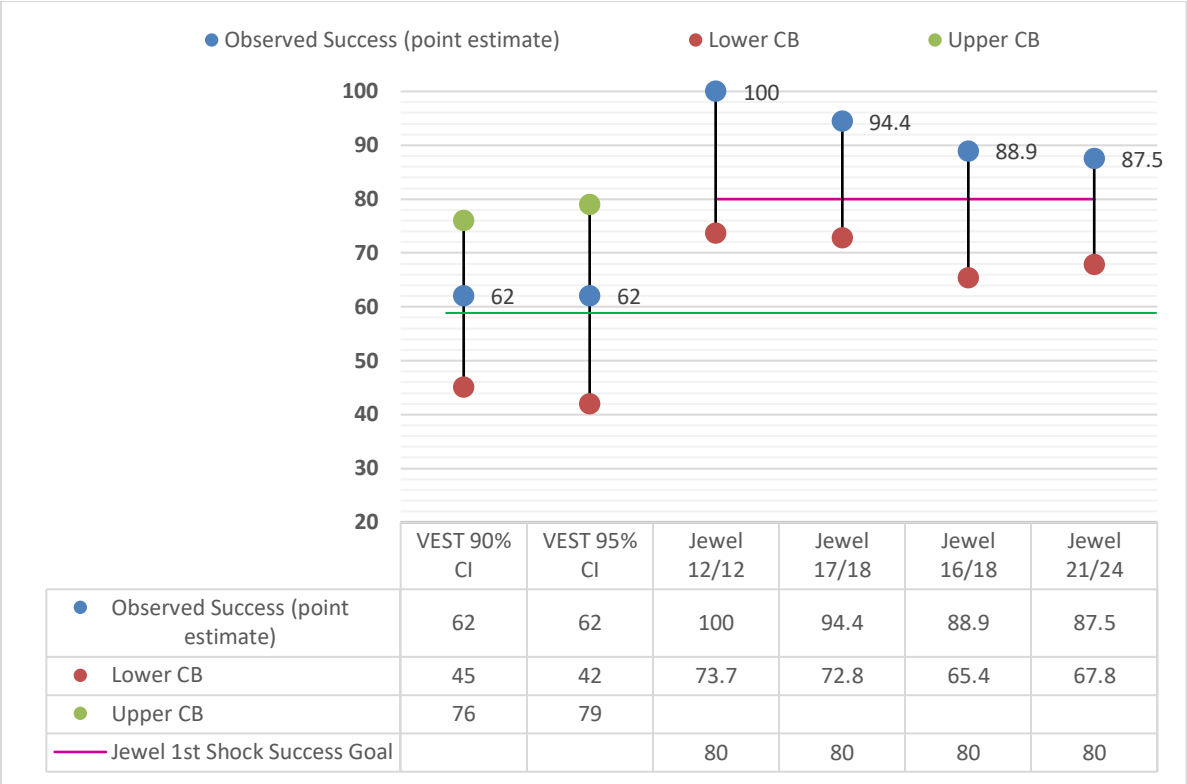
With a sample size of 18 subjects with 1 failure, the conversion rate is 94.4% with a one-sided lower 97.4% exact confidence bound of approximately 72.8% which also exceeds the 62% performance goal.

With a sample size of 18 subjects with 2 failures, the conversion rate is 88.9% with a one-sided lower 97.4% exact confidence bound of approximately 65.4% which also exceeds the 62% performance goal.

With a sample size of 24 subjects with 3 failures, the conversion rate is 87.5% with a one-sided lower 97.4% exact confidence bound of approximately 67.8% which also exceeds the 62% performance goal.

All of these scenarios result in a successful trial as the one-sided lower 97.4% exact confidence bound is above the performance goal of 62%. If at any point during the course of this study there are more than three (3) failures to convert a shockable rhythm (life-threatening VT or VF) due to the Jewel, the study will be stopped and deemed unsuccessful.

The graph below summarizes the group sequential study design, conversion success, and results of the one-sided lower 97.4% exact confidence bound.



	VEST 90% CI	VEST 95% CI	Jewel 12/12	Jewel 17/18	Jewel 16/18	Jewel 21/24
Observed Success (point estimate)	62	62	100	94.4	88.9	87.5
Lower CB	45	42	73.7	72.8	65.4	67.8
Upper CB	76	79				
Jewel 1st Shock Success Goal			80	80	80	80

Overall Type I Error Discussion:

The group sequential design of the Jewel EP Lab Study is meant to control the overall Type I error rate with 90% power. This design uses a Pocock alpha spending approach which controls the overall Type I error rate at 5%. The group sequential design of the Jewel EP Lab Study is being used in order to reduce the number of subjects put at risk through early stopping rules, while still providing sufficient data to demonstrate the effectiveness of the Jewel EP Lab System to successfully convert life-threatening VT and VF. Preliminary testing points and alpha expenditures were estimated using SAS version 9.3 which employs a normal approximation to designing sequential trials. The alpha spent at each testing point was used to determine the confidence level of the exact lower confidence bound. These confidence levels were then used to adjust the testing points to accommodate exact methods rather than the normal approximation. Simulations of 3000 trials of size 24 were used to confirm that the Type I error rate was controlled at the 5% level.

12. ADMINISTRATIVE CONSIDERATIONS

12.1. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

The Investigator should ensure that all persons assisting with the trial are adequately qualified and informed about the protocol, any amendments to the protocol, the study treatments, and their trial-related duties and functions. The Investigator must maintain a list of sub-investigators and other appropriately qualified persons to whom he/she has delegated significant trial-related duties.

12.2. INDEPENDENT ETHICS COMMITTEE (IEC) APPROVAL

The Investigator will not begin the study until the protocol and PIC have been approved by the IEC. As the product is investigational, national health authority approval is also required. The IEC will also review and approve all advertisements, if applicable. The IEC approval will be documented in writing and sent to the Investigator. The Investigator will forward a copy of the IEC approval document to the Sponsor. Any amendments to the protocol must also be approved in writing by the IEC, prior to implementation by the Investigator, except where necessary to eliminate an immediate hazard to study participants.

The Investigator will submit a progress report to the IEC at intervals as established by the IEC. The Investigator will retain a copy of this report in the Investigator's Site File.

12.3. ETHICAL CONDUCT OF THE STUDY

This study will be conducted in accordance with EN ISO 14155:2020, applicable local regulations, and the ethical principles that have their origin in the Declaration of Helsinki.

12.4. ADHERENCE TO PROTOCOL

By signing the Investigator Signature Page of this protocol, the Investigator confirms in writing that he/she has read, understands and will strictly adhere to the study protocol and will conduct the study in accordance with the Investigator Agreement and applicable regulatory requirements. By signing, the Investigator commits to ensuring that all site personnel involved in the execution of this study will be properly trained to perform their responsibilities prior to their involvement and that all personnel will be properly supervised during the course of this study.

12.5. PATIENT CONFIDENTIALITY

Patient names will not be supplied to the Sponsor. Only the patient identification number will be recorded in the CRF, and if the patient name appears on any other document (e.g. source documents), it must be redacted on the copy of the document to be supplied to the Sponsor. Study findings will be electronically stored in accordance with local data protection laws. The patients will be informed that representatives of the Sponsor, IEC, or regulatory authorities may inspect their medical records to verify information collected and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws.

The Investigator will maintain a personal patient identification list (patient numbers with the corresponding patient names) to enable records can be identified.

13. STUDY MONITORING

Monitoring visits will be conducted by representatives of the Sponsor in accordance with EN ISO 14155:2020 and relevant local regulations. The Investigator will permit the Sponsor's representative(s) to make regular study center visits during the study. At each previously arranged visit, the Investigator and staff will be expected to cooperate with the Sponsor's representative(s) for the review and verification of protocol compliance, AE/SAE reporting, CRFs, source documents, clinical supplies and inventory records, and any additional pertinent records. In addition to the monitoring visits, frequent communications (letter, telephone, email and fax) by the Study Monitor will ensure that the investigation is conducted according to protocol design and regulatory requirements.

13.1. TRAINING

The Sponsor will provide formal site initiation training for the Jewel EP Lab System procedure prior to activating each site. Training will review all critical aspects of study conduct as well as patient selection and eligibility, procedure methods, and follow-up required post treatment. On-site training will also be provided for patient treatments. The first case will be proctored at all sites and additional on-site support will be provided as needed.

13.2. ACCOUNTABILITY OF THE JEWEL EP LAB SYSTEM COMPONENTS

The Investigator is responsible for maintaining records relating to the receipt, inventory and return/destruction of Jewel EP Lab System components. The Investigator may delegate all or part of these responsibilities to qualified personnel.

13.3. CASE REPORT FORMS AND STUDY RECORDS

Electronic CRFs will be used for the collection of clinical data required by the protocol. The Principal Investigator is responsible for assuring the accuracy and completeness of all study documentation. The study will be monitored to check that all data collected for the study are recorded accurately and promptly. All documents and data shall be produced and maintained in a way that assures control and traceability. Where relevant, the accuracy of translations shall be guaranteed and documented. The Investigator shall assure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the CRFs. Where copies of the original source documents as well as printouts of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document.

The data reported on the CRFs shall be derived from the source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. The CRFs shall be electronically signed and dated by the Investigator or his/her designee(s). Any change or correction to the data shall be dated, signed with initials and explained as necessary, and shall not obscure the original entry (i.e. an audit trail shall be maintained); this applies to both written and electronic changes or corrections.

All clinical trial data will be recorded completely, promptly, and legibly, using indelible black or blue ballpoint ink. Errors made on any paper-based document must be corrected by drawing one line through the incorrect data, entering the correct data beside the incorrect entry, then initialing and dating the correction. Incorrect data should not be obliterated or obscured. The use of pencil, erasable ink, or correction fluid on study records is prohibited. All missing data must be explained. For instance, if the item was not done, mark "N/D" (or equivalent) should be used. If the item is not applicable to an individual case, mark the space "N/A" or equivalent.

Patients are not to be identified by name in the study database or on any study documents to be collected by the Sponsor or designee, but must be identified by the unique defined patient identifier.

Data management and handling will be conducted according to an approved Data Management Plan in accordance with applicable guidelines and the Sponsor's standard operating procedures (SOPs).

Any deviations, i.e. discrepancies and additions from the process defined in the Data Management Plan will be described in the investigation specific study report. The subject's personal data will be de-identified and coded as described in the Data Management Plan.

13.4. PROTOCOL DEVIATIONS

The Investigator will not alter this clinical study protocol without obtaining written agreement from the Sponsor. Once the study has started, amendments should be made only in exceptional cases. The amendment will become part of the clinical study protocol.

With the exception of an emergency situation, implementation of any change in the protocol that affects the safety of the patients, the scope of investigation, or the scientific quality of the study will not be permitted until the Sponsor, the Investigator, and the IEC responsible for review and approval of the study have reviewed and approved the amendment.

The Investigator will make every effort not to deviate from the protocol. In the event of an emergency, the Investigator shall implement any medical procedures deemed appropriate. However, all such procedures must have written documentation and be promptly reported to the Sponsor and IEC.

13.5. AMENDMENTS

Protocol modifications to the study may be made only after the approval of the Sponsor. Protocol amendments will be created if the changes affect the relative safety of subject, the scope of the investigation, the scientific quality of the study, the experimental design, the assessment variables, the number of subject treated, or any of the subject selection criteria.

Amendments may be generated only by the Sponsor, and require prospective review and approval by the Investigator's local IEC and the regulatory authorities, as applicable. The Sponsor/Monitor must receive IEC and regulatory authority (if applicable) approval/notification before the changes may be implemented.

If the protocol amendment changes the information in the PIC, the Investigator will submit an amended PIC to IEC for approval. The amended PIC must also be approved by the Sponsor.

13.6. ACCESS TO SOURCE DOCUMENTATION

The Investigator will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each patient enrolled in the study. The Investigator will allow the Sponsor's representatives, contract designees, and authorized regulatory authority inspectors to have direct access to all documents pertaining to the study.

The Investigator agrees that the Sponsor and its employees or agents, the IEC and governmental regulatory agencies have the right, from time to time, both during and after termination of this clinical study, to monitor, audit and review records relating to the clinical study, including patient medical and billing records. The Sponsor may request real time transmittal of some source data during the course of the study. Quality Assurance personnel from the Sponsor or its designee may audit the clinical trial site and/or study-related materials at any time during the study.

13.7. RETENTION OF DATA

A copy of the following documents must be retained by the investigator for at least two years after approval of the device, or two years following the completion of the study if marketing approval is not pursued, or longer if notified by the Sponsor to do so:

- Study protocol;
- Investigator's Brochure;
- Completed case report forms;
- Source medical records, including original test result reports, to verify all data entered on the case report form;
- Adverse event and protocol deviation documentation;
- Investigational device receipt, return, and accountability logs;
- All study related correspondence (including IEC and Sponsor correspondence);
- A copy of the written informed consent for each subject in the clinical trial; and,
- Any other documents pertaining to the conduct of this study.

No study document shall be destroyed without prior written agreement between the Sponsor and the Investigator. Should the Investigator wish to assign the study records to another party or to move them to another location, the Investigator must notify the Sponsor in writing and obtain written approval.

The Investigator will allow representatives of the Sponsor's monitoring team (and if applicable, the FDA and the local regulatory authority) to inspect all study records, CRFs, and corresponding portions of the study subjects' office and/or hospital medical records at regular intervals throughout the study. These inspections are for the purpose of verifying the adherence to the protocol, the completeness and exactness of the data being entered in the CRFs, and compliance with regulations.

14. SUPPLEMENTS

14.1. INVESTIGATOR'S AGREEMENT

Study Title: Jewel Electrophysiology (EP) Lab Study

I have read the attached protocol and agree that it contains all the necessary details for performing the study. I will ensure adequate and eligible patients are enrolled into the study.

I will provide copies of the protocol and the clinical information on the product, which was furnished to me by the Sponsor, to all members of the study team responsible to me who participate in the study. I will discuss this material with them to assure that they are fully informed regarding the product and the conduct of the study.

I understand that the study will not be started without the prior written approval of a properly constituted IEC. As the product is Investigational, National Health Authority approval is also required. No changes will be made to the study protocol. I will submit any informed consent modifications in writing to Element Science, Inc. and the IEC.

Written approval will be obtained before any modifications are implemented. I understand the protocol and will work according to it and according to the principles of Good Clinical Practice, EN ISO 14155:2020 and relevant local regulations. Information developed in this clinical study may be disclosed by the Sponsor to other clinical investigators, government health protection agencies, foreign or domestic, as required.

Subject confidentiality will be maintained at all times unless disclosure is required by government regulation or applicable law.

Signature of Investigator	Date
Name of Investigator	Title