NCT02714153
Bridge Occlusion Balloon in Lead Extraction Procedure
8/8/2016

YALE UNIVERSITY
HUMAN INVESTIGATION COMMITTEE

Application to Involve Human Subjects in Biomedical Research
100 FR1 (2015-2)

SECTION I: ADMINISTRATIVE INFORMATION

Title of Research Project: Bridge Occlusion Balloon in Lead Extraction Procedure			
Principal Investigator: **Jude Clancy, MD**		**Yale Academic Appointment:** **Assistant Professor of Medicine**	
Department: Internal Medicine, Section of Cardiology			
Campus Address: 330 Cedar Street, Dana 3 New Haven, CT 06520			
Campus Phone: 785-4126	**Fax:** 785-6506	**Pager:**	**E-mail:** jude.clancy@yale.edu
Protocol Correspondent Name & Address (*if different than PI*): Bemen Habashi 789 Howard Ave, DANA 345 New Haven CT 06520			
Campus Phone: 737-1330	**Fax:** 785-6457	**E-mail:** bemen,habashi@yale.edu	
Yale Cancer Center CTO Protocol Correspondent Name & Address (*if applicable*):			
Campus Phone:	**Fax:**	**E-mail:**	
Business Manager:			
Campus Phone :	**Fax :**	**E-mail**	

Faculty Advisor:(required if PI is a student, resident, fellow or other trainee) ☐ **N**				**ntment:**
Campus Address:				
Campus Phone:	**Fax:**	**Pager:**	**E-mail:**	

Investigator Interests:

Does the principal investigator, or do any research personnel who are responsible for the design, conduct or reporting of this project or any of their family members (spouse or dependent child) have an incentive or interest, financial or otherwise, that may affect the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? Note: The Principal Investigator (Project Director), upon consideration of the individual's role and degree of independence in carrying out the work, will determine who is responsible for the design, conduct, or reporting of the research.

See Disclosures and Management of Personal Interests in Human Research
http://www.yale.edu/hrpp/policies/index.html#COI

■ Yes ☐ No

Do you or does anyone on the research team who is determined by you to be responsible for the design, conduct or reporting of this research have any patent (sole right to make, use or sell an invention) or copyright (exclusive rights to an original work) interests related to this research protocol?

☐ Yes • No

If yes to either question above, list names of the investigator or responsible person:

Jude Clancy, relationships with industry have been disclosed to COI office

The Yale University Principal Investigator, all Yale University co-investigators, and all Yale University individuals who are responsible for the design, conduct or reporting of research must have a current financial disclosure form on file with the University's Conflict of Interest Office. Yale New Haven Hospital personnel who are listed as co-investigators on a protocol with a Yale University Principal Investigator must also have a current financial disclosure form on file with the University's Conflict of Interest Office. If this has not been done, the individual(s) should follow this link to the COI Office Website to complete the form: http://www.yale.edu/coi/

NOTE: The requirement for maintaining a current disclosure form on file with the University's Conflict of Interest Office extends primarily to Yale University and Yale-New Haven Hospital personnel. **Whether or not they are required to maintain a disclosure form with the University's Conflict of Interest Office, all investigators and individuals deemed otherwise responsible by the PI who are listed on the protocol are required to disclose to the PI any interests that are specific to this protocol.**

SECTION II: GENERAL INFORMATION

1. **Performing Organizations:** Identify the hospital, in-patient or outpatient facility, school or other agency that will serve as the location of the research. Choose all that apply:

a. Internal Location[s] of the Study:

☐ Magnetic Resonance Research Center (MR-TAC)
☐ Yale Cancer Center/Clinical Trials Office (CTO)
☐ Yale Cancer Center/Smilow
☒ Yale-New Haven Hospital
☐ Cancer Data Repository/Tumor Registry
☐ Specify Other Yale Location:
☐ Yale University PET Center
☐ YCCI/Church Street Research Unit (CSRU)
☐ YCCI/Hospital Research Unit (HRU)
☐ YCCI/Keck Laboratories
☐ Yale-New Haven Hospital—Saint Raphael Campus

b. External Location[s]:

☐ APT Foundation, Inc.
☐ Connecticut Mental Health Center
☐ Clinical Neuroscience Research Unit (CNRU)
☐ Other Locations, Specify:
☐ Haskins Laboratories
☐ John B. Pierce Laboratory, Inc.
☐ Veterans Affairs Hospital, West Haven
☐ International Research Site (Specify location(s)):

c. Additional Required Documents *(check all that apply)*: ☐ N/A

☐ *YCCI-Scientific and Safety Committee (YCCI-SSC)	Approval Date:
☐ *Pediatric Protocol Review Committee (PPRC)	Approval Date:
☐ *YCC Protocol Review Committee (YRC-PRC)	Approval Date:
☐ *Dept. of Veterans Affairs, West Haven VA HSS	Approval Date:
☐ *Radioactive Drug Research Committee (RDRC)	Approval Date:
☒ YNHH-Radiation Safety Committee (YNHH-RSC)	Approval Date: Pending
☐ Yale University RSC (YU-RSC)	Approval Date:
☐ Magnetic Resonance Research Center PRC (MRRC-PRC)	Approval Date:
☐ *Nursing Research Committee	Approval Date:
☐ YSM/YNHH Cancer Data Repository (CaDR)	Approval Date:

☐ Dept. of Lab Medicine request for services or specimens form

☐ Imaging on YNHH Diagnostic Radiology equipment request form (YDRCTO request) found at http://radiology.yale.edu/research/ClinTrials.aspx)

Approval from these committees is required before final HIC approval is granted. See instructions for documents required for initial submission and approval of the protocol. Allow sufficient time for these requests. Check with the oversight body for their time requirements.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

   1 Year.

3. **Research Type/Phase: (Check all that apply)**

   a. **Study Type**

   ☐ Single Center Study

   ☒ Multi-Center Study

   Does the Yale PI serve as the PI of the multi-site study? Yes ☒ No ☐

   ☒ Coordinating Center/Data Management

   ☐ Other:

   - ***List of the other sites:***

Dr. Bruce L. Wilkoff
Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH
Dr. Laurence M. Epstein
Brigham and Women's Hospital, 75 Francis St, Boston, MA
Dr. Roger G. Carrillo
University of Miami Health System, 1295 NW 14th St, Miami, FL
Dr. Jonathan Piccini Sr.
Duke University Hospital, 2301 Erwin rd, Durham, NC
Dr. John A. Andriulli
Cooper University Hospital, 1 Cooper Plaza, Camden, NJ
Dr. Pierce Vatterott
United Hospital, 333 N Smith Ave, St. Paul, MN
Dr. Rohit Mehta
Carolinas HealthCare System, Charlotte, North Carolina, United States, 28203

b. **Study Phase** ☐ **N/A**
☐ Pilot | Phase I | Phase II | Phase III | Phase IV
☒ Other (*Specify)*: Investigator initiated, post market study.

4. **Area of Research: (Check all that apply)** Note that these are overlapping definitions and more than one category may apply to your research protocol. Definitions for the following can be found in the instructions section 4c:

☒ Clinical Research: Patient-Oriented
☐ Clinical Research: Epidemiologic and Behavioral
☐ Translational Research #1 ("Bench-to-Bedside")
☐ Translational Research #2 ("Bedside-to-Community")
☐ Clinical Research: Outcomes and Health Services
☐ Interdisciplinary Research
☐ Community-Based Research

5. Is this study a clinical trial? Yes ☒ No ☐

NOTE the current ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events"

If yes, where is it registered?
Clinical Trials.gov registry ☒
Other (*Specify*)

*Registration of clinical trials **at their initiation** is required by the FDA, NIH and by the ICMJE.*

If this study is registered on clinicaltrials.gov, there is new language in the consent form and compound authorization that should be used.

For more information on registering clinical trials, including whether your trial must be registered, see the YCCI webpage, http://ycci.yale.edu/researchers/ors/registerstudy.aspx or contact YCCI at 203.785.3482)

6. Does the Clinical Trials Agreement (CTA) require compliance with ICH GCP (E6)?
Yes ☒ No ☐

7. Will this study have a billable service? *A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include*

x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

Yes ☒ No☐

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

8.. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes X_ No ___ *If Yes, please answer questions a through c and note instructions below. If No, proceed to Section III.*

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform? **Yes**

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? **Yes**

c. Will a novel approach using existing equipment be applied? **Yes**

If you answered "no" to question 8a, or "yes" to question 8b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. ***By signing this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH****.*

SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

1. **Funding Source:** Indicate all of the funding source(s) for this study. Check all boxes that apply. Provide information regarding the external funding source. This information should include identification of the agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the M/C# and Agency name (if grant-funded). If the funding source associated with a protocol is "pending" at the time of the protocol submission to the HIC (as is the case for most NIH submissions), the PI should note "Pending" in the appropriate section of the protocol application, provide the M/C# and Agency name (if grant-funded) and further note that University (departmental) funds support the research (until such time that an award is made).

PI	Title of Grant	Name of Funding Source	unding	unding Mechanism
Jude Clancy, MD	Bridge occlusion balloon initial use in humans – Investigator Initiated Study	Spectranetics	Federal ☐ State ☐ Non Profit ☒ Industry ☐ Other For rofit Other	Grant-M# ☐ Contract# ☐ Contract Pending ☒ Investigator/Department nitiated ☐ Sponsor Initiated Other, Specify:
			Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For rofit Other	Grant-M# ☐ Contract# ☐ Contract Pending ☐ Investigator/Department nitiated ☐ Sponsor Initiated Other, Specify:
			Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For rofit Other	Grant-M# ☐ Contract# ☐ Contract Pending ☐ Investigator/Department nitiated ☐ Sponsor Initiated Other, Specify:

IRB Review fees are charged for projects funded by Industry or Other For-Profit Sponsors. Provide the Name and Address of the Sponsor Representative to whom the invoice should be sent. ***Note: the PI's home department will be billed if this information is not provided.***

Send IRB Review Fee Invoice To:

Name: ATT: Rashmi Ram
Company: Spectranetics Corporation
Address: 9965 Federal Drive, Colorado Springs, CO 80921

2. **Research Team:** List all members of the research team. Indicate under the affiliation column whether the investigators or study personnel are part of the Yale faculty or staff, or part of the faculty or staff from a collaborating institution, or are not formally affiliated with any institution. **ALL members of the research team MUST complete Human Subject Protection Training (HSPT) and Health Insurance Portability and Accountability Act (HIPAA) Training before they may be listed on the protocol. See NOTE below.**

NOTE: The HIC will remove from the protocol any personnel who have not completed required training.

	Name	Affiliation: Yale/Other Institution (Identify)	NetID
Principal Investigator	Jude Clancy, MD	Yale	JFC25
Role: Investigator	Ryan Donovan PA-C	Yale	RJD43
Role: Investigator	Medhat Abdelmessih, MD	Yale	MA648

A personnel protocol amendment will need to be submitted when training is completed.

SECTION IV: PRINCIPAL INVESTIGATOR/FACULTY ADVISOR/ DEPARTMENT CHAIR AGREEMENT

As the **principal investigator** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- I assume full responsibility for the protection of human subjects and the proper conduct of the research.
- Subject safety will be of paramount concern, and every effort will be made to protect subjects' rights and welfare.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- All members of the research team will be kept apprised of research goals.
- I will obtain approval for this research study and any subsequent revisions prior to my initiating the study or any change and I will obtain continuing approval of this study prior to the expiration date of any approval period.
- I will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or have acquired the appropriate approval from the Dean's Office or Office of the Provost, or the Human Subject Protection Administrator at Yale-New Haven Hospital, or have a faculty advisor.
- I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities.

_____ _____

PI Name (PRINT) and Signature Date

As the **faculty advisor** of this research project, I certify that:

- The information provided in this application is complete and accurate.
- This project has scientific value and merit and that the student or trainee investigator has the necessary resources to complete the project and achieve the aims.
- I will train the student investigator in matters of appropriate research compliance, protection of human subjects and proper conduct of research.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- The student investigator will obtain approval for this research study and any subsequent revisions prior to initiating the study or revision and will obtain continuing approval prior to the expiration of any approval period.
- The student investigator will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set forth by the University and qualify to serve as the faculty advisor of this project.
- I assume all of the roles and responsibilities of a Principal Investigator even though the student may be called a PI.

_____ _____

Advisor Name (PRINT) and Signature Date

Department Chair's Assurance Statement

Do you know of any real or apparent institutional conflict of interest (e.g., Yale ownership of a sponsoring company, patents, licensure) associated with this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC.)
☐ No

As Chair, do you have any real or apparent protocol-specific conflict of interest between yourself and the sponsor of the research project, or its competitor or any interest in any intervention and/or method tested in the project that might compromise this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC)
☐ No

I assure the HIC that the principal investigator and all members of the research team are qualified by education, training, licensure and/or experience to assume participation in the conduct of this research trial. I also assure that the principal investigator has departmental support and sufficient resources to conduct this trial appropriately.

_____ _____

Chair Name (PRINT) and Signature Date

_____

Department

YNHH Human Subjects Protection Administrator Assurance Statement

Required when the study is conducted solely at YNHH by YNHH health care providers.

As Human Subject Protection Administrator (HSPA) for YNHH, I certify that:

- I have read a copy of the protocol and approve it being conducted at YNHH.
- I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.
- The principal investigator of this study is qualified to serve as P.I. and has the support of the hospital for this research project.

YNHH HSPA Name (PRINT) and Signature _____ Date _____

SECTION V: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

To evaluate the use of an occlusion balloon (Bridge Occlusion Balloon, Spectranetics) within the SVC in lead extraction patients.

2. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

Chronically implanted pacemaker and ICD leads often are encased in dense adherent fibrous tissue growth. This can lead to significant difficultly in extracting these leads and major complications and death may occur during transvenous lead extraction. A recent study of catastrophic complications occurring during lead extraction demonstrated a rate of 0.8% major complication and 0.4% for procedural mortality over a 16-year period in patients requiring an intervention [(1)]. Injury to the superior vena cava (SVC), a major thoracic vessel is uncommon and occurs at the rate of 0.4 % [(2)]. However, an SVC tear can be associated with hemodynamic instability, hemothorax, and tamponade. This is a life-threatening and potentially fatal complication if not recognized and treated promptly. Expeditious control of bleeding is of paramount importance to achieve a reasonable long-term outcome. Repair of an SVC perforation requires an open chest approach with emergency sternotomy or thoracotomy. According to the Heart Rhythm Society guidelines [(3)], a delay from the time of injury to open access to the heart (patient related comorbidities or re-operative open access) of more than 5-10 minutes was associated with a fatal outcome. Initiation of rescue efforts within this time period with prompt endovascular management with a device such as the Bridge occlusion balloon can result in a successful outcome. Inflating the Bridge device immediately when a tear is suspected can provide temporary occlusion in the tear area, resulting in control of hemorrhage, and maintenance of patient's hemodynamics prior to definitive surgical repair.

(1) Brunner MP, Cronin EM, Wazni O, Baranowski B, Saliba WI, Sabik JF, Lindsay BD, Wilkoff BL, Tarakji KG. Outcomes of patients requiring emergent surgical or endovascular intervention for catastrophic complications during transvenous lead extraction. Heart Rhythm. 2014 Mar;11(3):419-25

(2) Wazni, O et al. (2010). Lead extraction in the contemporary setting: the LExICon study: an observational retrospective study of consecutive laser lead extractions. J Am Coll Cardiol. Feb 9;55(6):579-86

(3) Wilkoff BL, Love CJ, Byrd CL, Bongiorni MG, Carrillo RG, Crossley GH 3rd, Epstein LM, Friedman RA, Kennergren CE, Mitkowski P, Schaerf RH, Wazni OM; Heart Rhythm Society; American Heart Association. Transvenous lead extraction: Heart Rhythm Society expert consensus on facilities, training, indications, and patient management: this document was endorsed by the American Heart Association (AHA). Heart Rhythm. 2009 Jul;6(7):1085-104.

3. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. **Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths**. Describe the setting in which the research will take place.

   This study will evaluate the use of an occlusion balloon (Bridge Occlusion Balloon, Spectranetics) within the SVC (Superior Vena Cava) in lead extraction patients. This will be performed in a non-emergent setting to allow for evaluation of how best to integrate this new technology into our clinical practice. The study will focus on the effect of the Bridge balloon on the patient preparation clinical workflow, ease of insertion/positioning/deployment, and the ability to recognize proper inflation and vein sealing under fluoroscopy. Understanding these factors will help build a more robust clinical workflow with the goal of better patient outcomes in the case of an injury to SVC. The images and data generated during this study can help in dissemination of the practical use knowledge to fellow lead extractors.

   The **study procedure steps** will be as follow:

   1. Record baseline vital signs (HR, BP, SPO2) and ABG post intubation but prior to study initiation
   2. Obtain baseline cine of superior vena cava (SVC) to document SVC integrity before using the balloon.
   3. Place a compatible guidewire via the right femoral vein and confirm position of the guidewire with fluoroscopy. Obtain cine of guidewire position from access vein to destination vein.
   4. Use a 12F sheath over the guidewire in the right femoral vein.
   5. Start time recording with a stopwatch (time=0); Open the sterile balloon packaging. Insert and advance the balloon until the proximal marker band (radiopaque mark) is located at the SVC/RA junction. Use cine to document balloon position.
   6. Record vital signs (HR, BP, SPO2) prior to balloon inflation.
   7. Using fluoroscopic guidance, properly inflate the balloon with 20/80 contrast/saline mix using the recommended 60cc syringe until the balloon conforms to the vasculature.
   8. Record the time to balloon deployment (i.e. complete conformance of the balloon to the vasculature based on fluoroscopy).
   9. Use fluoroscopy and cine to confirm and record the position of the balloon.
   10. Record vital signs (HR, BP, SPO2) post balloon inflation but prior to contrast injection.

11. Inject contrast from superior venous access and record cine to assess occlusion of the SVC.
12. Allow one repositioning of balloon if occlusion not obtained and record additional cine to reassess occlusion of SVC.
13. Record vital signs (HR, BP, SPO2) 1 min after occlusion has been confirmed.
14. Deflate the balloon fully using the 60cc syringe and remove the balloon from the body. Leave guidewire and femoral sheath in place (can be used to deliver a bridge balloon catheter in case if SVC tear occurred during the extraction procedure – this is a clinical indication and is not an investigational part). Repeat venogram after balloon deflation and removal to document SVC area post occlusion.
15. Record vital signs (HR, BP, SPO2) and ABG 5,10,15,20,25, and 30 minutes post balloon deflation.
16. Record all vital signs (HR,BP,SPO2) that is out of the expected reange for the patient within 30 minutes post balloon deflation.
17. Continue with the lead extraction procedure.

The extraction procedure itself is a standard of care procedure, it is clinically indicated in the targeted patient population. The deployment and use of the Balloon Bridge is a research related activity, will be done for the research purposes only.

All the procedures pertaining to lead extraction is standard of care and routinely used. The research portion of the study will consist of balloon inflation prior to initiation of the lead extraction procedure. There will be no control group for this study. The device itself will be provided at no cost.

This study will evaluate the use of the Bridge occlusion balloon in 3-5 lead extraction patients scheduled for lead extraction (patients indicated for lead extraction). This study will be performed prior to lead extraction in an intact SVC without prior SVC occlusion.
The following data will be collected:

- Cine at baseline and after removal of the Bridge occlusion balloon.
- Cine of the insertion/positioning/inflation of the Bridge occlusion balloon.
- Venogram: pre-occlusion, during occlusion confirming vein occlusion, and post-occlusion to evaluate vein integrity.
- Hemodynamics (BP, HR, and SPO2) at a pre-occlusion baseline, during occlusion, and post-occlusion and recovery time (5min).
- Time to insert, position, and deploy Bridge from sterile packaging.
- Any perioperative and post-24hr clinical complications the PI at each center feels is directly related to deployment of the Bridge occlusion balloon.

Study Endpoints:

Primary Endpoints

- Robust clinical workflow is established
- The Bridge occlusion balloon will:
  - ✓ Fit within an acceptable patient preparation clinical workflow.
  - ✓ Will be easy to insert, position, and deploy in vivo.

- ✓ Will be successful to achieve intact SVC occlusion with the Bridge balloon.

Secondary Endpoints

- Will be easy to recognize via fluoroscopy when occlusion.
- There will be no unacceptable hemodynamics during occlusion or post occlusion.
- There will be no perioperative clinical sequelae related to occlusion of the SVC area with the Bridge occlusion balloon.

Device Description

The Bridge Occlusion Balloon catheter is designed for temporary vessel occlusion of the superior vena cava in applications including perioperative occlusion and emergency control of hemorrhage associated with vascular tears that may occur during lead extraction procedures.
The subject device is packaged in a single sterile barrier system, is provided to the user sterile, and is intended for single use. The device does not include any accessories or additional components. ***(Figure.1)*** is an illustration of the Bridge Occlusion Balloon catheter. The device consists of a proximal hub, strain relief, catheter shaft, and a distal balloon. Three radiopaque markers are mounted on the catheter shaft inside the balloon. ***(Table.1)*** lists the dimensional specifications for the device.

Figure 1: Bridge Occlusion Balloon Catheter (top) and with balloon protector (bottom)

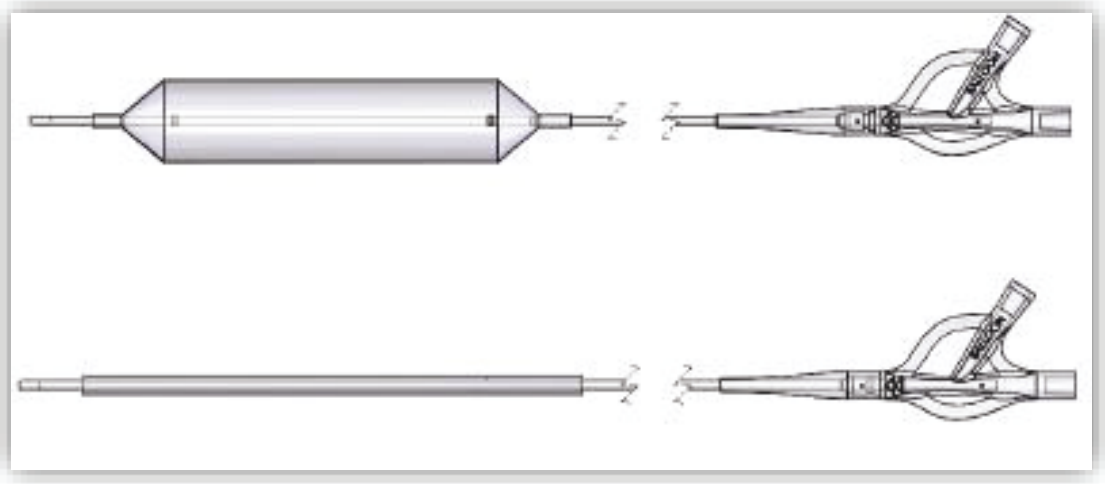

Table 1: Bridge Occlusion Balloon Specifications

Cat. #	Catheter Length (cm)	Balloon Diameter (mm)	Balloon Length (mm)	Maximum OD (Crossing Profile) (mm/in)	Minimum Tip/Guidewire Lumen ID (mm/in)	Maximum Inflation Volume (cc)
590-001	90	20 nominal 31 at max	80 nominal	4/0.157	0.9/0.036	60

Occlusion Balloon Catheter Description

The Bridge Occlusion Balloon catheter is designed to be delivered percutaneously to the superior vena cava (SVC) for the purpose of providing occlusion of the SVC and providing emergency control of hemorrhage and perioperative occlusion in the event of an SVC tear or perforation during a lead extraction procedure.

The Bridge Occlusion Balloon catheter is constructed of a compliant polyurethane balloon mounted on a dual lumen polyurethane shaft. The hub port, marked BALLOON, is connected to the balloon inflation lumen. The unmarked hub port is connected to the central lumen of the catheter, which terminates at the distal tip. This lumen is used to pass the catheter over a guidewire. A strain relief is mounted to the catheter shaft just distal of the proximal hub. Three platinum-iridium radiopaque markers are placed within the balloon segment of the catheter to provide visual reference points for balloon positioning within the SVC prior to inflation.

Plan to ensure training of staff at all sites:

- All site study coordinators are required to attend study protocol training over the phone (web conference). This training will be provided by the investigators at Yale and will cover the study purpose, the study protocol, and the data collection process in detail. This training will be documented in "Bridge Balloon Study – Protocol Training" form.
- All site study coordinators are then required to train their site physician(s) (if the physician(s) are unable to the phone training) on the study protocol. This training will be documented in the "Bridge Balloon Study – Protocol Training" form.
- Time will be given after each training session for questions and more clarification as needed.
- All site physicians are required to be trained on the Bridge Occlusion Balloon Catheter. This training will be performed by a qualified Spectranetics' sales representative and will be documented in the "Bridge Balloon Study – Device Training" form.
- Documentation of protocol and device training is required prior to enrolling patients.
- Documentation of the training will be kept in the regulatory binder.

Plan to ensure IRB approval is in place prior to starting:

- IRB approval tracking system is in place, excel sheet is created to track the IRB approvals at each site.
- Each site is required to send to Yale a copy of the IRB approval letter.
- Authorization letter will be sent out to start enrollment at other sites after receiving the appropriate IRB documentation.

Mechanism for registering each subject at Yale:

- Each subject has two different registration codes;
  - ✓ First ID: is done by each site which includes the site ID (2digits) and subject ID (3 digits) e.g. [XX-XXX] - This will allow us to know the enrolling site and enrollment order of each subject.
  - ✓ Second ID: is done here at Yale based on the order of receiving the data collection form e.g. [XXX]

Mechanism for routine communication with site investigators:

- The PI will send a weekly mass e-mail for the site investigators to discuss the study progress.
- A copy of the email communication will be kept in the regulatory binder.

Plan to ensure ongoing IRB approval at all sites and approval of any amendments:

- Based on the IRB approvals tracking system, 1st email reminder will be sent 3 months before study expiration date as a reminder of study reapproval. Follow up emails each week until a documentation of IRB submission is received.
- All sites are required to update the central site with any amendments submissions and a copy of the approval will be saved in the regulatory binder.

4. Genetic Testing N/A ☒

5. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

   Patients indicated for lead extraction. 5 patients per site can be tested as part of this study.

6. **Subject classification:** Check off all classifications of subjects that will be <u>specifically recruited for enrollment</u> in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐ Children	☐ Healthy	☐ Fetal material, placenta, or dead fetus
☐ Non-English Speaking	☐ Prisoners	☐ Economically disadvantaged persons
☐ Decisionally Impaired	☐ Employees	☐ Pregnant women and/or fetuses
☐ Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects? ☐ Yes ☒ No (If yes, see Instructions section VII #4 for further requirements)

7. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

Inclusion:

- Subject age more than 18 years.
- Lead extraction patients.

Exclusion:

Lead extraction patients with

- SVC occlusion or stenosis.
- Significant vegetation.
- Hemodynamic instability.
- Class IV NYHA heart failure
- Creatinine > 2.0mg/dL
- Mechanical assist devices
- Patients > 85 years old
- Patients felt to be high risk due to degree of acute illness or systemic comorbidities
- Patients who are placed on a heparin bridge, and are felt to be high risk for even brief discontinuation of anticoagulation

8. How will **eligibility** be determined, and by whom?

Eligibility will be determined by the PI and investigators based on the exclusion/inclusion criteria. Clinical evaluation will be done to evaluate the patient's eligibility for the study.

9. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The adverse events associated with an occlusion balloon procedure include, but are not limited to the following:

- *Allergic Reactions*
- *Death*
- *Embolization / thromboembolic episodes*
- *Hematoma*
- *Hemorrhage*
- *Sepsis/infection*
- *Short term hemodynamic deterioration*
- *Vascular thrombosis*
- *Vessel dissection*
- *Vessel Perforation*
- *Vessel Spasm*

There is a potential risk of privacy breach will be avoided by following HIPPA rules. All patients' personal information will be kept in safe encrypted devices. All the collected data will be kept on a protected device connected to secure server networks located in locked office.

10. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

Risks can be minimized through compliance with this protocol, using the devices in accordance with their applicable directions for use, performing the procedures following recommended standard practices/guidelines, performing procedures in the appropriate hospital environment, adherence to subject selection criteria, close monitoring of the subject's physiologic status during research procedures and/or follow-ups.

All the data will be kept in protected computers that are located in locked offices.

11. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.) For more information, see the Instructions, page 24.
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study?

       The risk assessment is greater than minimal.

    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study?

       No children will be enrolled in this study.

    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://www.yale.edu/hrpp/forms-templates/biomedical.html for
       i. Minimal risk
       ii. Greater than minimal

Greater Than Minimal Risk DSMP

1. Personnel responsible for the safety review and its frequency:

The principal investigator will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency, which must be conducted at a minimum of every 6 months (including when reapproval of the protocol is sought). During the review process, the principal investigator (monitor) will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment. Either the principal investigator, the IRB or have the authority to stop or suspend the study or require modifications.

All sites are required to document all the adverse events and complication in the data collection form with the site PI assessment. Each site will send de-identified source documents to the central site through secured academic email or fax to the central site. The fax is located in a locked office, to which only the research team has access.

Through the remote monitoring plan, the central PI will review all the adverse events and perioperative complication within 1 day of receiving the data collection form. Additional source

documents will be requested from the site. All the source documents will be stored in a locked research office in the cardiology department.

2. The risks associated with the current study are deemed greater than minimal for the following reasons: (choose those that apply)

1. We do not view the risks associated with the Bridge Balloon as minimal risks.

Although we have assessed the proposed study as one of greater than minimal risk, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of first-hand experience with the proposed study methods. Therefore, we provide a plan for monitoring the data and safety of the proposed study as follows:

An independent study monitor will have the oversight of the study. A remote monitoring plan is in place to validate the information collected from all sites.

The monitor will receive the documents form each site and will check the accuracy and completeness of the data entries, source documents, and other trial-related records against each other. The monitor specifically will verify that the data required by the protocol are reported accurately on the data collection sheet and are consistent with the source data/documents.

The study monitor will verify that all the adverse events, concomitant medications, and current illnesses are reported in accordance with the protocol. In addition, the monitor will determine whether all adverse events (AEs) are appropriately reported within the time periods.

The appointed monitor will verify that source documents and other trial records are accurate, complete, kept up-to-date, and maintained. Also will verifying that the investigator is enrolling only eligible subjects and report the subject recruitment rate.

The monitor will submit a written report to the sponsor after each monitoring action. The report will include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings, deviations and deficiencies, conclusions, actions taken or to be taken.

Review of documentation will begin for each site after the first subject's data is sent to the coordinating center. The review will take place within 5 days of receipt of the information. The monitor, after reviewing the data, will email the investigator with any queries. When all queries are responded to satisfactorily, the monitor will review additional subjects after the third subject is enrolled at the site.

All the qualification of the appointed monitor will be kept in the master binder.

3. Attribution of Adverse Events:

Adverse events will be monitored for each subject participating in the study and attributed to the study procedures / design by the principal investigator (Dr. Jude Clancy) according to the following categories:

a.) Definite: Adverse event is clearly related to investigational procedures(s)/agent(s).
b.) Probable: Adverse event is likely related to investigational procedures(s)/agent(s).
c.) Possible: Adverse event may be related to investigational procedures(s)/agent(s).
d.) Unlikely: Adverse event is likely not to be related to the investigational procedures(s)/agent(s).
e.) Unrelated: Adverse event is clearly not related to investigational procedures(s)/agent(s).

4. Plan for Grading Adverse Events:

The following scale will be used in grading the severity of adverse events noted during the study:

1. Mild adverse event
2. Moderate adverse event
3. Severe

5. Plan for Determining Seriousness of Adverse Events:

Serious Adverse Events:
In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it results in any of the following outcomes:

1. Death;
2. A life-threatening experience in-patient hospitalization or prolongation of existing hospitalization;
3. A persistent or significant disability or incapacity;
4. A congenital anomaly or birth defect; OR
5. Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its "seriousness" when determining whether reporting to the IRB is necessary.

6. Plan for reporting UPIRSOs (including Adverse Events) to the IRB

The principal investigator will report the following types of events to the IRB:

Any incident, experience or outcome that meets ALL 3 of the following criteria:

1. Is unexpected (in terms of nature, specificity, severity, or frequency) given (a) the research procedures described in the protocol-related documents, such as the IRB-

approved protocol and informed consent document and (b) the characteristics of the subject population being studied; AND

2. Is related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND
3. Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, legal, or social harm) than was previously known or recognized.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) may be medical or non-medical in nature, and include – but are not limited to – *serious, unexpected, and related adverse events* and *unanticipated adverse device effects*. ***Please note*** that adverse events are reportable to the IRB as UPIRSOs **only** if they meet all 3 criteria listed above.

These UPIRSOs/SAEs will be reported to the IRB in accordance with IRB Policy 710, using the appropriate forms found on the website. All related events involving risk but not meeting the *prompt* reporting requirements described in IRB Policy 710 should be reported to the IRB in summary form at the time of continuing review. If appropriate, such summary may be a simple brief statement that events have occurred at the expected frequency and level of severity as previously documented**.** In lieu of a summary of external events, a current DSMB report can be submitted for research studies that are subject to oversight by a DSMB (or other monitoring entity that is monitoring the study on behalf of an industry sponsor).

7. Plan for reporting adverse events to co-investigators on the study, as appropriate the protocol's research monitor(s), e.g., industrial sponsor, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), Protocol Review Committee (PRC), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies.

For the current study, the following individuals, funding, and/or regulatory agencies will be notified (choose those that apply):

■ All Co-Investigators listed on the protocol.

☐ Yale Cancer Center Data and Safety Monitoring Committee (DSMC)

☐ National Institutes of Health

☐ Food and Drug Administration (Physician-Sponsored IND #_____)

☐ Medical Research Foundation (Grant _)

■ Study Sponsor

■ Other Data Safety Monitoring Board (DSMB) or Committee (DSMC)

An independent DSMC has been established to oversight the study. The members of the DSMC are as follow:

Rachel Lampert, MD
Professor of Medicine, Yale University

Lynda Rosenfeld, MD
Professor of Medicine, Yale University

Charles Love, MD
Professor of Medicine, New York University

The committee will meet within the 1st week after the study initiation to establish a reviewing plan and a standard operating procedure for what the rules are for stopping the study and how adverse events will be reviewed. In addition, the committee will meet as frequent as needed to review any emerging safety issues and adverse events and finally at the time of study closure. Minutes will be maintained.

The data monitoring committee will review all the data after half the subjects in the study are enrolled according to the stopping and continuance rules established by the Committee.

The committee recommendations will be communicated to other sites on a regular basis. The central PI, Dr. Jude Clancy will create a secured Yale Box for data and document transfer. A copy of the committee members' CV and qualifications will be kept in the master file.

The principal investigator (*Dr. Jude Clancy*) will conduct a review of all adverse events upon completion of every study subject. The principal investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

d. For multi-site studies for which the Yale PI serves as the lead investigator:
   i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed?
      - **Any perioperative and post-24hr clinical complications the PI at each center feels is directly related to deployment of the Bridge occlusion balloon must be reported to the PI, the local site IRB and Yale HIC.**
      - **The PI will evaluate any unanticipated problems, will submit it to the HIC immediately.**
      - **Any adverse events or complications will be communicated to the co investigators through the weekly emails.**

The anticipated risks:

- Sudden drop in arterial blood pressure.
- Venous stasis that can induce arrhythmias and/or cardiac arrest.
- Cerebral venous hypertension.
- Temporary facial edema or facial cyanosis (bluish discoloration of the face).

- Groin hematoma or bleeding.
- Thrombus within SVC.

There is a section in the data collection form to document any other unknown adverse events.

ii. What provisions are in place for management of interim results?

- **The PI and investigators will review the data quarterly for safety issues. No statistical claims are being made with the data being collected, and there is no minimum**

•

- **sample size required.**

iii. What will the multi-site process be for protocol modifications?

- **The PI will request any protocol modifications to be applied to all sites. Protocol amendment will be requested with the need of local IRB acknowledgements to be collected from all sites.**
- **All the IRB related documentations are kept in the master regulatory binder in the research office. Copies of the PIs curriculum vitae and qualifications are kept in the regulatory binder.**
- **All sites are required to send their IRB approvals to the central site.**

12. **Statistical Considerations:** Describe the statistical analyses that support the study design.

A sample size of 3-5 patients per site was selected to allow for a sufficient physician experience to generate an ease of use and efficacy of occlusion determination (target 25 total)
No statistical claims are being made with the data being collected, there is no minimum sample size required.

SECTION VI: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, state N/A and delete the rest of the section.

A. DRUGS, BIOLOGICS and RADIOTRACERS N/A

B. DEVICES

1. Are there any investigational devices used or investigational procedures performed at Yale-New Haven Hospital (YNHH) (e.g., in the YNHH Operating Room or YNHH Heart and Vascular Center)? ☐Yes ☒No *If Yes, please be aware of the following requirements*:

a. A YNHH New Product/Trial Request Form must be completed via EPIC: **Pull down the Tools tab in the EPIC Banner, Click on Lawson, Click on "Add new" under the New Technology Request Summary and fill out the forms requested including the "Initial**

Request Form," "Clinical Evidence Summary, " and attach any other pertinent documents. Then select "save and submit" to submit your request; and

b. Your request must be reviewed and approved **in writing** by the appropriate YNHH committee before patients/subjects may be scheduled to receive the investigational device or investigational procedure.

2. What is the name of the device to be studied in this protocol?

Bridge Occlusion Balloon Catheter.

Has this device been FDA approved? ☒ Yes ☐ No
If yes, state for what indication.

Bridge Occlusion Balloon received FDA 510(k) clearance on 02/05/2016 for temporary vessel occlusion in cardiac lead extraction procedures (K153530).

Indication: The Bridge Occlusion Balloon catheter is indicated for use for temporary vessel occlusion of the superior vena cava in applications including perioperative occlusion and emergency control of hemorrhage.
Any use for procedures other than those indicated in these instructions is not recommended.

Background Information: Provide a description of previous human use, known risks, and any other factors that might influence risks. If this is the first time this device is being used in humans, include relevant data on animal models.

Five animal studies comprise the pre-clinical data sources. The study IDs are NGX017 (Intravascular Tear Model), NGX021 (Efficacy of Occlusion Balloon Shape), NGX023 (Safety of Occlusion Balloon Deployment), NGX027 (Efficacy of Bridge Occlusion Balloon), and NGX028 (Safety of Bridge Occlusion Balloon).

Results Summary:

Five pre-clinical animal studies were conducted at American Preclinical Services (APS), located in Minneapolis, MN, USA. Three of the animal studies were used to develop the clinical model, and to assess device design and safety. Two of the animal studies were conducted in accordance with FDA GLP regulations to assess the efficacy and safety of the final device design.
All studies were conducted in the porcine animal model due to the anatomical and physiological similarities to the human cardiovascular system. Study results demonstrated that the Bridge Occlusion Balloon significantly reduced blood loss when deployed at the site of a SVC tear, which allowed all animals to be kept in a clinically stable condition for the full

duration of every procedure. Deployment of the Bridge Occlusion Balloon did not produce any clinically significant histological findings or neurological or physical deficiencies. Taken together, these results suggest that the Bridge Occlusion balloon is safe and effective for temporary occlusion of the SVC.

The Bridge occlusion balloon is designed based on human SVC (superior vena cava) measurements to inflate and cover the entire SVC with a single device with a balloon working length of 80mm.

Clamping a patent unobstructed SVC can have adverse hemodynamic consequences such as a sudden drop in mean arterial blood pressure and venous stasis that can induce arrhythmias and/or cardiac arrest. Additional consequences may be cerebral venous hypertension, decrease in cerebral perfusion, and alteration of cerebral arteriovenous gradient leading to brain damage[1, 2, and 3] While there is limited evidence for temporary balloon occlusion during an SVC tear, the efficacy of temporary venous occlusion to minimize or stop blood flow during a cardiac surgical repair, reconstruction, or a minimally invasive procedural treatment with little to no neurological impairment or cerebral damage has been studied in the literature. Although there is a risk to occluding the SVC, the studies described herein demonstrate that such procedures can be done safely. [4]

Snaring of the caval veins to occlude flow prior to right atrial incision during tricuspid valve surgery is associated with a risk of sudden injury and untreatable bleeding. As an alternative, Foley and Fogarty balloon catheters [5, 6] and Swan-Ganz [7] catheters have been described in the use of temporary SVC occlusion. The utility of Swan-Ganz catheter with SVC clamping was described in 7 patients undergoing thoracic surgical SVC reconstruction or replacement with SVC bypass. This system allowed hemodynamic stability with no overall change in blood pressure, heart rate, and oxygen saturation values. In one patient, facial edema and cyanosis was observed during SVC clamping, although this rapidly resolved following SVC reconstruction. Clinical postoperative neurological examination after extubation revealed no neurological impairment or deficit in any patient. One patient presented with severe agitation during awakening and required additional sedation and extubation time. There was no 90 day postoperative mortality. The mean SVC occlusion time was 24±3 minutes in this study.

Other uses for occlusion balloon in the SVC have been described during minimally invasive surgical procedure for removal of migrated foreign bodies. Lu et al. [8] reported placement of a balloon catheter in the internal jugular vein and SVC to keep a foreign body from embolizing to the heart or pulmonary arteries during surgical removal. The entire procedure took 30 minutes, including 15 minutes for balloon inflation. The patient made an uneventful postoperative recovery and was discharged at day 5 post-procedure with no evidence of complication.

Finally, it is also pertinent to recognize the presence of ***collateral routes*** of the SVC in humans for maintenance of venous drainage in the event of SVC occlusion [9, 10]. The azygos-hemiazygos pathway is the predominant system and includes the azygos (that drains directly into the SVC), hemiazygos, intercostal, and lumbar veins. Accidental ligation of the SVC

during pneumonectomy has been reported to be tolerated for a few hours before being noticed and repaired [(11)].

Given the Bridge device is a temporary occlusion balloon for deployment within the SVC, it can be safely inflated for up to 30 minutes. Other collateral pathways are the internal thoracic, vertebral, and lateral thoracic venous systems. The internal thoracic venous system drains into the inferior vena cava from the internal thoracic vein through the superior epigastric vein, inferior epigastric vein, external iliac vein, and common iliac vein. The vertebral venous system drains blood from the sinus venous and bilateral brachiocephalic veins into the intercostal vein, lumbar vein, and sacral vein into the inferior vena cava.
The lateral thoracic venous system is the superficial collateral circulatory system where blood from the subclavian and axillary vein reaches the lateral thoracic vein and drains into the femoral vein. Since the collateral pathways maintain flow in the presence of an SVC obstruction, a temporary occlusion to the SVC, as demonstrated above, appears to be safe and achievable within a limited timeframe and is critical in the event of an SVC tear for maintenance of hemostasis and patient stabilization.

The literature summarized here supports the conclusion that the SVC can be occluded for 30 minutes without negatively affecting physiologic or neurologic states and therefore should be considered a safe procedure for timely rescue of the patient.

1 Gonzalez-Fajardo JA, Garcia-Yuste M, Florez S, Ramos G, Alvarez T, et al. Hemodynamic and cerebral repercussions arising from surgical interruption of the superior vena cava. Experimental model. J Thorac Cardiovasc Surg 1994;107: 1044-1049

2 Galatoudis Z, Soumpasis I, Vretzakis G. Anesthetic considerations for surgery involving clamping of superior vena cava. Greek E-Journal Perioper Med 2005;3:49-59

3 Leo F, Della Grazia L, Tullii M, Gasparri R, Borri A, Venturino M, Spaggiari L. Hemodynamic instability during superior vena cava cross-clamping: predictors, management, and clinical consequences. J Thorac Cardiovasc Surg 2007;133:1105–1106

4 Ishiguchi T, Nishikimi N, Usui A, Ishigaki T. Endovascular stent-graft deployment: temporary vena caval occlusion with balloons to control aortic blood flow-experimental canine study and initial clinical experience. Radiology. 2000 May;215(2):594-9.

5 Sansone F, del Ponte S, Zingarelli E, Casabona R. Internal snaring of the caval veins by Foley catheters in case of reoperation via right thoracotomy. Interact Cardiovasc Thorac Surg. 2011 Oct;13(4):370-2.

6 Capestro F, Matteucci S, Rescigno G, Torracca L. A simplified technique for caval occlusion in reoperative small thoracotomies. J Thorac Cardiovasc Surg. 2011 Aug;142(2):460-2.

7 Perentes JY, Erling CC, Ris HB, Corpataux JM, Magnusson L. A simple bypass technique for superior vena cava reconstruction. Interact Cardiovasc Thorac Surg. 2011 Jan;12(1):15-9.

8 Lu G, Bao J, Pei Y, Jing Z. Temporary balloon occlusion of both the superior vena cava and the internal jugular vein to achieve removal of a migrated foreign body. Ann Vasc Surg 2009;23:687.e9-13.

9 McIntire FT, Sykes EM Jr. Obstruction of the superior vena cava; a review of the literature and report of two personal cases. Ann Intern Med. 1949 May;30(5):925-60.

[10] Dahan H, Arrivé L, Monnier-Cholley L, Le Hir P, Zins M, Tubiana JM. Cavoportal collateral pathways in vena cava obstruction: imaging features. Am J Roentgenol. 1998 Nov;171(5):1405-11.

[11] Ohri SK, Lawrence DR, Townsend ER. Homograft as a conduit for superior vena cava syndrome. Ann Thorac Surg 1997; 64: 531-533

3. **Source:**
   a) Identify the source of the device to be used.
   Bridge Occlusion Balloon.

   b) Is the device provided free of charge to subjects? ☒ Yes ☐ No

4. What is the PI's assessment of risk level (significant or non-significant) associated with the use of the device?

☐ **Significant Risk (SR) Device Study:** A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Significant Risk Devices require an Investigational Device Exemption (IDE) issued by the FDA.

What is the **IDE number** assigned by the FDA?

Did the FDA approve this IDE as **Category A** (experimental/investigational) or as **Category B** (non-experimental/investigational)?

Who holds the IDE?

☒ **Non-Significant Risk (NSR) Device Study:** A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants. Note that if the HIC concurs with this determination, an IDE is not required.

5. **Abbreviated IDE or Exempt IDE:** There are abbreviated requirements for an IDE and there also are exemptions to the requirement for an IDE. *See the criteria in the HIC Application Instructions,* Section VI.B.4 at http://www.yale.edu/hrpp/resources/docs/100FR1aHICProtocol_Application_Instructions5-25-11.pdf *to determine if these pertain to this study.*

☒ **Abbreviated IDE or Exempt IDE** – *If criteria set forth in the HIC Application Instructions are met, copy and paste the completed relevant section from the Instructions into this application.*
b.) Does the device fulfill one of the IDE exemption categories (21 CFR 812.2(c))?

• The device, other than a transitional device, was introduced into commercial distribution on or after May 28, 1976, the FDA determined the device to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and the device will be used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

_X Yes___No

6. Investigational device accountability:

State how the PI, or named designee, ensures that an investigational device is used only in accordance with the research protocol approved by the HIC, and maintains control of the investigational device as follows:

The PI and research staff will receive training regarding the device prior to the start of the study. Training will include protocol specific handling of the device.

Maintains appropriate records, including receipt of shipment, inventory at the site, dispensation or use by each participant, and final disposition and/or the return of the investigational device (or other disposal if applicable):

Receipt of device shipment, inventory at the site, device dispensation/participant use, and return of the investigational device will be documented and maintained by research staff in the on-site study binder/files.

Documents pertinent information assigned to the investigational device (e.g., date, quantity, batch or serial number, expiration date if applicable, and unique code number):

The Principal Investigator or an authorized designee shall keep records documenting the receipt, storage, use, return and disposal of the investigational devices/equipment, which shall include the following:

• Date of receipt
• Identification of each investigational device/piece of equipment (batch number or unique code)
• Expiration date, as applicable
• Date of use
• Subject identification
• Date on which the investigational device/piece of equipment was returned, if applicable
• Date of return of unused

Study spreadsheets documenting site inventory and device dispensation will be maintained and updated with each new participant/procedure. These files will be kept on a server that is back up daily.

Stores the investigational device according to the manufacturer's recommendations with respect to temperature, humidity, lighting, and other environmental considerations:

The devices will be kept in the EP lab under environmental conditions that are prescribed by the sponsor.

Ensures that the device is stored in a secure area with limited access in accordance with applicable regulatory requirements:

The Bridge Balloon will be stored in the Operative Room at YNHH. It will be stored in a locked cabinet. Access to this cabinet will only be available to PI and the investigators.

Distributes the investigational device to subjects enrolled in the IRB-approved protocol:

The devices will be distributed to the PI prior to the extraction procedure. The enrollment status will also be confirmed as the participants enrollment will be highlighted on EPIC.

SECTION VII: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. **Targeted Enrollment: Give the number of subjects:**
   a. targeted for enrollment at Yale for this protocol_5___
   b. If this is a multi-site study, give the total number of subjects targeted across all sites_25_ (8 sites including Yale)

2. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

☐ Flyers	☐ Internet/Web Postings	☐ Radio
☐ Posters	Mass E-mail Solicitation	Telephone
☐ Letter	☐ Departmental/Center Website	☐ Television
☒ Medical Record Review	Departmental/Center Research Boards	Newspaper
☐ Departmental/Center Newsletters	Web-Based Clinical Trial Registries	
☐ YCCI Recruitment database	☐ Clinicaltrials.gov Registry (do not send materials to HIC)	

☒ Other (describe): **Patients who are already scheduled for elective lead extraction.**

3. **Recruitment Procedures:**
   a. Describe how potential subjects will be identified.

The patients will be identified through the clinic evaluation and the EP schedule. Patients who are eligible or scheduled for Lead Extraction will be approached to participate in the study. The investigators will review the patients' charts and they will determine eligible patients based on inclusion and exclusion criteria.

   b. Describe how potential subjects are contacted.

The patients will be approached by the study team in the clinic or before the procedure to explain the study and to answer any questions.

   c. Who is recruiting potential subjects?

All the investigators will be involved in recruiting potential subjects

4. **Screening Procedures**
   a. Will email or telephone correspondence be used to screen potential subjects for eligibility prior to the potential subject coming to the research office? ☐ Yes ☒ No
   b. If yes, identify below all health information to be collected as part of screening and check off any of the following HIPAA identifiers to be collected and retained by the research team during this screening process.

HEALTH INFORMATION TO BE COLLECTED:

HIPAA identifiers:

☐ Names

☐ All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

☐ Telephone numbers

☐ Fax numbers

☐ E-mail addresses

☐ Social Security numbers

☐ Medical record numbers

☐ Health plan beneficiary numbers

☐ Account numbers

☐ All elements of dates (except year) for dates related to an individual, including: birth date, admission date, discharge date, date of death, all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

☐ Certificate/license numbers

☐ Vehicle identifiers and serial numbers, including license plate numbers

☐ Device identifiers and serial numbers

☐ Web Universal Resource Locators (URLs)

☐ Internet Protocol (IP) address numbers

☐ Biometric identifiers, including finger and voice prints

☐ Full face photographic images and any comparable images

☐ Any other unique identifying numbers, characteristics, or codes

5. **Assessment of Current Health Provider Relationship for HIPAA Consideration:**

   Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

   ☒ Yes, all subjects

   ☐ Yes, some of the subjects

   ☐ No

   If yes, describe the nature of this relationship.

   All the patients at YNHH will be under the care of Dr. Clancy in the clinic or electrophysiology service.

6. **Request for waiver of HIPAA authorization:** (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

   Choose one:

☐ For entire study
☒ For recruitment purposes only
☐ For inclusion of non-English speaking subject if short form is being used

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data;

Review of records is required to determine who would be eligible for the study.

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data; **N/A**

By signing this protocol application, the investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

7. **Required HIPAA Authorization:** If the research involves the creation, use or disclosure of protected health information (PHI), separate subject authorization is required under the HIPAA Privacy Rule. Indicate which of the following forms are being provided:
   ☒ Compound Consent and Authorization form
   ☐ HIPAA Research Authorization Form

8. **Consent Personnel:** List the names of all members of the research team who will be obtaining consent/assent.

   Jude Clancy, MD, Ryan Donovan, PA-C, Medhat Abdelmessih, MD

9. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   The patient will be approached by the study team to explain the study, and to answer any questions. If the patient is in agreement, will sign the consent form and then will be enrolled in the study.

10. E**valuation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

The investigator will evaluate the subject's capacity to consent base on the communication with the subject, his/her age (adult), no history of significant psychiatric illnesses.

11. Documentation of Consent/Assent: Specify the documents that will be used during the consent/assent process. Copies of all documents should be appended to the protocol, in the same format that they will be given to subjects.

The patient will sign a consent form, will be given a copy of the signed consent form. A consent process note will be signed by the consenting personnel and the PI.

12. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.

12(a) As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment?
YES ☐ NO ☒

Non- English speaking individual will not be considered for the study.

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are found on our website at: http://www.yale.edu/hrpp/forms-templates/biomedical.html. If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via amendment prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

13. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐ **Not Requesting a consent waiver**
☐ **Requesting a waiver of signed consent**
☒ **Requesting a full waiver of consent**

A. Waiver of **signed** consent: (Verbal consent from subjects will be obtained. **If PHI is collected, information in this section must match Section VII, Question 6**)

☐ **Requesting a waiver of signed consent for Recruitment/Screening only**

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research?
☐ Yes ☐ No

b. Does a breach of confidentiality constitute the principal risk to subjects?
☐ Yes ☐ No

OR

c. Does the research activity pose greater than minimal risk?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity
☐ No

AND

d. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☐ No

☐ **Requesting a waiver of signed consent for the Entire Study (**Note that an information sheet may be required.)

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research?
☐ Yes ☐ No

b. Does a breach of confidentiality constitute the principal risk to subjects?
☐ Yes ☐ No

OR

c. Does the research pose greater than minimal risk? ☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** ☐ No

AND

d. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☐ No

B. Full waiver of consent: (No consent from subjects will be obtained for the activity.)

☒ **Requesting a waiver of consent for Recruitment/Screening only**

a. Does the research activity pose greater than minimal risk to subjects?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity
☒ No

b. Will the waiver adversely affect subjects' rights and welfare? ☐ Yes ☒ No
c. Why would the research be impracticable to conduct without the waiver?

Review of records is required to determine who would be eligible for the study.

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

The results from the study sites will be generated as a single manuscript to be published in the Heart Rhythm Journal.

☐ **Requesting a full waiver of consent for the <u>Entire Study</u> (Note: If PHI is collected, information here must match Section VII, question 6.)**

If requesting a full waiver of consent, please address the following:

a. Does the research pose greater than minimal risk to subjects?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.***
☐ No
b. Will the waiver adversely affect subjects' rights and welfare? ☐ Yes ☐ No
c. Why would the research be impracticable to conduct without the waiver?
d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

SECTION VIII: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

a. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

For each patient, the investigators will obtain the following baseline information: demographics information (age, sex, MRN, address, emergent contact, referring physician), medical history, Extraction procedure's information and post-operative follow up information to determine the occurrence of any adverse events.

b. How will the research data be collected, recorded and stored?

All data will be collected and stored using encrypted digital forms

c. How will the digital data be stored? ☐ CD ☐ DVD ☒ Flash Drive ☐ Portable Hard Drive ☒ Secured Server ☒ Laptop Computer ☒ Desktop Computer ☐ Other

d. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

1. **Data on the excel spreadsheet will be stored in a in an encrypted format, password protected, on an encrypted Yale University computer/laptop connected to a secure server.**

2. **If there be any reason to transfer data from one location to another, an encrypted data stick (iron key) issued by the Yale IT department, will be used. This will ensure data in encrypted format and not readable to others in the event it does fall into the wrong hands.**

3. **The research data will be coded; all data used in the analysis and reporting of this study will be without identifiable reference to specific subject name.**

Do all portable devices contain encryption software? ☒ Yes ☐ No
If no, see http://hipaa.yale.edu/guidance/policy.html

e. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

The data will be secured in the department data base using secured encrypted computers on secured servers.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), SSC, etc.)? (please distinguish between PHI and de-identified data)

Only the investigators and research staff.

g. If appropriate, has a Certificate of Confidentiality been obtained? **N/A**

h. Are any of the study procedures likely to yield information subject to mandatory reporting requirements? (e.g. HIV testing – reporting of communicable diseases; parent interview -incidents of child abuse, elderly abuse, etc.). Please verify to whom such instances will need to be reported.

NO

SECTION IX: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

There is no direct benefit for the subjects in this study. Also in the unlikely event the patient has an SVC tear the balloon is FDA approved and would be used in the emergent management of SVC tear.

The study will focus on the effect of the Bridge balloon on the patient preparation clinical workflow, ease of insertion/positioning/deployment, and the ability to recognize proper inflation and vein sealing under fluoroscopy.

Understanding these factors will help build a more robust clinical workflow with the goal of better patient outcomes in the case of an SVC injury. The images and data generated during this study can help in dissemination of the practical use knowledge to fellow lead extractors.

SECTION X: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?

   Outside of this research, there is no utility of the balloon unless there is an SVC tear as a complication of the lead extraction procedure.

2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   No compensation will be provided.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   All the procedures are standard of care and routinely used during the lead extraction procedures except the use of balloon which is the research part of this study. The device itself will be provided at no cost.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk.
   a. Will medical treatment be available if research-related injury occurs? **YES**
   b. Where and from whom may treatment be obtained?

   Treatment will be obtained from the study doctor, Dr. Jude Clancy at Yale-New Haven Hospital
   c. Are there any limits to the treatment being provided? **NO**
   d. Who will pay for this treatment?

   If patients are injured while on study, they should seek treatment and contact the study doctor as soon as possible. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If patient is injured as a result of their participation in this study, treatment will be provided. The patient or their insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. Patients do not give up any of your legal rights by signing this form.

e. How will the medical treatment be accessed by subjects?

In the event of research related injury; subjects should contact Dr. Jude Clancy or any member of the research team.