RADIAL ACCESS FOR NAVIGATION TO YOUR CHOSEN LESION FOR PERIPHERAL VASCULAR INTERVENTION: (REACH PVI)

[redacted]

[redacted]

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NCT 03943160

SPONSOR:

Cardiovascular Systems, Inc.
1225 Old Highway 8 NW
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1.0 Protocol Summary

Title:	Radial accEss for nAvigation to your CHosen lesion for Peripheral Vascular Intervention: REACH PVI
Study Design:	Prospective, observational, single-arm, multi-center post-market clinical study.
Study Purpose:	The purpose of this study is to prospectively evaluate acute clinical outcomes of orbital atherectomy (OA) via transradial access (TRA) for treatment of peripheral artery disease (PAD) in lower extremity lesions.
Devices:	This clinical study is designed to collect prospective clinical data on the use of CSI devices cleared for commercial use by the United States Food and Drug Administration (FDA), for the treatment of peripheral artery disease. There will be no investigational devices allowed in this study. Cardiovascular Systems Inc. (CSI) devices may include: • CSI Diamondback 360® Peripheral Orbital Atherectomy System • CSI Stealth 360® Peripheral Orbital Atherectomy System • [redacted]
Study Population:	All patients undergoing peripheral vascular intervention (PVI) via transradial access (TRA) and for whom TRA has been successfully achieved and peripheral lesion deemed appropriate for treatment via TRA per physician discretion.
Number of Sites:	Up to ten (10) active sites in the United States (U.S.).
Number of Subjects:	Approximately 50 subjects.
Primary Objective:	The objective of this study is to evaluate acute clinical results of orbital atherectomy (OA) via radial artery access, including complication rates and cost effectiveness.
Outcome Measures:	Acute procedure data and device-related data.
Primary Outcome and Secondary Outcome:	The primary and secondary outcomes will be assessed for all enrolled subjects. **Primary Outcome:** Procedural Success: Successful completion of OA (orbital atherectomy) treatment of target lesion via transradial access without serious transradial access related events. **Secondary Outcome:** Treatment Success: Treatment success is defined as <50% residual stenosis post-procedure and without significant angiographic complications without stent placement, or <30% residual stenosis post-procedure and without angiographic complications with stent placement.

[redacted]	[redacted]
Follow-Up Visits:	All subjects will be followed post-procedure through the first standard of care follow-up visit (7-45 days post-procedure).
Duration:	This study is expected to enroll for approximately 6-12 months. Subjects will be followed through their first standard of care visit.
[redacted]	[redacted]
Sponsor Contact Information:	Cardiovascular Systems, Inc. (CSI) Clinical Affairs Department – REACH PVI Clinical Study 1225 Old Highway 8 NW Saint Paul, MN 55112 United States 651-259-1600
National Primary Investigator (NPI) Contact Information:	Ankur Lodha, MD Cardiovascular Institute of the South [redacted]

2.0 Abbreviations & Definitions

2.1 Abbreviations

Abbreviation	Term
AE	Adverse Event
BA	Balloon Angioplasty
BARC	Bleeding Academic Research Consortium
CABG	Coronary Artery Bypass Grafting
CFR	Code of Federal Regulations
CLI	Critical Limb Ischemia
CMP	Clinical Monitoring Plan
CSI	Cardiovascular Systems, Inc.
DS	Diameter Stenosis
DUS	Duplex Ultrasound
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IFU	Instructions for Use
IRB	Institutional Review Board
MDR	Medical Device Reporting
OA	Orbital Atherectomy
OAS	Orbital Atherectomy System
PAD	Peripheral Artery Disease
PCI	Percutaneous Coronary Interventions
PI	Principal Investigator
PVI	Peripheral Vascular Intervention
QVA	Quantitative Vascular Angiography
RMA	Returned Materials Authorization
RVD	Reference Vessel Diameter
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	Standard of Care

SFA	Superficial Femoral Artery
TFA	Transfemoral access
TRA	Transradial Access
TIA	Transient Ischemic Attack
TLR	Target Lesion Revascularization
TVR	Target Vessel Revascularization
US	United States

2.2 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational medical device.
Bleeding (Bleeding Academic Research Consortium, BARC)	Type 0: No Bleeding Type 1: Bleeding that is not actionable and does not cause the patient to seek treatment Type 2: Any clinically overt sign of hemorrhage that "is actionable" and requires diagnostic studies, hospitalization, or treatment by a health care professional Type 3: a. Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL (provided hemoglobin drop is related to bleed); transfusion with overt bleeding b. Overt bleeding plus hemoglobin drop of < 5 g/dL (provided hemoglobin drop is related to bleed); cardiac tamponade; bleeding requiring surgical intervention for control; bleeding requiring IV vasoactive agents c. Intracranial hemorrhage confirmed by autopsy, imaging, or lumbar puncture; intraocular bleed comprising vision Type 4: CABG-related bleeding within 48 hours Type 5: a. Probably fatal bleeding b. Definite fatal bleeding (overt or autopsy or imaging confirmation)
Dissection Classification	Type 0: None Type A: Small radiolucent area within lumen of the vessel Type B: Linear, non-persisting extravasation of contrast Type C: Extraluminal, persisting extravasation of contrast Type D: Spiral shaped filling defect Type E: Persistent lumen defect with delayed ante/retrograde flow Type F: Filling defect accompanied by total arterial occlusion *Note: Type A,B and C are generally considered benign and minor dissections.*
Investigator	Any physician designated and supervised by the Principal Investigator who is participating on the study at the site.
Percent Diameter Stenosis (% DS)	The percent stenosis at minimum lumen diameter as reported using quantitative vascular angiography (QVA) or visual estimation.
Reference Vessel Diameter (RVD)	Defined as the average of normal segments within 10 mm proximal and 10 mm distal to the target lesion from two orthogonal views using QVA or visual estimation.
Rutherford Classification	**Class 0**: Asymptomatic; no hemodynamically significant occlusive disease. **Class 1**: Mild Claudication; there is no limitation with ordinary physical activities (e.g., walking several blocks, climbing stairs). Limiting symptoms may occur with marked exertion (e.g., strenuous, rapid or prolonged exertion at work or recreation). **Class 2**: Moderate Claudication; there is a slight limitation of ordinary physical activities (e.g., walking uphill, or more than two level blocks, or climbing stairs

Term	Definition
	rapidly). Patient is comfortable at rest. **Class 3**: Severe Claudication; there is marked limitation of ordinary physical activities (e.g., walking 1-2 level blocks or climbing one flight of stairs). Patient is comfortable at rest. **Class 4**: Ischemic rest pain. **Class 5**: Minor tissue loss, non-healing ulcer, focal gangrene with diffuse pedal ischemia. **Class 6**: Major tissue loss extending above transmetatarsal level; functional foot no longer salvageable.
Serious Adverse Event (SAE) (ISO 14155 definition)	a) Led to a death, injury or permanent impairment to a body structure or a body function. b) Led to a serious deterioration in health or the subject, that either resulted in: • a life-threatening illness or injury, or • a permanent impairment of a body structure or a body function, or • in-patient hospitalization or prolongation of existing hospitalization, or • medical or surgical intervention to prevent life threatening illness. c) Led to foetal distress, foetal death or a congenital abnormality or birth defect.
Procedural Success (per subject)	Procedural success is defined as successful completion of OA (orbital atherectomy) treatment of target lesion via transradial access without serious transradial access related events.
Significant Angiographic Complications	▪ Dissections (D-F) ▪ Perforations ▪ Serious slow flow/no reflow ▪ Serious acute vessel closure ▪ Serious distal embolization ▪ Serious thrombus formation
Target Area	Peripheral arterial anatomy extending from the common femoral artery to the ankle (distal boundary largely dependent on patient height)
Target Lesion	Stenotic segment appropriate (e.g., location/morphology) for treatment with the Orbital Atherectomy System study device(s) via transradial access. The target lesion will be: • The first lesion with Orbital Atherectomy attempted OR • The first lesion with Orbital Atherectomy attempted after other successful peripheral intervention(s) without the occurrence of a reportable adverse event. This study will be limited to one (1) target lesion per enrolled subject.
Target Lesion Revascularization (TLR)	A repeat procedure occurring after the index procedure which includes all or part of a target lesion treated during the index procedure.
Target Vessel Revascularization TVR)	A repeat procedure occurring after the index procedure which includes all or part of a target vessel treated during the index procedure.
Target Vessel	The entire vessel in which the target lesion is located.

Term	Definition
Treatment Success (per target lesion)	Treatment success is defined as <50% residual stenosis post-procedure and without significant angiographic complications without stent placement, or <30% residual stenosis post-procedure and without significant angiographic complications with stent placement.

3.0 Introduction

Historically, endovascular treatment of coronary and peripheral artery disease has been performed via transfemoral access (TFA).[1,2] In the past decade, however, access through the radial artery has emerged as a valid alternative approach for percutaneous coronary interventions (PCI) and has significantly decreased the rate of access site bleeding, major vascular complications, and mortality in patients undergoing PCI.[3,4] Transradial access (TRA) leads to shorter post-procedural monitoring, earlier ambulation, reduced length of hospital stay and less discomfort compared to TFA.[5]

Recent data suggest that TRA may be a safe treatment approach for selected peripheral lesions above-the-knee, especially in patients who are not suitable for TFA, including obese patients, patients with heavily calcified femoral arteries, history of femoral surgery, or in the absence of palpable femoral pulses.[6,7] The first report on transradial peripheral intervention was published in 2005 and it was a case of a common iliac artery stenting.[8] In the next year, the first report of bilateral iliac artery stenting via TRA performed in the same procedure was published. This is one of the many advantages of TRA, the possibility of the treatment of bilateral lesions in the same procedure without a second access site.[9] Since then, dozens of case reports, feasibility- and single-center studies have been published with high procedural success rates, low rates of access-site and bleeding complications, better patient comfort, and simplified post-procedure care. Studies have shown an increase radiation exposure and longer procedure time compared to TFA.[10–12]. Complications related to TRA are uncommon.[13,14] Radial artery occlusion is the most significant complication, occurring in 2% to 16% of patients.[12,13,15–17] Other complications include spasm, pseudoaneurysm, nerve damage, perforation, and hematoma.[5,14,18] Femoral crossover (1.9%) is another TRA-related incidence and causes include vessel spasm/small vessel diameter, radial loops, proximal occlusion, and catheter length limitations.[19]

Retrospective studies that compared the TRA and TFA in peripheral interventions also demonstrate a comparable safety profile between the two approaches.[10–12,20,21] In a study of 68 subjects with claudication and critical limb ischemia (CLI) who underwent aorto-iliac interventions, there were no minor access-site complications in the TRA group, but 7.3% of the patients had such complications in the TFA group.[10] Furthermore, the time to discharge was significantly shorter for the TRA group compared to the TFA group (14.4 hours vs. 20.9 hours). In their small feasibility study, Cortese et al. reported a 6% major bleeding complication rate for the TFA group compared to 0% in the TRA group.[21] Finally, in a single center study of 188 patients with claudication or CLI who underwent aorto-iliac or femoropopliteal interventions, access site complications occurred in 6% of the TFA patients vs. 3.7% of the TRA patients.[11]

The main barrier to the adoption of TRA is the lack of dedicated equipment with adequate length and small enough outer diameter.[18,22] Shaft length of balloons and stents needs to be at least 170-180 cm in order to be used for femoropopliteal interventions. Atherectomy devices are limited by both shaft length and outer diameter. The only atherectomy devices that could be used from TRA are the Diamondback 360 Peripheral Orbital Atherectomy System (OAS)[15,18,22,23] and the Stealth 360 Peripheral Orbital Atherectomy System (OAS). This device is the only 6 Fr compatible (4 Fr and 5 Fr with the Micro- and Solid Crowns) atherectomy catheter with shaft lengths of 145 cm - up to 200 cm (longer lengths available for select Solid Crowns).

There are only two case studies that report on OAS use via TRA in the lower extremities. The first study is a case of transradial intervention of severe common femoral artery stenosis with OAS.[24] The intervention was successful, the patient was discharged home four hours after the procedure, and after a month his symptoms disappeared (Rutherford class 0). In the second study, Hanna and colleagues treated 6 patients

with superficial femoral artery (SFA) disease with OAS and adjunctive balloon angioplasty (BA) via TRA.[23] They concluded that for simple SFA disease stand-alone transradial recanalization is feasible and may be performed with high success rate.

The objective of this study is to evaluate acute clinical results of orbital atherectomy (OA) via radial artery access including complication rates and cost effectiveness.

4.0 Risks and Benefits

4.1 Risks

All devices that will be used in this study have been cleared or approved by FDA. Clinical risks to subjects enrolled in this study are the same risks encountered if treated outside of the study. The choice of treatment for enrolled subjects will be determined by the Investigator. The Investigator should refer to the manufacturer's Instructions for Use (IFU) for each technology used in the study for specific device related risks, contraindications, restrictions, warnings and precautions.

Since this study will enroll subjects who otherwise would be indicated for treatment, the pre-procedure preparation and follow-up care will be the same and do not present different risks from those not participating in the study. Subjects may undergo additional tests per the Investigator's discretion if he/she desires to monitor the subject's disease state more closely.

4.2 Benefits

Subject's participation in this study is voluntary. There is no direct additional benefit to subjects enrolled in the study. However, information gathered from this study may help increase the understanding of the clinical and economic outcomes of transradial access with lower extremity PAD. Ultimately, this knowledge can inform future PAD clinical trials, provide data to help physicians choose the best care for patients, and advance the knowledge of transradial access for treatment of lower extremity PAD.

5.0 Devices Used in Study

This clinical study is designed to evaluate OAS use via TRA. Only endovascular devices cleared or approved for commercial use by the FDA can be used in this study, please refer to the appropriate device-specific IFU. There will be no investigational devices allowed in this study.

Cardiovascular Systems Inc. (CSI) devices designed for use via TRA include:

- CSI Diamondback 360® Peripheral Orbital Atherectomy System
- CSI Stealth 360® Peripheral Orbital Atherectomy System
- [redacted]

6.0 Study Objective

The objective of this study is to evaluate acute clinical results of orbital atherectomy (OA) via radial artery access, including complication rates and cost effectiveness.

7.0 Outcome Measures

The primary and secondary outcomes will be assessed for all enrolled subjects.

7.1 Primary Outcome: Procedural Success

Procedural success is defined as successful completion of OA treatment of the target lesion via transradial access without serious transradial access related events.

7.2 Secondary Outcome: Treatment Success

Treatment success is defined as <50% residual stenosis post-procedure and without significant angiographic complications without stent placement, or <30% residual stenosis post-procedure and without significant angiographic complications with stent placement.

[redacted]

8.0 Sample Size

Approximately 50 subjects treated with OA will be enrolled in this study. As a hypothesis generating study, this study is not powered.

[redacted] Subjects must meet ALL of the inclusion criteria and NONE of the exclusion criteria to be eligible to participate in this study. Subject will be approached and consented for participation in the study prior to the index procedure, during which index inclusion and exclusion criteria will be confirmed. Subjects found to not meet index inclusion criteria or to meet index exclusion criteria will be considered consented screen failures.

9.0 Study Enrollment

9.1 General Inclusion Criteria

1. Subject is ≥ 18 years
2. Subject is willing and able to sign the IRB-approved informed consent form (ICF)
3. Subject presents with a Rutherford Classification of 2 to 5
4. Subject has a positive Allen's Test
5. Subject to undergo peripheral angiography and/or PVI via TRA approach per physician discretion

9.2 Index Procedure Inclusion Criteria

1. Physician obtains successful radial artery access (Note: snuffbox access is allowed)
2. Target lesion appropriate (i.e. location/morphology) for OA treatment via TRA within target area
3. OAS use attempted (defined as ViperWire introduced into the body)

9.3 General Exclusion Criteria

1. Subject has no palpable radial artery on the planned access arm
2. Subject has a previous failed radial access attempt on planned access arm
3. Subject has a dialysis fistula on planned access arm
4. Subject has a known subclavian stenosis or occlusion
5. Subject has a previous subclavian stent or previous subclavian intervention
6. Subject has a shunt in the radial artery on the planned access arm
7. Subject has evidence of osteomyelitis
8. Subject is currently participating in an investigational drug or device study
9. Subject is pregnant within the study period

9.4 Index Procedure Exclusion Criteria

1. Physician unable to obtain radial artery access
2. Physician determines TRA is not acceptable due to patient anatomy, lesion characteristics, and/or disease severity
3. OAS use not attempted (defined as ViperWire introduced into the body)

Prior to insertion of ViperWire:

4. Femoral access is obtained
5. Unsuccessful peripheral intervention
6. A reportable adverse event has occurred

9.5 Treatment of Target Lesion

The target lesion will be:

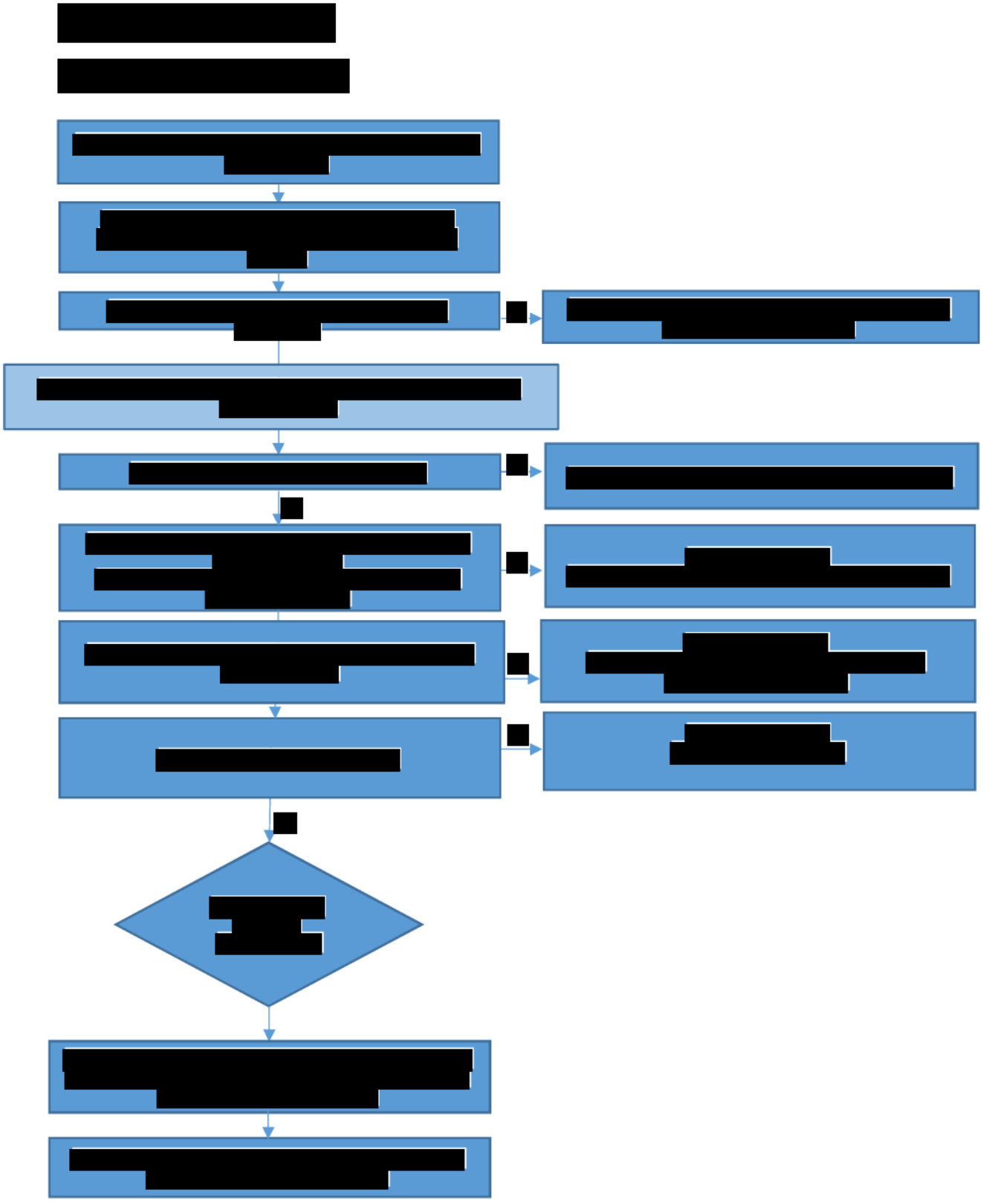
- The first lesion with Orbital Atherectomy attempted OR
- The first lesion with Orbital Atherectomy attempted after other successful peripheral intervention(s) without the occurrence of a reportable adverse event.

[redacted]

9.6 Point of Enrollment

Enrollment is defined as point when a subject has signed an IRB-approved ICF, have met all inclusion criteria and none of the exclusion criteria, and the ViperWire has been inserted into the body.

[redacted]



11.0 Follow-Up Visit

All subjects will be followed post-procedure through the first standard of care follow-up visit (7-45 days post-procedure) only.

[redacted]

[redacted]

13.0 Adverse Event

13.1 Adverse Event Collection

The reporting of adverse events (AEs) will begin immediately after the subject has been enrolled. For the purposes of this study, pre-planned interventions noted at baseline are not considered reportable AEs. The AEs collected in this study will include:

TRA Related Events are defined for the purpose of the data analyses of the study's outcome and include access site complications such as:

- Serious TRA site bleeding (BARC Type 2-5)
- Serious TRA site hematoma
- Serious radial artery spasm
- Serious hand ischemia
- Stroke
- Transient Ischemic Attack (TIA)
- Serious nerve damage
- Perforation
- TRA site pseudoaneurysm

Significant Angiographic Events that occur during the treatment procedure regardless of device relatedness including:

- Dissections (D-F)
- Perforations
- Serious slow flow/no reflow
- Serious acute vessel closure
- Serious distal embolization
- Serious thrombus formation

[redacted]

- [redacted]

13.2 Adverse Event Definitions

Serious Adverse Event (SAE) means:

a) Led to a death, injury or permanent impairment to a body structure or a body function.
b) Led to a serious deterioration in health or the subject, that either resulted in:
    - a life-threatening illness or injury, or
    - a permanent impairment of a body structure or a body function, or
    - in-patient hospitalization or prolongation of existing hospitalization, or
    - medical or surgical intervention to prevent life threatening illness.
c) Led to foetal distress, foetal death or a congenital abnormality or birth defect.

Permanent means irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage.

Medical interventions may include hospitalizations or prolonged hospitalizations due to the use of the interventional devices used in this study.

Device related means related to any CSI device used during index procedure on the target lesion.

Access Site Bleeding: Bleeding Academic Research Consortium, BARC. Access site BARC Type 2 – Type 5 bleeding events that occur during the index procedure through study exit will be collected.

Type 0: No Bleeding

Type 1: Bleeding that is not actionable and does not cause the patient to seek treatment

Type 2: Any clinically overt sign of hemorrhage that "is actionable" and requires diagnostic studies, hospitalization, or treatment by a health care professional

Type 3:
a. Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL (provided hemoglobin drop is related to bleed); transfusion with overt bleeding
b. Overt bleeding plus hemoglobin drop of < 5 g/dL (provided hemoglobin drop is related to bleed); cardiac tamponade; bleeding requiring surgical intervention for control; bleeding requiring IV vasoactive agents
c. Intracranial hemorrhage confirmed by autopsy, imaging, or lumbar puncture; intraocular bleed comprising vision

Type 4: CABG-related bleeding within 48 hours

Type 5:
a. Probably fatal bleeding
b. Definite fatal bleeding (overt or autopsy or imaging confirmation)

13.3 Adverse Event Relatedness

The relatedness of the AE to the treatment device(s) and procedure(s) will be classified by the Investigator and reviewed by the Sponsor. The Investigator will use the following definitions in classifying the relationship of the AE:

- **Device Related:** AE is directly related to any CSI device used in treatment of the lesion.
- **Procedure Related:** AE is directly attributable to the index procedure.

13.4 Adverse Event Reporting

Protocol reportable adverse events must be collected until each subject's completion of or exit of the study. Adverse events must be reported to the Sponsor on the AE electronic case report form (eCRF) as well as the reviewing IRB, if necessary. FDA Medical Device Reporting (MDR) requirements will be followed for this study.

[redacted]

[redacted]

[redacted]

15.0 Protocol Deviations

A protocol deviation is defined as an event where the study is not conducted according to the protocol, FDA regulations 21 CFR Parts 50 and 56, and requirements imposed by the reviewing IRB. Protocol deviations that will be collected include, but are not limited to the following:

- Failure to obtain informed consent
- Enrolling a subject who did not meet inclusion criteria, or met exclusion criteria
- [redacted]

[redacted]

16.0 Site Non-Compliance

As a result of deviation, appropriate corrective actions are to be developed by the study staff and implemented promptly. If excessive protocol deviations are noted, the Sponsor reserves the right to suspend study enrollment until a sufficient system is in place at the site to reduce further deviations, or withdraw the site from participation in the study.

17.0 Study Exit

All subjects will be followed post-procedure through first standard of care follow-up visit (7-45 days post-procedure).

[redacted]

20.0 Study Termination

The Sponsor may terminate this study at any time due to the following reasons, but not limited to: low subject recruitment/enrollment, competing studies and financial reasons. Appropriate notification will be provided to all participating Investigators.

21.0 Data Analysis

Study data will be analyzed as indicated in the Statistical Analysis Plan (SAP).

[redacted]

[redacted]

23.0 Study Responsibilities

23.1 Sponsor Responsibilities

Sponsor responsibilities include but are not limited to:

- Selection of Principal Investigators, study sites, and Core Laboratories, if applicable, who participate in the study;
- Training of participating study sites including the Investigator and staff conducting the study;
- Providing financial support to each study site which is fair, reasonable, and equitable to fair market value;
- Following all applicable regulatory standards per applicable regulations at each study site; and,
- Ownership and control of the use of data, including review and approval of study-related publications/presentations, etc.

23.2 Investigator Responsibilities

The Investigator is responsible for the following:

- Protecting the rights, safety, and welfare of subjects.
- Conducting the investigation in accordance with the Clinical Trial Agreement with the Sponsor, the Protocol, applicable FDA regulations, including 21 CFR Part 50 and 56, and any conditions of approval imposed by the IRB.
- Delegation of study-related tasks to qualified personnel under their supervision as may be applicable; however, the Principal Investigator remains responsible for the proper conduct of the clinical study.
- Ensuring that the Sponsor has received all required documentation, including but not limited to the signed Clinical Trial Agreement and IRB approvals.
- Appropriate procedures are followed to maintain subject confidentiality according to the Health Insurance Portability and Accountability Act (HIPAA) regulations. Each site may have its own internal procedures or requirements for use and release of subject medical information in research studies. Each Investigator is responsible for obtaining appropriate approvals, consents, or releases of medical information as dictated by their site's relevant patient privacy laws.
- The study is not transferable to other sites attended by the Principal Investigator unless prior approval is obtained from the appropriate IRB and the Sponsor.

- All records pertaining to this study will be kept for a minimum of two (2) years following the date on which the study is completed or terminated. If an Investigator wishes to withdraw from the responsibility for keeping the study records, custody per written notice must be submitted to the Sponsor, or designee, indicating the name and address of the person accepting primary responsibility. The IRB must also be notified in writing of the name and address of the new custodian.

23.3 Investigator Records and Reports

23.3.1 Investigator Records

Investigator is responsible for preparing and/or retaining the following records:

- Subject's case history records, including: signed/dated ICF, observations of adverse events, relevant medical history, results of tests and/or exams performed in this study, and dates and data collected at office visits and telephone follow-up;
- Protocol and any amendments; and
- IRB approval documents and related correspondence.

[redacted]

[redacted]

[redacted]

24.0 Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Subject names will not be supplied to the Sponsor. Only the subject number will be recorded in the eCRF, and if the subject name appears on any other document (e.g. source document), it must be de-identified before a copy of the document is supplied to the Sponsor. Trial findings stored on a computer will be stored in accordance with local data protection laws. As part of the informed consent process, the subjects will be informed in writing that representatives of the Sponsor. IRB, or regulatory authorities may inspect their medical records to verify the 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. If the results of the trial are published, the

subject's identity will remain confidential. The Investigator will maintain an onsite listing to enable subjects to be identified.

25.0 Regulatory Adherence

The trial will be adhering to 21 CFR parts 50, 56, 803 and ISO 14155 Serious Adverse Event (SAE) reporting throughout the duration of the trial.

26.0 Use of Information and Publication

Publication of data from this trial will be in accordance with the clinical trial agreements fully executed with Investigators and the Steering Committee Charter. All information and data relating to the clinical trial are the sole property of CSI. The Sponsor reserves the right to review and approve all publications and presentations utilizing the trial data.

For publication purposes, this trial will be submitted for inclusion in the clinical trial registry at: http://www.ClinicalTrials.gov.

27.0 References

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