Clinical Study Protocol

Evaluation of Safety and Efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System in the Treatment of Iliac and Femoropopliteal Lesions via Transradial Access
RADIANCY

Product Names:	S.M.A.R.T. RADIANZ™ Vascular Stent System BRITE TIP RADIANZ™ Guiding Sheath SABERX RADIANZ™ PTA Balloon Catheter
Protocol Number:	P21-7701
CIV-ID Number:	CIV-22-02-039027
Version:	7.0
Version Date:	March 21, 2023
Sponsor's Name/Address:	Cordis US Corp. 14201 NW 60th Ave Miami Lakes, FL 33014
Sponsor's Legal Representative:	Cordis Cashel Cahir Road, Cashel County Tipperary, Ireland
NCT number	NCT05399680

TO CONTACT THE SPONSOR REGARDING SAFETY MATTERS:

The Medical Monitor and other members of the study team (see "Study Management Team" section) can be reached using the Study Contact List provided by the sponsor.

Version History

Version Number	Version Date	Summary of Revisions
1.0	December 22, 2021	N/A (original version)
2.0	February 15, 2022	Added/clarified/reorganized content within Safety Reporting section, clarified medication regimen, added anticipated study start/end dates
3.0	April 25, 2022	Added/changed content to Study Design section (with clarifications on the "roll-in" cohort), Subject Early Discontinuation section and Statistics/Data Analyses section (including removal of interim analysis), minor clarifications in Products and Screen Failures sections

4.0	June 02, 2022	Increased total sample size, clarified primary safety endpoint, updated Statistics/Data Analyses section with revisions to assumed technical success and safety rates and addition of performance goals; updated number of sites and countries
5.0	June 09, 2022	Minor clarifications/additions to numerous sections (Background, Risks, Inclusion Criteria, Informed Consent, Safety Reporting, Quality Control/Quality Assurance, Record Retention, Participating Sites), additions to Appendix B
6.0	July 29, 2022	Addition of lead (coordinating) Investigator, SMART RADIANZ risk/anticipated AE occurrence corrections, rearrangement of secondary safety endpoints and inclusion/exclusion criteria for clarity, addition of Overall Process section (10.1), minor clarifications/additions/corrections in Screening/Enrollment, Reporting, Data Quality Assurance and Monitoring sections.
7.0	March 21, 2023	Change of CRO (entity performing medical monitor, monitoring and safety management roles); removal of "- 7" window for discharge assessments; modifications to endpoints; modifications to inclusion/exclusion criteria and bilateral stenosis treatment; inclusion of additional radial duplex ultrasound; addition of Risk/Benefit Analysis and Risk Management sections (5.4 & 5.5), clarifications to telephone/virtual follow-up, updates/additions to Participating Investigators and Sites

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Approval Signatures

I am the primary author of this study protocol and confirm, to the best of my knowledge, that it is complete and accurate.

Name	Role	Signature	Date
Rajesh Nathan	Clinical Project Manager	Rajesh Nathan	*Electronically signed by: Rajesh Nathan Reason: Author Date: Mar 23, 2023 18:54 EDT*

I have reviewed the study protocol and confirm, to the best of my knowledge, that it is complete and accurate.

Nusrath Sultana, MD, MBA	Clinical Management	Nusrath Sultana	*Electronically signed by: Nusrath Sultana Reason: Approved Date: Mar 23, 2023 16:09 PDT*
Nusrath Sultana, MD, MBA	Medical Monitor	Nusrath Sultana	*Electronically signed by: Nusrath Sultana Reason: Approved Date: Mar 23, 2023 16:09 PDT*
Steven Ullery	Statistician (NAMSA)	Steven Ullery	*Electronically signed by: Steven Ullery Reason: Reviewed Date: Mar 23, 2023 17:57 PDT*
Linda Ruedy	Regulatory Affairs	Linda Ruedy	*Electronically signed by: Linda Ruedy Reason: Approved Date: Mar 23, 2023 16:02 PDT*

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Investigator Protocol Signature Page

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study in accordance with the design and specific provisions outlined herein.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the investigational product and the conduct of the study.

I will use the informed consent form approved by Cordis US Corp. or its designee and the Ethics Committee (EC) and will fulfill all responsibilities for submitting pertinent information to the EC responsible for this study.

I also agree to report all information or data in accordance with the protocol and, in particular, I agree to report all adverse events, device deficiencies, and complaints, as defined in the protocol.

I further agree that sponsor and/or designee have access to any original source documents from which case report form (CRF) information may have been generated.

I also agree to have control over all clinical supplies (including all product) provided by sponsor and/or designees and collect and handle all clinical specimens in accordance with the protocol.

The below signed confirm herewith to have read and understood this study protocol and/or amendment and appendices; furthermore, to accomplish this study in accordance with the protocol, ICH/GCP guidelines, applicable international standards and all applicable country, local and federal regulations; and to accept respective revisions conducted by authorized personnel of sponsor and by regulatory authorities.

_____	
Principal Investigator (print)	
_____	_____
Principal Investigator (signature)	Date
_____	
Institution Name/Location	

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Evaluation of Safety and Efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System in the Treatment of Iliac and Femoropopliteal Lesions via Transradial Access

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Protocol Synopsis

Protocol Title	Evaluation of Safety and Efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System in the Treatment of Iliac and Femoropopliteal Lesions via Transradial Access
Abbreviated Title	RADIANCY
Name of Sponsor	Cordis US Corp.
Products	S.M.A.R.T. RADIANZ™ Vascular Stent System (investigational) BRITE TIP RADIANZ™ Guiding Sheath (CE marked) SABERX RADIANZ™ PTA Balloon Catheter (investigational for 9 and 10 mm diameters; CE marked for 2 through 8 mm diameters)
Reference/Control Treatment	N/A
Intended Use	The S.M.A.R.T. RADIANZ™ Vascular Stent System, when used with the BRITE TIP RADIANZ™ Guiding Sheath and SABERX RADIANZ™ PTA Balloon Catheter, is intended for treatment of lesions in the iliac, superficial femoral or proximal popliteal arteries via radial artery access.
Study Purpose	The primary objective of this clinical investigation is to evaluate acute safety and efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System, when used with the BRITE TIP RADIANZ™ Guiding Sheath and SABERX RADIANZ™ PTA Balloon Catheter, to deploy the S.M.A.R.T.™ Nitinol Stent, in the treatment of patients with obstructive iliac or femoropopliteal arterial disease via radial artery access.
Study Design	Multi-center, single-arm, non-randomized, prospective, pivotal (pre-market) clinical study
Study Centers	Approximately 15 investigational sites across Europe
Timeline	Actual start (first subject enrollment): Q2 2022 Anticipated completion (last subject last visit): Q4 2023
Primary Endpoints	Primary Safety Endpoint: • Occurrence rate of CEC-adjudicated, major radial access site complications attributed to study device or procedure through time of hospital discharge. Primary Efficacy Endpoint: Technical success at the conclusion of the index procedure, defined as successful insertion of the S.M.A.R.T. RADIANZ™ Vascular Stent System into the peripheral vasculature through the radial artery, successful

	deployment of the study device (S.M.A.R.T.™ stent) at the intended location, and successful withdrawal of the delivery system without conversion from radial to femoral artery access.

Secondary Endpoints	Secondary Safety Endpoints:
	• Peri-procedural (within 30 days post-index procedure):
	  ○ Rate of device deficiencies for each of the three (3) devices
	  ○ Rate of adverse events
	  ○ Rates of death, index limb amputation and target lesion revascularization
	  ○ Rate of procedural complications
	
	Secondary Efficacy Endpoints:
	• Technical success associated with use of the BRITE TIP RADIANZ™ Guiding Sheath, defined as successful insertion of the device into the peripheral vasculature through the radial artery (allowing for introduction of interventional and/or diagnostic devices) and successful withdrawal of the device.
	
	• Procedural success associated with use of the SABERX RADIANZ™ PTA Balloon Catheter for pre-dilation and/or post-deployment stent dilatation (whenever applicable), defined as successful insertion of the device into the peripheral vasculature through the radial artery, successful inflation and deflation of the balloon, successful withdrawal of the device, and achievement of a final residual diameter stenosis of < 30% at the conclusion of the index procedure.

Additional Data Points	• Data will be collected to evaluate the following health economics outcomes:
	  ○ Fluoroscopy time and procedural time, defined as the time of sheath introduction to time of vascular closure
	  ○ Time to achieve hemostasis, defined as the time elapsed from removal of the BRITE TIP RADIANZTM Guiding Sheath to the time that hemostasis was first observed
	  ○ Time to ambulation, defined as when the subject can stand up and walk any distance
	  ○ Time to hospital discharge
	  ○ Time to hospital discharge eligibility (when physician examines and if all is well, gives discharge orders).
	  ○ Method to achieve closure of the transradial artery access site
	
	• Quality of Life Assessments: Data will be also collected to evaluate health-related, quality of life in all subjects by administering both the SF-36 and the EuroQOL-5 Dimension (EQ-5D) standardized, validated questionnaires to assess general and disease-specific outcomes.

Sample Size	This study is planned to enroll approximately 159 subjects, of which approximately 30 subjects will constitute the “roll-in” cohort for the study and consist of the first two (2) enrolled subjects at each study site, as applicable (see “Statistics/Testing Methods” section below). To adequately assess the efficacy and safety of both iliac and femoropopliteal artery treatment under study, a minimum of 30 subjects will be required for each of the two indications (femoropopliteal and iliac).

	A goal of this study is to collect data on 30 uses of the SABERX device. Ideally those uses will be evenly distributed across the iliac and femoropopliteal arteries.
Treatment Plan	All enrolled subjects will be followed up to 30 days post-procedure. A patient with bilateral stenosis (lesions in both limbs) can have both lesions treated without a waiting period (e.g., during the index procedure). In all cases, a lesion on the second/contralateral limb can **ONLY** be treated with the study devices, via transradial approach and if it meets all applicable study eligibility criteria.
Eligibility Criteria	**Inclusion Criteria** **ALL patients must meet the following criteria prior to enrollment**: 1. Age ≥ 18 years 2. For women of child-bearing potential, a negative pregnancy test within seven (7) days prior to the index procedure 3. Symptomatic leg ischemia or ischemic ulcerations that do NOT exceed digits of the foot (Rutherford/Becker Classification category 2, 3, 4 or 5) 4. Palpable radial artery with diameter ≥ 2.5 mm, as assessed by duplex ultrasound 5. Eligibility for standard surgical repair, if necessary 6. A patient who requires a coronary intervention should have it performed at least seven (7) days prior to treatment of the target lesion 7. The patient must provide documented informed consent and any other documented authorization, as required, prior to initiation of the study procedure 8. Per Investigator assessment, the patient is willing and able to be followed up to 30 days post-procedure for evaluation and complete all required assessments per the study protocol. ***Inclusion criteria 9 and 10 AND 11a through 14a OR 11b through 16b (whichever is applicable) would be assessed via baseline angiography performed at the time of index procedure*:** 9. The Investigator has assessed that the patient is a suitable candidate (i.e, meets all inclusion criteria and none of the exclusion criteria), for treatment of a lesion in the iliac, superficial femoral and/or proximal popliteal arteries via transradial approach and is eligible for conversion from a transradial to transfemoral approach, if it becomes necessary. 10. The guidewire is across the target lesion(s) and located intraluminally within the distal vessel following a transradial approach **Patients whose target lesion is in the iliac artery must meet these additional criteria prior to enrollment**: 11a. A single *de novo* or restenotic lesion ≥ 50% stenosis in the common and/or external iliac artery 12a. Stenotic lesion (one long or multiple serial/tandem lesions) ≤ 100 mm, by visual assessment, within or across the common or external iliac

	arteries. The stenosis must be treatable with no more than two stents (while minimizing stent overlap) 13a. Reference vessel diameter (RVD) ranging from 4.0 to 9.0 mm by visual assessment 14a. Angiographic evidence of a patent profunda or superficial femoral artery in the diseased (target) limb **Patients whose target lesion is in the SFA and/or PPA must meet these additional criteria prior to enrollment**: 11b. A single *de novo* or restenotic lesion ⩾ 50% stenosis in the SFA and/or PPA 12b. Stenotic lesion (one long or multiple serial/tandem lesions) ≤ 150 mm, by visual assessment, within or across the SFA and/or PPA. The stenosis must be treatable with no more than two stents (while minimizing stent overlap) 13b. RVD ranging from 4.0 to 7.0 mm by visual assessment 14b. All lesions are to be located at least three centimeters proximal to the superior edge of the patella 15b. Patent infrapopliteal artery, i.e., single vessel runoff or better with patency (<50% stenosis) of at least one of three vessels to the ankle or foot 16b. Adequate aortoiliac or common femoral "inflow" (defined as < 30% stenosis after PTA or stenting) prior to treatment of the target lesion (defined as < 30% stenosis after PTA or stenting) prior to treatment of the target lesion **Exclusion Criteria** **Patients will be excluded if ANY of the following exclusion criteria apply**: 1. The patient has had/experienced any prior intervention/treatment to the target vessel within 90 days prior to enrollment (e.g., previously implanted graft in the aorta or target vessel; stroke; cryoplasty, laser or atherectomy; abdominal aortic aneurysm or aneurysm of the iliac, superficial femoral or popliteal artery). 2. Previously deployed stent at the site of the target lesion 3. The patient has post-surgical stenosis and anastomotic suture treatments of the target vessel 4. Requires general anesthesia for percutaneous transluminal angioplasty (PTA) and/or the stenting procedure 5. Use of mechanical devices on or thrombolysis of the target vessel within 72 hours prior to the index procedure without complete resolution of the thrombus 6. The patient is receiving any form of dialysis. 7. The patient is receiving any form of immunosuppressant therapy. 8. Planned amputation

	9. Established vasospastic disease 10. Glomerular filtration rate (GFR) < 30 mL/min within 7 days prior to the index procedure 11. The patient has a history of neutropenia, coagulopathy, and/or thrombocytopenia. 12. Thrombophlebitis, uremia, or deep venous thrombus, within past 30 days prior to the index procedure 13. Bleeding diathesis 14. Known allergies or intolerance to antiplatelet, anticoagulant or thrombolytic medications including but not limited to aspirin, clopidogrel bisulfate (Plavix®), ticlopidine (Ticlid®) or heparin that cannot be medically managed. 15. Known allergy or intolerance to Nitinol (nickel titanium) 16. Known allergy to contrast agent that cannot be medically managed before treatment with steroids and/or antihistamines. 17. Known or suspected active infection at the time of the index procedure. 18. Patient is currently participating in another investigational drug or medical device study that has not completed primary endpoint(s) evaluation or clinically interferes with the endpoints from this study or is planning to participate in such a study prior to their completion of this study. 19. Patient has had a major surgical or interventional procedure unrelated to this study within 30 days prior to enrollment or is anticipated/planned to have such a procedure within 30 days after enrollment. ***Exclusion criteria 20 through 25 would be assessed via baseline angiography performed at the time of index procedure*:** 20. Significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device 21. Noted perforation of the target vessel 22. Stent placement required across or within 0.5 cm of the SFA/profunda femoris artery (PFA) bifurcation 23. Cases of chronic total occlusion/in-stent restenosis/severe calcification in which there is pre-determined inability to treat the target lesion with a single stent, or procedures pre-determined to require stent-in-stent placement to obtain patency 24. Presence of thrombus prior to crossing the lesion 25. Successful PTA treatment of a target lesion in the SFA/PPA (defined as < 50% stenosis after PTA treatment)

Statistics/Testing Methods	Approximately 129 of the 159 enrolled subjects will be studied to demonstrate the safety and effectiveness of the new S.M.A.R.T. RADIANZ™ Vascular Stent System for delivery of the S.M.A.R.T.™ stent to obstructive iliac or femoropopliteal lesions by radial artery access. The remaining subgroup of approximately 30 subjects, consisting of the first two (2) enrolled subjects at each study site (as applicable) will constitute the "roll-in" cohort for the study. Such subjects will be pre-specified as "roll-in" subjects prior to their enrollment and must meet all criteria for enrollment, however, they will be followed up and evaluated to 30 days post-procedure only for safety and not included in any endpoint analyses. The intent of including a "roll-in" cohort is to enable less experienced investigators to overcome the learning curve in performing the study procedure and for all investigators to become better accustomed to the use of the various study devices. It is assumed that the technical success rate will be 98% and this rate will be compared to a performance goal of 93% which is derived from literature. The testing will be done using exact methods. A sample size of 129 limbs will provide 88% power to demonstrate that the observed technical success rate is greater than the performance goal of 93% at the 0.05 level of significance. The assumed complication rate associated with radial access is 2.0% as reported in the literature. This rate has been reported as being less than that associated with femoral access. The performance goal is set at 7.0% and the Type I error rate is set to 5%. Testing again is done using exact methods. A sample size of 129 subjects provides 88% power to demonstrate that the observed complication rate associated with radial access is less than the performance goal of 7.0%. To adequately assess the efficacy and safety of both iliac and femoropopliteal artery treatment under study, a minimum of 30 subjects will be required for each of the two indications (femoropopliteal and iliac). In order to characterize the safety and efficacy of the SABERX RADIANZ device, it is a goal of this study to collect information on 30 distinct uses of the device. This is a goal and not a minimum since use of the SABERX RADIANZ device is dictated by the attending physician. Ideally, the 30 uses will be evenly distributed between the iliac and femoropopliteal arteries. Data will be collected on occurrence rate of complications associated with transradial artery access, successful index procedure, which is defined as successful insertion of the delivery system through the vasculature, successful deployment of the study device at the intended location, and successful withdrawal of the delivery system without conversion to femoral access. Additional secondary endpoints will report on device deficiencies, adverse events, rates of death, index limb amputation, target lesion revascularization, rate of procedural complications, health economics outcomes, and demographic characteristics. For continuous variables, the mean, median, standard deviation, interquartile range, number of observations, minimum and maximum values, and 95% confidence intervals (CI), as appropriate, will be presented. For categorical variables, the numerator, denominator, rate (%) and exact 95% CI will be calculated. Data distribution will be tested, and correlations between variables will be explored. Additional subgroup analyses will be conducted and reported on. All calculations will be conducted using SAS version 9.4.

Time and Event Schedule

All required assessments from screening to 30 days post-procedure are presented in Table 1.

Table 1: Time and Event Schedule

Assessment	Screening	Index Procedure	Discharge (+7 days)	30 days (+/- 7 days) Post-Procedure
Informed Consent[1]	X			
Medical History	X			
Physical Examination[2]	X			
Inclusion/Exclusion Criteria Verification	X	X		
Labs[2]	X			
Duplex Ultrasound of the radial access artery	X[2]		X[3] (see footnote)	
Angiogram		X		
Adverse Event Assessment		X	X	X
Concomitant Medication	X	X	X	X
Quality of Life (SF-36 and EQ-5D) Assessments	X[2]		X	X

[1]Documented informed consent must be obtained within 60 days prior to the index procedure. The reflection period (time between explaining the study/providing written information to the prospective subject and obtaining documented consent) can vary based on individual circumstances but should be at least 24 hours in duration or per standard practice or institutional policies at each site.
[2]Must be completed within seven (7) days prior to the index procedure
[3]**Post-procedure duplex ultrasound can be completed any time between discharge and the 30-day follow-up visit per standard practice. If not standard-of-care at the site, this assessment must be completed at discharge.**

Study Management Team

The entities that will be responsible for managing various aspects of this study are presented in Table 2. Please refer to the Study Contact List provided by the sponsor for more specific contact information for each of these entities, which will be updated throughout the study as needed.

Table 2: Study Management Team

Sponsor	Cordis US Corp.
Sponsor's Legal Representative	Cordis Cashel
Medical Monitor	North American Science Associates, LLC (NAMSA)
Lead (Coordinating) Investigator	Prof. Raphael Coscas
Imaging Core Laboratory	NAMSA
Monitoring	NAMSA
Electronic Data Capture (EDC) System/Study Database	Medrio
Data Management	Cordis US Corp.
Safety Management	NAMSA
Statistics	NAMSA
Medical Writing	Cordis US Corp.

1 Introduction

1.1 Background

Peripheral arterial disease (PAD) affects more than 41 million people throughout the United States and Western Europe.[1] Disabilities from PAD continue to increase each year with growing prevalence of risk factors, including but not limited to: tobacco use, diabetes, hypertension, and hypercholesterolemia.[2] Although medical control of modifiable risk factors, and adherence to a structured regimen, are widely accepted as first-line treatment to slow disease progression, the majority of patients with critical limb ischemia require endovascular or surgical revascularization to prevent limb loss.[2] Many patients with PAD are high-risk surgical candidates, and endovascular intervention has increasingly become the first line of therapy for the invasive management of PAD.[2]

Traditionally, the majority (approximately 97%) of endovascular interventions throughout the body have been performed through transfemoral arterial (TFA) access, to accommodate larger diameter or large bore devices for various interventions, however, TFA access is difficult to perform for patients that are morbidly obese and unable-to-lie-flat patients with hostile groin anatomy (e.g. multiple diffuse lesions, chronic limb ischemia) and history of aortoiliac occlusive disease (e.g., multiple diffuse lesions, chronic limb ischemia).[1,3] TFA access is associated with increased risk of vascular complications and mortality.[3]

For interventions that do not have significant size requirements, alternative approaches including the transradial arterial (TRA) access have been extensively studied.[1] It has been well established that the TRA compared to the TFA approach may reduce access site complications and serious adverse events, including mortality.[4] Radial access approach is performed mostly from the left side as it is easier to approach target vessels due to shorter distance and since the aortic arch and cerebral vessels are avoided when inserting a guidewire or sheath.[3] Safety and performance data on this approach is sparse due to lack of devices.

The examination time for a procedure involving TRA access is similar to that for a procedure involving the TFA approach.

1.2 RADIANCY Clinical Study

In this clinical study, Cordis is evaluating the safety and efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System (S.M.A.R.T. RADIANZ), when used with the BRITE TIP RADIANZ™ Guiding Sheath (BRITE TIP RADIANZ) and SABERX RADIANZ™ PTA Balloon Catheter (SABERX RADIANZ) to deploy the S.M.A.R.T.™ Nitinol Stent (S.M.A.R.T. stent) for the treatment of patients with iliac and/or femoropopliteal [which includes the superficial femoral artery (SFA) and proximal popliteal artery (PPA)] lesions via transradial artery access.

- All S.M.A.R.T. RADIANZ products and all SABERX RADIANZ products in 9 and 10 mm diameters are not CE marked (hereafter referred to as “investigational products”).
- All other sizes (in 8 mm and smaller diameters) of the SABERX RADIANZ product and all BRITE TIP RADIANZ product are CE marked.

Both the investigational and CE marked products that will be used in this study are currently NOT commercially available in Europe and are being made available exclusively for use in this clinical study.

Individually or collectively, both investigational and CE marked products may be referred to as “study devices” hereafter.

The investigational study population is representative of the target population, which includes the following:

- individuals requiring treatment for atherosclerotic lesions in the SFA and/or PPA
- individuals requiring treatment in the common and external iliac arteries to improve luminal diameters in patients with symptomatic vascular stenotic and/or occlusive disease.

The target population is based on the patient's anatomy and compatibility with the study devices.

A list of all Investigators and sites (institutions) selected for participation in this clinical study is presented in Appendix C.

1.3 Literature Reviews

Summaries of the literature reviews that are related to the two (2) investigational products in this study (S.M.A.R.T. RADIANZ and 9 and 10 mm diameters of SABERX RADIANZ) and similar devices are provided below.

Literature Review Related to S.M.A.R.T. RADIANZ and Similar Devices

S.M.A.R.T. RADIANZ is a new device which has not been studied in any prior clinical investigations, however, the stent component of S.M.A.R.T. RADIANZ, the S.M.A.R.T. stent, is the same as that in previous generations of the S.M.A.R.T. device family. The only difference is the stent delivery system in that S.M.A.R.T. RADIANZ delivers the stent via transradial arterial access to the target lesion(s). The S.M.A.R.T. device family has been evaluated for performance in lower extremity arterial disease indications (SFA, PPA and iliac arteries) in numerous studies.

A recent literature search on the S.M.A.R.T. stent revealed that 10 publications reported outcomes in the SFA/PPA indication while four (4) publications reported outcomes in the iliac indication. To analyze the safety and performance of the S.M.A.R.T. device family in relation to similar self-expanding stents, an additional evaluation of the available literature data relative to the current state of the art (i.e., on similar/competitor/benchmark devices) was also performed based on 50 publications reporting outcomes in the SFA/PPA indication and eight (8) publications reporting outcomes in the iliac indication.

SFA/PPA Indication

The 10 publications[5-14] reporting outcomes on use of the S.M.A.R.T. stent in the SFA/PPA indication included 1,617 subjects, 33.4% of whom were female, and whose mean lesion length was 105.4 mm (77.3-157). The 50 publications[15-64] reporting outcomes on use of similar devices in the SFA/PPA indication included 7,599 subjects, 32.8% of whom were female, and whose mean lesion length was 117.88 mm (10-251).

Both groups (S.M.A.R.T. and similar devices) had comparable rates of technical success, generally defined as successful completion of the procedure with less than or equal to 30% residual stenosis, of 99.5% and 98.8%, respectively. The 30-day death rate [all-cause mortality (ACM)] was low for both groups with 0.0% and 1.0% rate for S.M.A.R.T. stent devices (one study reporting) and similar devices, respectively. At the one-year mark, ACM increased in both groups with 3.9% (n = 505) and 4.6% (n = 4,042) rate for S.M.A.R.T. stent devices and similar devices, respectively.

The S.M.A.R.T. stent group saw a higher 1-year primary patency rate of 82.4% (6 studies) compared to the 80.0% patency rate (33 studies) for the similar devices group. Neither group had a noteworthy number of cases of target lesion revascularization at 30 days (S.M.A.R.T.: 0.0%, similar devices: 0.6%), though rates increased at 1-year follow-up (S.M.A.R.T.: 10.3%, similar devices: 19.9%). Out of 3,568 patients in the similar device group, only 1.5% required major limb amputation after 1 year while 0.6% of the 276 patients treated with S.M.A.R.T. required major limb amputation.

Iliac Indication

The four (4) publications[65-68] reporting outcomes on use of the S.M.A.R.T. stent in the iliac indication included 2,328 subjects, 19.7% of whom were female, and whose mean lesion length was 56.8 mm (24.7-60.0). The eight (8) publications[69-76] reporting outcomes on use of similar devices in the iliac indication included 876 subjects, 27.9% of whom were female, and whose mean lesion length was 36 mm (25-57).

Patients treated with the S.M.A.R.T. stent devices exhibited a technical success rate of 97.0% (n = 193) while the similar device group exhibited a similar rate at 97.6% (n = 560). The 30-day ACM rate was 2.0% and 1.4% for S.M.A.R.T. stents and similar devices, respectively. The patency rate at 1-year for S.M.A.R.T. stents and similar devices was 92.0% and 92.9%, respectively. The slightly lower weighted averages are explained by the small cohort sizes for S.M.A.R.T. stents; however, the rates are similar and both results do overlap each other's confidence interval.

Literature Review Related to SABERX RADIANZ and Similar Devices

The new, 9 and 10 mm diameters are a line extension of the existing SABERX RADIANZ device available in 2-8 mm diameters and have not been studied in any prior clinical investigations. The SABERX RADIANZ device is a line extension of the previously commercialized SABERX™ PTA Dilatation Catheter (SABERX).

There is currently no literature available which report outcomes of using the SABREX RADIANZ, SABERX or any other Cordis PTA dilatation catheter in procedures involving a radial-to-peripheral treatment approach. A literature search performed on other PTA catheters used in a radial-to-peripheral approach revealed the following:

In the prospective, observational, REACH PVI (Radial accEss for nAvigation to your cHosen lesion for Peripheral Vascular Intervention) study, 49 out of 50 patients were deemed procedurally successful. Therefore, the conclusion was that transradial orbital atherectomy by percutaneous transluminal angioplasty (PTA) for lower extremity PAD is feasible and demonstrates a favorably safety profile, however, as the study points out, more studies and devices are needed so the transradial arterial access approach can be taken for any endovascular procedure.[3]

2 Products

Cordis US Corp. is the legal manufacturer of all investigational and CE marked product used in this study.

2.1 Investigational Products

S.M.A.R.T. RADIANZ

The S.M.A.R.T. RADIANZ device is designed to deliver the S.M.A.R.T. ™ self-expanding stent (S.M.A.R.T. stent) to the iliac arteries, superficial femoral arteries and/or proximal popliteal arteries using a 6F (2.0 mm) sheathed delivery system introduced through the radial artery. The S.M.A.R.T. stent is composed of a nickel titanium alloy (nitinol). A total of 12 (6 at each end) tantalum radiopaque markers are located on the ends of the stent. The stent is a flexible, fine mesh tubular prosthesis that expands upon deployment to appose the vessel wall. Upon deployment, the stent imparts an outward radial force on the luminal surface of the vessel to establish patency. The S.M.A.R.T. stent is already CE marked for treating lesions in the iliac, superficial femoral and proximal popliteal arteries whereas the S.M.A.R.T. RADIANZ device is a new/investigational product.

The S.M.A.R.T. RADIANZ device is available in stent diameters ranging from 6 to 10 mm. Stent lengths range from 20 to 150 mm for 6, 7 and 8 mm stent diameters and from 20 to 80 mm for 9 and 10 mm stent

diameters. Stents with 6 and 7 mm diameters are available only in a delivery system with a 190 cm length; stents with an 8 mm diameter are available in a 190 cm or 150 cm long delivery system; stents with a 9 or 10 mm diameter are available only in a 150 cm long delivery system. The complete matrix showing all sizes in which the S.M.A.R.T. RADIANZ device is supplied is presented as Table 3.

Table 3: S.M.A.R.T. RADIANZ Size Matrix

Delivery System Length (cm)	Stent Diameter (mm)	Stent Length (mm)							
		20	30	40	60	80	100	120	150
190	6	X	X	X	X	X	X	X	X
190	7	X	X	X	X	X	X	X	X
190	8	X	X	X	X	X	X	X	X
150		X	X	X	X	X	X	X	X
150	9	X	X	X	X	X			
150	10	X	X	X	X	X			

All sizes of the S.M.A.R.T. RADIANZ device will be labeled as "Exclusively for Clinical Investigation".

The Instructions for Use (IFU) and the Investigator's Brochure (IB) for the S.M.A.R.T. RADIANZ device will be provided by the sponsor and should be referred to for a more detailed description of the device and information on its intended purpose, indications/contraindications, warnings, precautions, potential complications, storage, handling, directions for use, necessary training and experience for use, etc. prior to the enrollment of and use of the device on any subjects in this study.

SABERX RADIANZ: 9 and 10 mm Diameters

The SABERX RADIANZ device is a catheter with a distal inflatable balloon. The catheter utilizes a rapid exchange design, consisting of a single inflation lumen and a distal guidewire lumen. The guidewire lumen begins at the distal tip and terminates at the guidewire exit port. The proximal hub is used as a balloon inflation port. Radiopaque marker bands indicate the dilating section of the balloon and aid in balloon placement. For balloon lengths greater than or equal to 10 cm, the distal section will have one (1) marker band and proximal section will consist of two (2) adjacent marker bands. For balloon lengths less than 10 cm, the distal and proximal section will have each one (1) marker band. The catheter tip is tapered to ease entry into peripheral arteries and to facilitate the crossing of tight stenoses. SABERX RADIANZ balloons are coated with a hydrophilic material designed to increase lubricity throughout the lifetime of the device.

Currently, the SABERX RADIANZ device is CE marked for diameters of 2, 2.5, 3, 3.5, 4, 5, 6, 7, and 8 mm (see **Section 2.2.2** below). The 9 and 10 mm diameters for this device are new/investigational, for which available balloon lengths range from 2 through 10 cm, as presented in Table 4.

Table 4: SABERX RADIANZ 9 and 10 mm Diameter Size Matrix

Balloon Length (cm)	Balloon Diameter (mm)	
	9	10
2	X	X
3	X	X
4	X	X
6	X	X
8	X	X
10	X	X

All SABERX RADIANZ units with 9 and 10 mm diameters will be labeled as "Exclusively for Clinical Investigation".

The IFU for the 9 and 10 mm diameters of the SABERX RADIANZ device and the IB for the SABERX RADIANZ device will be provided by the sponsor and should be referred to for a more detailed description of the device and information on its intended purpose, indications/contraindications, warnings, precautions, potential complications, storage, handling, directions for use, necessary training and experience for use, etc. prior to the enrollment of and use of the device on any subjects in this study.

2.2 CE Marked Products

BRITE TIP RADIANZ

The CE marked, BRITE TIP RADIANZ device is a catheter guiding sheath that facilitates percutaneous entry of an intravascular device into the peripheral vasculature through the radial artery. The sheath surface has a hydrophilic coating to enhance entry and withdrawal during vessel access. A hemostasis valve facilitates entry and withdrawal of intravascular devices through the catheter guiding sheath and minimizes the back-flow of blood. It has a hydrophilic coating and a multi-segmented braided design for optimal pushability, kink resistance and back-up support. The BRITE TIP RADIANZ device is available in working lengths of 110 cm and 135 cm.

The IFU for the BRITE TIP RADIANZ device will be provided by the sponsor and should be referred to for a more detailed description of the device and information on its intended purpose, indications/contraindications, warnings, precautions, potential complications, storage, handling, directions for use, etc. prior to the enrollment of and use of the device on any subjects in this study.

SABERX RADIANZ: 2 through 8 mm Diameters

The SABERX RADIANZ device is CE marked for all diameters from 2 through 8 mm. Balloons that are 2 through 6 mm in diameter are available in lengths from 2 through 30 cm; balloons that are 7 or 8 mm in diameter are available in lengths from 2 through 10 cm as shown in Table 5.

Table 5: SABERX RADIANZ 2 through 8 mm Diameter Size Matrix

Balloon Length (cm)	Balloon Diameter (mm)								
	2	2.5	3	3.5	4	5	6	7	8
2	X	X	X	X	X	X	X	X	X
3	X	X	X	X	X	X	X	X	X
4	X	X	X	X	X	X	X	X	X
6	X	X	X	X	X	X	X	X	X
8	X	X	X	X	X	X	X	X	X
10	X	X	X	X	X	X	X	X	X
15	X	X	X	X	X	X	X		
20	X	X	X	X	X	X	X		
25	X	X	X	X	X	X	X		
30	X	X	X	X	X	X	X		

Of all the CE marked sizes for the SABERX RADIANZ device, only those in diameters from 4 through 8 mm will be available in this study.

The IFU for the 2 through 8 mm diameters of the SABERX RADIANZ device and the IB for the SABERX RADIANZ device will be provided by the sponsor and should be referred to for a more detailed description of the device and information on its intended purpose, indications/contraindications, warnings, precautions, potential complications, storage, handling, directions for use, etc. prior to the enrollment of and use of the device on any subjects in this study.

3 Study Objectives

The primary objective of this clinical investigation is to evaluate acute safety and efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System, when used with the BRITE TIP RADIANZ™ Guiding Sheath and SABERX RADIANZ™ PTA Balloon Catheter, to deploy the S.M.A.R.T.™ Nitinol Stent, in the treatment of patients with obstructive iliac or femoropopliteal arterial disease via radial artery access.

4 Indications

4.1 Investigational Products

S.M.A.R.T. RADIANZ

The S.M.A.R.T. RADIANZ device is indicated for use to improve luminal diameter for the treatment of patients with *de novo* or restenotic, native lesion(s) of the superficial femoral artery and/or proximal popliteal artery with total lesion length up to 150 mm and a reference vessel diameter ranging from 4 mm to 7 mm, or of the Iliac artery with total lesion length up to 100 mm and a reference vessel diameter ranging from 4 mm to 9 mm.

SABERX RADIANZ: 9 and 10 mm Diameters

The SABERX RADIANZ device in the 9 and 10 mm diameters is indicated to dilate stenoses in the iliac, femoral, and proximal popliteal arteries. The device is also indicated for post-dilatation of balloon-expandable and self-expanding stents in the peripheral vasculature.

4.2 CE Marked Products

BRITE TIP RADIANZ

The BRITE TIP RADIANZ device is indicated for intravascular introduction of interventional and/or diagnostic devices into the peripheral vasculature through the radial artery. In this study, this device will be used within its approved indications.

SABERX RADIANZ: 2 through 8 mm Diameters

The SABERX RADIANZ device in the 2 through 8 mm diameters is indicated to dilate stenoses in the iliac, femoral, ilio-femoral, popliteal, infra popliteal and renal arteries. The device is also indicated for post-dilatation of balloon-expandable and self-expanding stents in the peripheral vasculature. As this device will be used for stenoses in the iliac and/or femoropopliteal arteries in this study, it will be used within its approved indications.

5 Benefits/Risks

5.1 S.M.A.R.T. RADIANZ

5.1.1 *Benefits*

The potential benefits of using S.M.A.R.T. RADIANZ via radial artery access include:

- Reduced access site and major complications
- Lower bleeding risk
- Faster mobilization
- Cost-effectiveness

The potential benefit of the S.M.A.R.T. stent within the S.M.A.R.T. RADIANZ device includes improved arterial luminal diameter in patients with peripheral artery disease.

5.1.2 *Risks*

The following are possible risks, categorized by occurrence (Improbable, Remote, Occasional, Probable, Frequent), associated with use of S.M.A.R.T. RADIANZ and S.M.A.R.T. stent.

Occurrence Rate: Improbable, <0.002%

- Abrupt closure
- Access failure
- Access site complications
- Allergic/anaphylactoid reaction to anticoagulant and/or antithrombotic therapy or contrast medium
- Allergic reaction to nitinol
- Allergic reaction
- Amputation
- Anemia/blood loss
- Arrhythmia
- Blue toe syndrome
- Bradycardia
- Worsened claudication or rest pain
- Death
- Encephalopathy (new or worse) (altered mental state or confusion)
- Fever
- Fistulization
- Gangrene
- Gastrointestinal bleed from anticoagulation/antiplatelet medication
- Hematoma
- Hemorrhage
- Hypotension/hypertension
- Iliac artery spasm
- Infection
- Infection and/or sepsis
- Intimal tear/dissection
- Ischemia
- Multi-organ failure
    - Muscle hemorrhage
- Pain
- Pneumothorax
- Pseudoaneurysm
- Renal failure
- Respiratory arrest
- Sepsis
- Stent embolization
- Stent migration
- Stent occlusion
- Stroke
- Transient Ischemic Attack (TIA)
- Trauma to adjacent structures
- Worsened claudication or rest pain

Occurrence Rate: Remote, 0.002%-<0.02%

- Aneurysm
- Angina/coronary ischemia/myocardial infarction
- Arterial restenosis
- Arterial stenosis or dissection
- Arteriosclerosis
- Arteriovenous fistula
- Disseminated intravascular coagulation
- Edema, peripheral
- Embolism
- Emergent repeat hospital intervention or surgery
- Necrosis
- Restenosis of the stented segment
- Tissue necrosis
- Vascular injury, including perforation, rupture and dissection
- Vasospasm
- Vessel occlusion/thrombosis, puncture site (restenosis or recurrent stricture)

Occurrence Rate: Occasional, 0.02% to <1%

No risks

Occurrence Rate: Probable, 1% to <10%
No risks

Occurrence Rate: Frequent, >10%
No risks

5.2 BRITE TIP RADIANZ

NOTE: As BRITE TIP RADIANZ is a CE marked device to be used within its intended purpose, the same benefits and risks apply as they do for the use for which the device has been approved.

5.2.1 *Benefits*

The BRITE TIP RADIANZ device allows for radial artery access to successfully complete diagnostic and treatment procedures. The potential benefits of using BRITE TIP RADIANZ are similar to other access sheaths that have been intended and optimized for use via a transradial approach. In general, when vascular access is obtained by needle puncture, avoiding a surgical incision, the need for analgesia and sedation is reduced. Percutaneous access often results in shorter recovery times and thereby, length of hospital stay.[77] Compared to traditional femoral access, the transradial approach is associated with a lower bleeding rate, faster time to ambulation and shorter hospital stay.[78] Also, these benefits allow a wider range of patients to be treated, including those who otherwise would be contraindicated from undergoing surgery due to operative risk and comorbidities.

5.2.2 *Risks*

The following are possible risks, categorized by occurrence (Improbable, Remote, Occasional, Probable, Frequent), associated with use of BRITE TIP RADIANZ.

Occurrence Rate: Improbable, <0.002%
- Air Embolism
- Allergic reaction (contrast medium and medications)
- Hematoma at puncture
- Hemorrhage
- Inflammation / Infection / Sepsis
- Perforation of vessel wall
- Peripheral nerve injury
- Thrombus formation

Occurrence Rate: Remote, 0.002% to <0.02%
- Abrupt vessel closure
- Additional intervention
- Embolic Stroke/Cerebral Infarct
- Intimal tear
- Necrosis
- Pain
- Vascular complications (e.g., intimal tear, dissection, pseudoaneurysm, perforation, rupture, spasm, occlusion)

Occurrence Rate: Occasional, 0.02% to <1%
No risks

Occurrence Rate: Probable, 1% to <10%
No risks

Occurrence Rate: Frequent, >10%
No risks

5.3 SABERX RADIANZ

NOTE: The benefits and risks associated with using the SABERX RADIANZ device with the investigational, 9 and 10 mm diameters are the same as those which apply for the uses for which the device with the CE marked, 2 through 8 mm diameters have been approved.

5.3.1 *Benefits*

The potential benefits of using SABERX RADIANZ in patients with arterial stenosis are that it allows for improved arterial luminal diameter (opens the arterial lumen), prepares the lesion for stenting and/or ensures the stent has been fully expanded and apposing the arterial wall.

5.3.2 *Risks*

The following are possible risks, categorized by occurrence (Improbable, Remote, Occasional, Probable, Frequent), associated with use of SABERX RADIANZ.

Occurrence Rate: Improbable, <0.002%

- Acute Myocardial Infarction
- Allergic reaction (contrast medium and medications)
- Amputation
- Arrhythmias
- Arteriovenous fistula
- Bradycardia
- Death
- Hypotension/hypertension
- Inflammation/infection/sepsis
- Neurological events, including peripheral nerve injury, transient ischemic attack, and/or stroke
- Organ failure (single, multiple)
- Procedural complications: bleeding, hypotension, access site complications
- Pseudoaneurysm
- Renal failure
- Vascular complications (e.g., intimal tear, dissection, pseudoaneurysm, perforations, rupture, spasm, occlusion)

Occurrence Rate: Remote, 0.002% to <0.02%

- Abrupt vessel closure
- Access site complication

- Dissection
- Embolism
- Hematoma at puncture site
- Hemorrhage
- Ischemia
- Necrosis
- Pain
- Restenosis of the dilated vessel
- Thrombosis

Occurrence Rate: Occasional 0.02% to <1%

- Potential for balloon burst and potential complications (rated burst pressure)

Occurrence Rate: Probable, 1% to <10%
No risks

Occurrence Rate: Frequent, >10%
No risks

5.4 Benefit and Risk Assessment

A comprehensive analysis of the individual risks, the overall residual risk, and the anticipated medical benefits as well as risk management for the Cordis SMART Stent Family and for the family of Cordis PTA catheters are detailed in the documents, “Risk Management Report for SMART RADIANZ Self-Expanding Stent (SES) Family” (100617627/Rev. 1), and “Risk Management Report for PTA Catheters” (100235021/Rev.8), respectively.

5.4.1 *Benefits*

Transradial access (TRA) is a safe and feasible alternative to transfemoral access for a range of peripheral interventions, achieving success in 93.2% of cases.[79]

Most of the disadvantages of the femoral artery access approach are non-existent when accessing the radial approach. Even in obese patients, the radial artery is close to the skin surface, making the initial needle puncture simple and straightforward. In addition, any bleeding can be readily seen and addressed immediately - a short compression of the radial artery can stop bleeding even when the patient has been aggressively anticoagulated. Lastly, the radial artery is not close to a major nerve (as opposed to the femoral artery’s proximity to the femoral nerve).[80]

Overwhelming evidence demonstrating these advantages as well as reduced access-related complications, early ambulation and discharge, cost savings, and patient preference because of improved post-procedure comfort with faster recovery are some of the important reasons for the increased adoption of transradial approach for coronary, peripheral, and cerebrovascular endovascular procedures worldwide.[81,82,83,84,85,86,87,88,89,90] Led by the interventional cardiology community, large randomized multicenter trials such as the Radial versus Femoral Access for Coronary Angiography and Intervention in Patients with Acute Coronary Syndrome (RIVAL) and Minimizing Adverse Haemorrhagic Events by Transradial Access Site and the Systemic Implementation of AngioX (MATRIX) studies, with over 7,000

patients each, have reported a greater than 60% reduction in vascular complications as well as significant decreases in all-cause mortality and net adverse clinical events with TRA.[90,91] From the PREVAS study, immediate ambulation as opposed to bed rest after femoral procedures, reduced post-procedure nursing care, reduced hospital stay, and therefore cost, with an overwhelming patient preference for transradial angiography have all been reported.[92]

5.4.2 *Risks*

The TRA approach, however, does come with access challenges. Failure to access the radial artery is typically due to puncture error or radial artery spasm (RAS). These two reasons for failure are intimately linked as failed attempts at piercing the radial artery quickly result in RAS, which in turn results in even greater difficulty in accurately puncturing and cannulating the small artery in spasm.[93]

Imaging modalities have shown to improve and/overcome this technical barrier. The routine use of ultrasound for radial artery puncture nearly eliminates access failure and improves efficiency. In a randomized, multicenter trial of 692 patients, ultrasound guidance resulted in a significantly reduced number of attempts (mean 1.65±1.2 vs 3.05±3.4, p<0.0001) and time to access (88±78s vs 108±112s, p=0.006), as well as improved first-pass success (64.8% vs 43.9%, p<0.0001)[93] This reduction in attempts is important in decreasing the likelihood of RAS as well as preventing patient pain, swelling, and hematomas at the access site. Of note, when radial artery access failure occurs distally, attempts to cannulate the radial artery more proximally can be done prior to conversion to TFA. The entire length of the radial artery distal to the brachioradialis muscle (in which the artery dives below the fascia) is easily accessed and associated with minimal risk.

Additionally, it is expected that enrolled subjects will be exposed to some amounts of radiation from the angiogram imaging required in this study. The total radiation dose to which subjects (of average size) will be exposed from their participation in this study ranges from approximately 0.05 mSv to 5 mSv (depending on the artery undergoing treatment) and may or may not be comparable to what they would be otherwise exposed to if they did not take part in this study, based on standard of care at the study institution. Nevertheless, the total radiation exposure from angiography would be a multiple of natural radiation exposure for an individual who does not undergo this type of procedure.

5.4.3 *Summary of Assessment*

As mentioned above, a comprehensive review and analysis of the benefits and risks involving the investigational study devices are provided within the respective risk management reports.

Additionally, the risk/benefit analyses summarized above, the Clinical Evaluation Reports and post-market surveillance data (obtained from active customer feedback, complaints, quality and production information and periodic literature reviews), which provide objective evidence to support the risk/benefit profile, conclude that the potential benefits associated with the medical procedures in which the SMART RADIANZ Self-Expanding Stent (SES) Family and Cordis PTA catheters are used outweigh the potential risks.

From a clinical perspective, the devices achieve their intended performance during normal conditions of use as stated in the labeling materials. Known and foreseeable risks and adverse events are minimized and acceptable when weighed against the benefits of the intended performance. At this time, no unknown device or procedural interaction is suspected, and the device is generally used as indicated by the label. Based on the analysed information, the SMART RADIANZ SES Family of devices and Cordis PTA catheters

have been demonstrated as safe and effective devices when used in accordance with their Instructions for Use.

Analysis of published literature and post-market surveillance data have identified no new/previously unknown hazards (safety or performance issues) and/or increased frequency/severity of known hazards during use of these products. The safety profile and types/incidences of complications reported in the published literature were consistent with hazards identified by risk assessment for these devices and with reported complaints. Review of the complaints database, which includes the rate of occurrence for all categories of complaints, also showed that these and other, commercially-available devices, which have been on the market for over twenty years, have similar potential risks and a known and stable history of adverse events, with most events being an inherent risk of the percutaneous vascular procedure.

Based on the results and completeness of the risk management process as listed above as well as the criteria defined in the Risk Management Plan, it is concluded that the SMART Stent Family of devices and Cordis PTA catheters remain safe and effective treatment options for treating stenotic lesions. Considering the risk profile and evidence of the same when compared to the benefits, it is believed that the potential risks are outweighed by the potential benefit to the patients.

6 Study Design

This is a multi-center, single-arm, non-randomized, prospective, pivotal (pre-market) clinical study enrolling approximately 159 subjects with obstructive iliac or femoropopliteal arterial disease.

- **"Roll-in" cohort**: A subgroup of approximately 30 subjects, consisting of the first two (2) enrolled subjects at each study site (as applicable), will constitute the "roll-in" cohort for the study. Such subjects will be pre-specified as "roll-in" subjects prior to their enrollment and must meet all criteria for enrollment, however, they will be followed up and evaluated to 30 days post-procedure only for safety and not included in any endpoint analyses.

  The "roll-in" cohort is intended to allow less experienced investigators to overcome the learning curve in performing the study procedure and for all investigators to become better accustomed/acclimated to the operation/use of all study devices through the first couple study subjects treated at their respective sites, but without including such subjects in endpoint analyses.

- All enrolled subjects (including those in the "roll-in" cohort) will be followed up to 30 days post-procedure.

- To adequately assess the efficacy and safety of both iliac and femoropopliteal artery treatment under study, a minimum of 30 subjects will be required for each of the two indications (femoropopliteal and iliac).

- A goal of this study is to collect data on 30 uses of the SABERX device. Ideally those uses will be evenly distributed across the iliac and femoropopliteal arteries.

There will be approximately 15 participating study sites across Europe.

The RADIANCY study started (first subject enrollment) in Q2 2022 and is anticipated for completion (last subject last visit) in Q4 2023.

The sponsor, Cordis US Corp. (Cordis), will finance the study and arrange for all liability insurance needs. All devices (both investigational and CE marked) will be provided free of charge to all participating sites by

the sponsor as none are yet commercially available. The costs for all non-standard-of-care tests required by this study protocol will be covered by the sponsor.

Each study site will be contracted with Cordis via a Clinical Trial Agreement to execute all study activities as described in this protocol.

7 Inclusion and Exclusion Criteria

Prior to any study-specific activities, all subjects must sign and date the most current, EC approved Informed Consent Form (ICF).

7.1 Inclusion Criteria

Subjects must meet ALL of the following inclusion criteria to be enrolled in the study:

1. Age ≥ 18 years
2. For women of child-bearing potential, a negative pregnancy test within seven (7) days prior to the index procedure
3. Symptomatic leg ischemia or ischemic ulcerations that do NOT exceed digits of the foot (Rutherford/Becker Classification category 2, 3, 4 or 5)
4. Palpable radial artery with diameter ≥ 2.5 mm, as assessed by duplex ultrasound
5. Eligibility for standard surgical repair, if necessary
6. A patient who requires a coronary intervention should have it performed at least seven (7) days prior to treatment of the target lesion
7. The patient must provide documented informed consent and any other documented authorization, as required, prior to initiation of the study procedure
8. Per Investigator assessment, the patient is willing and able to be followed up to 30 days post-procedure for evaluation and complete all required assessments per the study protocol.

***Inclusion criteria 9 and 10 AND 11a through 14a OR 11b through 16b (whichever is applicable) would be assessed via baseline angiography performed at the time of index procedure*:**

9. The Investigator has assessed that the patient is a suitable candidate (i.e, meets all inclusion criteria and none of the exclusion criteria), for treatment of a lesion in the iliac, superficial femoral and/or proximal popliteal arteries via transradial approach and is eligible for conversion from a transradial to transfemoral approach, if it becomes necessary.
10. The guidewire is across the target lesion(s) and located intraluminally within the distal vessel following a transradial approach

Patients whose target lesion is in the iliac artery must meet these additional criteria prior to enrollment:

11a. A single *de novo* or restenotic lesion ≥ 50% stenosis in the common and/or external iliac artery

12a. Stenotic lesion (one long or multiple serial/tandem lesions) ≤ 100 mm, by visual assessment, within or across the common or external iliac arteries. The stenosis must be treatable with no more than two stents (while minimizing stent overlap)

13a. Reference vessel diameter (RVD) ranging from 4.0 to 9.0 mm by visual assessment

14a. Angiographic evidence of a patent profunda or superficial femoral artery in the diseased (target) limb

Patients whose target lesion is in the SFA and/or PPA must meet these additional criteria prior to enrollment:

11b. A single *de novo* or restenotic lesion ≥ 50% stenosis in the SFA and/or PPA

12b. Stenotic lesion (one long or multiple serial/tandem lesions) ≤ 150 mm, by visual assessment, within or across the SFA and/or PPA. The stenosis must be treatable with no more than two stents (while minimizing stent overlap)

13b. RVD ranging from 4.0 to 7.0 mm by visual assessment

14b. All lesions are to be located at least three centimeters proximal to the superior edge of the patella

15b. Patent infrapopliteal artery, i.e., single vessel runoff or better with patency (<50% stenosis) of at least one of three vessels to the ankle or foot

16b. Adequate aortoiliac or common femoral "inflow" (defined as < 30% stenosis after PTA or stenting) prior to treatment of the target lesion
(defined as < 30% stenosis after PTA or stenting) prior to treatment of the target lesion

7.2 Exclusion Criteria

Subjects will be excluded if they meet ANY of the following exclusion criteria:

1. The patient has had/experienced any prior intervention/treatment to the target vessel within 90 days prior to enrollment (e.g., previously implanted graft in the aorta or target vessel; stroke; cryoplasty, laser or atherectomy; abdominal aortic aneurysm or aneurysm of the iliac, superficial femoral or popliteal artery).
2. Previously deployed stent at the site of the target lesion.
3. The patient has post-surgical stenosis and anastomotic suture treatments of the target vessel.
4. Requires general anesthesia for percutaneous transluminal angioplasty (PTA) and/or the stenting procedure.
5. Use of mechanical devices on or thrombolysis of the target vessel within 72 hours prior to the index procedure without complete resolution of the thrombus.
6. The patient is receiving any form of dialysis.
7. The patient is receiving any form of immunosuppressant therapy.
8. Planned amputation.
9. Established vasospastic disease.
10. Glomerular filtration rate (GFR) < 30 mL/min within 7 days prior to the index procedure.
11. The patient has a history of neutropenia, coagulopathy, and/or thrombocytopenia.
12. Thrombophlebitis, uremia, or deep venous thrombus, within past 30 days prior to the index procedure
13. Bleeding diathesis.
14. Known allergies or intolerance to antiplatelet, anticoagulant or thrombolytic medications including but not limited to aspirin, clopidogrel bisulfate (Plavix®), ticlopidine (Ticlid®) or heparin that cannot be medically managed.
15. Known allergy or intolerance to Nitinol (nickel titanium).

16. Known allergy to contrast agent that cannot be medically managed before treatment with steroids and/or antihistamines.
17. Known or suspected active infection at the time of the index procedure.
18. Patient is currently participating in another investigational drug or medical device study that has not completed primary endpoint(s) evaluation or clinically interferes with the endpoints from this study or is planning to participate in such a study prior to their completion of this study.
19. Patient has had a major surgical or interventional procedure unrelated to this study within 30 days prior to enrollment or is anticipated/planned to have such a procedure within 30 days after enrollment.

***Exclusion criteria 20 through 25 would be assessed via baseline angiography performed at the time of index procedure*:**

20. Significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device.
21. Noted perforation of the target vessel.
22. Stent placement required across or within 0.5 cm of the SFA/profunda femoris artery (PFA) bifurcation.
23. Cases of chronic total occlusion/in-stent restenosis/severe calcification in which there is pre-determined inability to treat the target lesion with a single stent, or procedures pre-determined to require stent-in-stent placement to obtain patency.
24. Presence of thrombus prior to crossing the lesion.
25. Successful PTA treatment of a target lesion in the SFA/PPA (defined as ≤ 50% stenosis after PTA treatment).

This study is designed to exclude children, pregnant women, and immunocompromised subjects, due to the nature of the procedure, device and indications.

8 Study Endpoints

8.1 Primary Endpoints

8.1.1 *Primary Safety Endpoint*

The primary safety endpoint is the occurrence rate of CEC-adjudicated, major radial access site complications attributed to study device or procedure through time of hospital discharge.

8.1.2 *Primary Efficacy Endpoint*

Technical success at the conclusion of the index procedure, defined as successful insertion of the S.M.A.R.T. RADIANZ™ Vascular Stent System into the peripheral vasculature through the radial artery, successful deployment of the study device (S.M.A.R.T.™ stent) at the intended location, and successful withdrawal of the delivery system without conversion from radial to femoral artery access.

8.2 Secondary Endpoints

8.2.1 *Secondary Safety Endpoints*

Secondary safety endpoints include the following:

- Peri-procedural (within 30 days post-index procedure):
  - Rate of device deficiencies for each of the three (3) devices
  - Rate of adverse events
  - Rates of death, index limb amputation and target lesion revascularization
  - Rate of procedural complications

Secondary Efficacy Endpoints

- Technical success associated with use of the BRITE TIP RADIANZ™ Guiding Sheath, defined as successful insertion of the device into the peripheral vasculature through the radial artery (allowing for introduction of interventional and/or diagnostic devices) and successful withdrawal of the device.
- Procedural success associated with use of the SABERX RADIANZ™ PTA Balloon Catheter for pre-dilation and/or post-deployment stent dilatation (whenever applicable), defined as successful insertion of the device into the peripheral vasculature through the radial artery, successful inflation and deflation of the balloon, successful withdrawal of the device, and achievement of a final residual diameter stenosis of < 30% at the conclusion of the index procedure.

8.3 Additional Data Points

Data will be collected to evaluate the following health economics outcomes:

- Fluoroscopy time and procedural time, defined as the time of sheath introduction to time of vascular closure.
- Time to achieve hemostasis,
-
- defined as the time elapsed from removal of the BRITE TIP RADIANZ™ Guiding Sheath to the time that hemostasis was first observed.Time to ambulation, defined as when the subject can stand up and walk any distance
- Time to hospital discharge
  - Time to hospital discharge eligibility (when physician examines and if all is well, gives discharge orders).

  Method to achieve closure of the transradial artery access site

Quality of Life Assessments: Data will be also collected to evaluate health-related, quality-of-life in all subjects by administeringthe 36-item Short Form Health Survey (SF-36) and the EuroQOL-5 Dimension (EQ-5D) standardized, validated questionnaires to assess general and disease-specific outcomes. Brief descriptions of these two questionnaires are as follows

- The SF-36 is a patient-reported survey of general health and well-being. It consists of 36 items grouped in these dimensions: physical functioning, physical and emotional limitations, social functioning, bodily pain, general and mental health. Higher scores indicate better health status.
- The EQ-5D questionnaire is used for the assessment of health state utility and visual analog rating, which is a quantitative measure of overall health status. It consists of five (5) dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

8.4 Rationale for Study Endpoints

Each of the primary and secondary safety and/or efficacy endpoints above aligns with the primary objective of the study in evaluating acute safety and efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System,

when used with the BRITE TIP RADIANZ™ Guiding Sheath and SABERX RADIANZ™ PTA Balloon Catheter in treating femoropoliteal or iliac artery lesions via a radial artery approach.

Regarding the S.M.A.R.T. RADIANZ device in particular: since the investigational S.M.A.R.T. RADIANZ delivery system incorporates the CE marked S.M.A.R.T. stent, for which there is an abundance of short-term and long-term clinical data available from its evaluation in previous, Cordis-sponsored studies, the main purpose of this study is to assess the safety and performance (outcomes) of the delivery system versus the stent. There is proven, long-term primary patency through 10 years and low stent fracture rate through 3 years following implantation of the S.M.A.R.T. stent. Therefore, rates of vessel patency, restenosis, stent fractures, etc. have not been included as pre-specified endpoints for this study.

The various health economic endpoints will be used to determine if there are cost savings/benefits, such as decreased procedural/treatment and hospitalization costs, for patients who are eligible for and undergo procedures that can be completed via a transradial versus transfemoral arterial approach. General and disease-specific outcomes assessed via the SF-36 and EQ-5D standarized, validated questionnaires will help determine if there is overall, improved quality-of-life in the short-term in patients that undergo stenting procedures via transradial approach to 30 days post-procedure.

9 Informed Consent

Prior to enrollment and performance of any study-specific activities or procedures, the study team shall:

1. Provide each prospective subject with a full explanation of the study (including all potential benefits and risks) that is also documented (i.e., informed consent form) and ensure they have understood all information that has been presented to them.

    a. The informed consent form (ICF) should enable the subject to understand:
        i. the nature, objectives, benefits, implications, risks and inconveniences of the clinical investigation;
        ii. the subject's rights and guarantees regarding his/her protection, in particular his/her right to refuse to participate in and the right to withdraw from the clinical investigation at any time without any resulting detriment and without having to provide any justification;
        iii. the conditions under which the clinical investigations are to be conducted, including the expected duration of the subject's participation in the clinical investigation; and
        iv. the possible treatment alternatives, including the follow-up measures if the participation of the subject in the clinical investigation is discontinued.
    b. The ICF shall:
        i. Be comprehensive, concise, clear, relevant and understandable to the subject;
        ii. Be provided in a prior interview with a member of the clinical investigation team who is appropriately qualified under national law and delegated to this responsibility; gives special attention to the information needs of specific patient populations and individual subjects as well as to the methods used to provide the information; verifies the subject has understood the information;
        iii. Include information about an applicable damage compensation system; and
        iv. Include the unique, study identification number and information about the availability of clinical study results to the subject, to the extent possible, via a clinical study report and summary presented in terms understandable to the intended user, irrespective of the outcome of the clinical study.

2. Allow adequate time for the prospective subject to read the most current EC-approved informed consent form (ICF) and consider participation in the study and for addressing any/all of their questions.

3. Obtain documented consent [handwritten or electronic (if applicable) signature and date on the ICF] from the prospective subject after it is certain they understand all implications of participating in the study. The ICF shall also be signed by the Investigator or person performing the interview. Alternatively, in situations where the subject is unable to write, consent may be provided in the presence of at least one impartial witness, who shall sign and date the ICF.

The reflection period (time between explaining the study/providing written information to the prospective subject and obtaining documented consent) can vary based on individual circumstances, but should be at least 24 hours in duration or per standard practice or institutional policies at each site.

A copy of the ICF (or other record by which informed consent had been provided) that is signed by the subject and the Investigator and/or designee obtaining consent will be provided to the subject.

The Investigator and/or designee must clearly document the process for obtaining informed consent, including the date and time of obtaining consent, in the subject's medical record. It is the Investigator's responsibility to ensure that the informed consent process is performed in accordance with ICH-GCP applicable international standards and all applicable local and federal regulations.

Documented informed consent must be obtained within 60 days prior to the index procedure.

Exceptions to obtaining documented informed consent prior to the initiation of study-specific procedures would be in cases where necessary to eliminate an immediate apparent hazard and protect the life or physical well-being of a study subject, as determined by the investigator. See section 15.5.3 (Emergency Deviations). In such cases, informed consent must be obtained from the subject following the same process as described above as soon as possible following the index procedure.

10 Screening and Enrollment

10.1 Overall Process

The sequence of steps in the evaluation of potential patients for study enrollment is described as follows and diagrammed in **Figure 1**. Refer to **Section 7** for a list of all inclusion and exclusion criteria.

1. **Pre-Screening**: The potential patient will be evaluated against all inclusion and exclusion criteria that can be assessed via review of their medical records.
2. **Informed Consen**t: A patient who is shown to qualify for the study based on medical record review alone will be asked to provide documented informed consent to participate in the study as described in **Section 9**.
3. **Screenin**g: A patient who provides informed consent will be evaluated against all other inclusion and exclusion criteria via study-specific assessments performed through the time of index procedure (i.e., angiography).
4. **Enrollmen**t: A patient who meets all criteria as outlined in **Section 10.3** can be enrolled into the study.

Figure 1: Patient Evaluation Process

10.2 Pre-Screening and Screening

10.2.1 *Data Collection and Assessments*

In addition to obtaining documented informed consent within 60 days prior to the index procedure, the following must be (except as indicated below) performed or obtained. Subjects will be verified to meet all inclusion criteria and none of the exclusion criteria prior to device implantation.

1. **Demographic Data:** Including but not limited to age, sex, weight, height, and race
2. **Medical/Surgical History:** Including but not limited to vascular and non-vascular clinical history, risk factors, medical and surgical cardiovascular background (i.e., history of cardiac, kidney or peripheral vascular disease, diabetes, hypertension, bleeding history, hypercholesterolemia, TIA, stroke, renal insufficiency, allergies, tobacco use)
3. **Physical Examination:** Complete review of systems must be completed within seven (7) days prior to the day of the index procedure
4. **Concomitant Medications (recommended):** Aspirin AND either Clopidogrel bisulfate (Plavix®) or Ticlopidine (Ticlid®). Please see **section 11.5.**
5. **Laboratory Evaluations:** Non-fasting results are acceptable. The patient should be adequately hydrated prior to obtaining laboratory tests. The following tests must be completed within seven (7) days prior to the day of the index procedure.
    a. Glomerular filtration rate assessment
    b. Pregnancy test (if the patient is female and of child-bearing potential)
6. **Duplex Ultrasound**: This must be completed of the radial artery that will be used as the access site within seven (7) days prior to the day of the index procedure. Refer to the Core Lab reference manual for guidelines on performing and submitting this assessment.
7. **Health-Related Quality of Life:** Assessed via the SF-36 and EQ-5D questionnaires that are completed by the subject or administered to the subject by a study team member at the site (if possible) within seven (7) days prior to the day of the index procedure.
8. **Baseline Angiography:** Performed at the time of index procedure

The baseline angiography (assessment 8) will be done at the time of the index procedure. The site's visual assessment from the baseline angiography will be used to determine the subject's eligibility for the study according to all anatomically-related inclusion/exclusion criteria, however, all angiograms will also be sent to the core lab for further analysis.

10.2.2 *Screen Failures & Pre-Screen Failures*

Pre-screen Failures: Pre-screen failures are defined as patients who are confirmed to not qualify for study participation according to the eligibility criteria after review of their medical records (i.e., prior to providing informed consent). Such subjects will neither be treated with the study devices nor followed per protocol.

Screen Failures: Any consented patient who is confirmed to not qualify for study participation according to the eligibility criteria will be considered a screen failure and will neither be treated with the study devices nor followed per protocol.

Signed informed consent forms and all applicable documentation including source records indicating rationale for screen failure classification and Screening/Enrollment logs or equivalent forms/screens in the Electronic Data Capture (EDC) system will be reviewed during monitoring visits for all screen failure patients.

10.2.3 *Duration*

The screening of potential patients for this study is anticipated to occur over a 4-6 month period.

10.3 Enrollment

The subject will be considered enrolled into the study after ALL of the following criteria have been met:

- ICF has been signed/dated by all parties
- All pre-screening and screening assessments have been completed
- Vascular access has been obtained in the radial artery (i.e., time of puncture)
- Subject has been assessed by the site against all study eligibility criteria, including those determined by angiography

11 Treatment Plan

11.1 Index Procedure

The Instructions for Use (IFU) provides detailed information on the product, safety, storage, design, deliverability, and sizing specifications for all three (3) devices: S.M.A.R.T. RADIANZ, BRITE TIP RADIANZ and SABERX RADIANZ. All information within the IFU for each device should be reviewed prior to initiation of the index procedure and implantation of the study stent.

NOTE: Left side radial artery access is recommended/preferred for all subjects.

NOTE: There is currently no data available to support use of the study devices via the distal radial artery as the access site.

CAUTION: The height of each subject must be considered to ensure the S.M.A.R.T. RADIANZ delivery system is adequate in length to be tracked to the site of the target lesion.

1. **Initial Angioplasty using SABERX RADIANZ PTA Balloon Catheter (if appropriate)**
   a. An angioplasty balloon catheter should be selected to correspond to the diameter of the superficial femoral artery proximal to the lesion. The side arm of the introducer should be connected to a pressure transducer to record the arterial pressure distal to the obstruction. An initial dilation of the lesion should be made with an appropriately sized balloon catheter. Whenever there is doubt about the dispensability of the lesion, the smallest appropriate balloon catheter should be used for the initial dilatation.
   Note: Stent placement is not indicated if the primary angioplasty is not technically successful. A technically successful angioplasty is one in which the guidewire and dilation catheter are passed through the lesion and dilatation of the lesion produces a lumen adequate to accommodate introduction of the stent delivery system.

b. Following dilatation of the lesion, an arteriographic image should be recorded in order to determine the adequacy of the primary procedure.

2. Select S.M.A.R.T. Stent Size

a. Measure the length of the target lesion to determine the length of stent(s) required, as per Table 3. Size the stent length(s) to extend slightly proximal and distal to the lesion.
b. The appropriate stent length(s) should be selected to cover the entire length of the lesion.
c. The appropriate unconstrained stent diameter should be selected based on the vessel lumen diameter as per
Table 6.

Table 6: Stent Size Selection Guide

Vessel Lumen Diameter	Unconstrained Stent Diameter
4.0 – 5.0 mm	6 mm
5.0 – 6.0 mm	7 mm
6.0 – 7.0 mm	8 mm
7.0 – 8.0 mm	9 mm
8.0 – 9.0 mm	10 mm
Note: Refer to product labeling for stent length information	

3. Insertion of BRITE TIP RADIANZ Guiding Sheath or Guide Catheter and Guidewire

a. Access the treatment site utilizing the appropriate accessory equipment compatible with the 6F (2.0 mm) delivery system.
b. Place a 6F guiding sheath of an appropriate length (110cm for a 150cm long delivery system and a 135cm for a 190cm long delivery system) with an internal diameter of at least 2.2 mm.
c. Place an .018” (0.46 mm) guidewire of sufficient length across the lesion to be stented via the guiding sheath or guide catheter.

4. Dilation of Lesion with SABERX RADIANZ PTA Balloon Catheter (if appropriate)

a. Pre-dilate the lesion using standard PTA balloon catheter techniques.
b. Remove the PTA balloon catheter from the patient while maintaining lesion access with the guidewire.

5. Stent Deployment

a. Verify that the delivery system’s radiopaque stent markers (leading and trailing ends) are proximal and distal to the target lesion.

b. Initiate stent deployment by rotating the thumbwheel in a clockwise direction while holding the handle in a fixed position.
c. While using fluoroscopy, maintain position of the radiopaque stent markers relative to the target lesion site. Watch for the distal radiopaque markers to begin separating. Separation of the distal stent markers signals that the stent is deploying. Continue turning the tuning dial to cause further separation of the distal radiopaque markers until the distal end of the stent obtains full wall apposition.
d. Deployment is complete when the proximal markers oppose the vessel wall and the outer sheath radiopaque marker is proximal to the support member stent stop.

6. **Post-deployment Stent Dilatation with SABERX RADIANZ PTA Balloon Catheter (if appropriate)**
   a. While using fluoroscopy, withdraw the entire delivery system as one unit, over the guidewire, into the guiding sheath and out of the body. Remove the delivery device from the guidewire. Do not rotate the handle during withdrawal.
   b. Using fluoroscopy, visualize the stent to verify full deployment. Post-deployment balloon dilatation can be performed within the stent at any point along the lesion where there was incomplete expansion.
   c. Select an appropriate size PTA balloon catheter, dilate the lesion with conventional technique and remove the PTA balloon from the patient.

7. **Post Stent Placement**
   a. Remove the guidewire and sheath from the body.
   b. Close entry wound as appropriate.

NOTE: It is required to use S.M.A.R.T. RADIANZ as the stent delivery system, BRITE TIP RADIANZ as the guiding sheath and SABERX RADIANZ as the PTA balloon catheter (if pre-dilation and/or post-dilatation is performed) during the index procedure to be able to adequately evaluate the performance of all three (3) devices.

Though subjects are considered enrolled only from the time they are confirmed to qualify for study participation according to the eligibility criteria (i.e., upon completion of angiography), all events for enrolled subjects, which include all adverse events and device deficiencies, will be reported retroactive to when vascular access was established in the radial artery (i.e., time of puncture), in the case of adverse events, or initial use or handling of a study device, in the case of device deficiencies.

11.2 Treatment of Bilateral Stenosis

A patient with bilateral stenosis (lesions in both limbs) can have both lesions treated without a waiting period (e.g., during the index procedure). In all cases, a lesion on the second/contralateral limb can **ONLY** be treated with the study devices, via transradial approach and if it meets all applicable study eligibility criteria.

11.3 Treatment Failures

In the event of a device deficiency, detailed information on the product, circumstances of the deficiency as well as any complications and their management will be collected and reported to the sponsor, as described in Section 13.6.

Failure to implant the assigned study device will be recorded on the CRF as a treatment failure. In the event of a treatment failure, each site will follow their standard-of-care procedures (and/or use commercially-available products) to ensure the safety of the subject.

Any subject enrolled in this clinical study that does not receive the study device (S.M.A.R.T. stent) will be followed to 30 days post-procedure to be monitored for safety (adverse events and overall health) but will not be required to complete any of the study-specific procedures/assessments scheduled for the 30-day follow-up visit. If applicable, the Investigator must return any malfunctioned/damaged/unused investigational devices to the sponsor or its designee in accordance with the instructions provided.

11.4 Post-Procedure Care/Discharge (+7 days)

Following the index procedure, the site will notify the sponsor of the subject enrollment status (i.e., whether the subject was enrolled or was a screen failure).

In addition to the standard-of-care procedures at each participating site, all subjects will undergo these assessments at time of discharge (+ 7 days):

1. **Concomitant Medications (recommended):**
   Post Procedure: Clopidogrel bisulfate (Plavix®) – 75 mg qd
   or
   Ticlopidine (Ticlid®) – 250 mg b.i.d.

   After Discharge: Aspirin – 75-325 mg qd indefinitely
   Clopidogrel bisulfate (Plavix®) – 75 mg qd for at least 30 days

   or
   Ticlopidine (Ticlid®) – 250 mg b.i.d. for at least 30 days
2. **Adverse Event Monitoring**
3. **Quality of Life Assessment:** SF-36 & EQ-5D
4. **Duplex Ultrasound*:** This must be completed of the radial artery that was used as the access site during the index procedure. Refer to the Core Lab reference manual for guidelines on performing and submitting this assessment.

If a hospital's standard-of-care requires additional imaging assessments prior to discharge that are not required per the study protocol, copies should be sent to the Core Lab.

Upon discharge, subjects must be given a Stent Implant Card with specific "MR Conditional" information included.

* **Post-procedure duplex ultrasound can be completed any time between discharge and the 30-day follow-up visit per standard practice. If not standard-of-care at the site, this assessment must be completed at discharge.**

11.5 Recommended Medication Regimen

Pre-Procedure	Aspirin AND Clopidogrel bisulfate (Plavix®) OR Ticlopidine (Ticlid®)	75-325 mg (non-enteric coated water soluble) starting at least 24 hours prior to procedure Loading dose of 300-375 mg within 24 hours pre-procedure Loading dose of 250 mg within 24 hours pre-procedure
During Procedure	Heparin (If administered)	Initial bolus IV with additional boluses to maintain an activated clotting time (ACT) > 250 seconds
Post-Procedure	Clopidogrel bisulfate (Plavix®) OR Ticlopidine (Ticlid®)	75 mg qd 250 mg b.i.d.
After Discharge	Aspirin AND Clopidogrel bisulfate (Plavix®) OR Ticlopidine (Ticlid®)	75-325 mg qd indefinitely 75 mg qd for at least 30 days 250 mg b.i.d. for at least 30 days

The above medications are NOT required. An alternative medication regimen that is standard of care at the institution may be used instead. Any medications utilized must adhere to the recommendation specified by each medication's package insert.

11.6 Follow-up Visit/Assessments

Subjects are required to complete the follow-up visit at 30 days (+/- 7 days) post-procedure **at the investigational site (study institution/office/clinic)**. The following assessments will be completed at this visit:

1. **Concomitant Medications Assessment**
2. **Adverse Event Monitoring**
3. **Quality of Life Assessment:** SF-36 & EQ-5D

NOTE: Please refer to section 11.4 for the requirements and timing of a duplex ultrasound of the radial artery to be done post-procedure.

11.7 Telephone/Virtual Follow-Up

The 30-day follow-up visit may be conducted by telephone or other virtual means of communication (i.e., audio/video conferencing) **ONLY in exceptional circumstances** (e.g., due to COVID infection). If the visit is conducted by telephone/virtually, concomitant medications, safety information and quality of life assessment (SF-36 and EQ-5D) data should be collected from the subject or from a friend/family member, if possible.

Every occurrence of a telephone/virtual 30-day follow-up visit will be captured as a protocol deviation with an explanation recorded as to why the visit was not completed at the site (e.g., due to COVID infection).

11.8 Lost to Follow-up

For all active subjects, the site must first make three (3) telephone contact attempts to reach the subject for the 30-day follow-up visit. If unsuccessful, the Investigator must then send a certified letter to the subject. All contact attempts must be adequately documented in the subject's source documents. When possible, the patient's primary care physician should also be asked for assistance with contacting the subject.

The subject will be considered lost to-follow-up only under the following circumstances:

- The site learns that all methods of contacting the subject are no longer viable (e.g., telephone number not in service, no forwarding address provided, no current/correct contact information available from the patient's primary care physician).
- The site fails to reach/hear from the subject for the 30-day follow-up visit after all required contact attempts have been made using a valid telephone number and address on record.

11.9 Unscheduled Visits

Unscheduled follow-up visits may be required to ensure the safety of study subjects. All complications and adverse events will be evaluated by the Investigator and reported according to sponsor and EC regulations.

If an unscheduled follow-up visit is required, the site study team will assess if the subject has undergone any interventional treatment or experienced any adverse events since the last protocol-specified visit and will record such information on the appropriate CRF pages. Any additional imaging obtained must be forwarded to the Core Lab. All relevant information required to assess any adverse event reported should be maintained in the subject's medical records and all relevant documentation required for event adjudication should be provided as requested by the sponsor.

Assessments that may be completed at an unscheduled visit include, but are not limited to, the following:

1. **Concomitant medications**
2. **Physical examination**
3. **Imaging studies**
4. **Adverse event monitoring**
5. **Quality of Life Assessment:** SF-36 & EQ-5D

11.10 Subject Study Exit/Discontinuation

Every subject should be encouraged to remain in the study until they have completed the final, protocol-required, follow-up visit at 30 +/- 7 days post-procedure.

As required, the investigator(s)/institution(s) will arrange for the care of subjects after their participation in the study has ended, per institutional standard-of-care and/or the investigator's best clinical judgement.

If subject participation is prematurely discontinued, the reason for such must be documented in the subject's source documents and the CRF. Possible reasons for a subject's early exit from the study may include, but are not limited to, the following:

- Withdrawal of consent – Subject decides to withdraw from the study. This decision must be "independent" (i.e., made by the subject). The reason for withdrawal of consent should also be inquired from the subject and documented if provided.
- Physician discretion – The Investigator may choose to withdraw a subject from the study for reasons which include, but are not limited to, safety concerns. A detailed reason for the withdrawal should be documented.
- Death

- Lost to follow-up – all methods of contacting the subject are no longer viable or the subject is unable to be reached, or heard back from, to complete the 30-day follow-up visit

Subjects who discontinue early from the study will not be replaced and cannot re-enter the study. The investigator(s)/institution(s) must arrange for any continued safety monitoring, treatment and/or follow-up of subjects who withdraw/are withdrawn from the study or determined as lost to follow-up as per standard-of-care/best clinical judgement, unless it has been determined by the Investigator that the continued follow-up may jeopardize the rights, safety, and/or welfare of the subject. The investigator(s)/institution(s) must also maintain traceability of the study device that has been implanted in each of these subjects in the event they are to report any safety-related events or complaints attributed to the study device to the sponsor.

11.11 End of Study

The clinical study will be considered complete when the last enrolled subject has completed the 30-day follow-up visit or protocol-required assessment or has otherwise exited the study.

The sponsor will provide end-of-study notification to all Member States in which the clinical study was conducted within 15 days of the end of the clinical study across all Member States.

12 Core Laboratory

All sites will be required to submit the duplex ultrasound and baseline angiogram at the time of screening/index procedure and any imaging of the same type obtained at other timepoints such as from unscheduled visits or per routine, standard-of-care until the time of subject exit, for independent review and analysis by a core laboratory.

Instructions for filming technique and film submission will be provided as part of the Study Reference Manual.

13 Safety Reporting

Any person who identifies an event or information that could impact subjects', users', or other persons' safety has an obligation to inform the Investigator and the sponsor of their concerns.

13.1 Adverse Events

An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device and whether or not anticipated. Therefore, all anticipated adverse events listed in **section 13.2** are included within the scope of overall AE reporting requirements.

In this study, the investigational products are:

- S.M.A.R.T. RADIANZ
- 9 and 10 mm diameters of SABERX RADIANZ

Though subjects are considered enrolled only from the time they are confirmed to qualify for study participation according to the eligibility criteria (i.e., upon completion of angiography), all adverse events for all enrolled subjects, including those from the "roll-in" cohort of the study, will be reported retroactive to when vascular access was established in the radial artery (i.e., time of puncture) until their exit from the study (i.e., point of study completion or premature discontinuation). Each new AE or change to a previously

reported AE (based on any new findings) will be recorded and followed until resolution or stabilization of the event or until the subject has exited the study.

Subjects should be encouraged to report AEs spontaneously and may volunteer information at any time. At each evaluation, the Investigator will assess if an adverse event has occurred and will obtain all information required to complete the appropriate AE CRF(s). If an event occurs at an outside institution, the Investigator should obtain all or as much of the required AE information as possible.

For each AE, the Investigator should report at a minimum, the term/description, start/end dates, severity, serious/non-serious classification, treatment and outcome of the AE and determine its causality/association to the study devices or study procedures. During causality assessment, clinical judgement shall be used and the relevant documents, such as the Investigator's Brochure or the study protocol shall be consulted, as all the foreseeable SAEs and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

The following categorizations will be used when reporting the severity and causality for AEs:

Severity:

- Mild: Awareness of a sign or symptom that does not interfere with the subject's usual activity or is transient, resolved without treatment and with no sequelae;
- Moderate: Interferes, but does not hinder the subject's usual activity and may require treatment;
- Severe: Symptom(s) causing severe discomfort and significant impact of the subject's usual activity and requires treatment or intervention.

Causality:

- Not related: Relationship to the study devices or procedures can be excluded when:
  - the event has no temporal relationship with the use of the study devices, or the procedures related to application of the study devices
  - the adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
  - the discontinuation of medical device application or the reduction of the level of activation/exposure, when clinically feasible, and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the AE;
  - the event involves a body-site or an organ that cannot be affected by the device or procedure;
  - the serious adverse event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
  - the event does not depend on a false result given by the study device used for diagnosis, when applicable;

In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the AE.

- Possible: The relationship with the use of the study device or the procedures is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
- Probable: The relationship with the use of the study device or the procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

  Causal relationship: The AE is associated with the study device or procedures beyond reasonable doubt when: - the AE is a known side effect of the product category the device belongs to or of similar devices and procedures;

  - the AE has a temporal relationship with study device use/application or procedures;

  - the AE involves a body-site or organ:
    - to which the study devices or procedures are applied;
    - on which the study devices or procedures have an effect;

  - the AE follows a known response pattern to the medical device (if the response pattern is previously known);

  - the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the AE (when clinically feasible);

  - other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;

  - harm to the subject is due to error in use;

  - the AE depends on a false result given by the study devices used for diagnosis, when applicable;

  In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of devices/procedures and the AE.

The sponsor and the investigators will distinguish between AEs related to the study devices and those related to the procedures (any procedure specific to the clinical investigation). An AE can be related both to procedures and the study devices. Complications caused by concomitant treatments not required by the study protocol or routine diagnostic or patient management procedures applied to patients regardless of the study protocol are considered not related. If routine procedures are not required by the study protocol, complications caused by them are also considered not related. In some particular cases, the AE may not be adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The sponsor and the Investigators will make the maximum effort to define and categorize the event and avoid these situations.

The sponsor/designee will review/screen source documents during on-site and/or remote interim monitoring visits (IMV) to ensure any new adverse events or changes to previously-reported adverse events have been reported appropriately by the study site or otherwise, request they be promptly reported.

13.2 Anticipated Adverse Events

The following is a list of anticipated AEs categorized by occurrence (Improbable, Remote, Occasional, Probable, Frequent) for S.M.A.R.T. RADIANZ™ Vascular Stent System.

Occurrence Rate: Improbable, <0.002%

- Abrupt closure
- Access failure
- Access site complications
- Allergic/anaphylactoid reaction to anticoagulant and/or antithrombotic therapy or contrast medium
- Allergic reaction to nitinol
- Allergic reaction
- Amputation
- Anemia/blood loss
- Arrhythmia
- Blue toe syndrome
- Bradycardia
- Worsened claudication or rest pain
- Death
- Encephalopathy (new or worse) (altered mental state or confusion)
- Fever
- Fistulization
- Gangrene
- Gastrointestinal bleed from anticoagulation/antiplatelet medication
- Hematoma
- Hemorrhage
- Hypotension/hypertension
- Iliac artery spasm
- Infection
- Infection and/or sepsis
- Intimal tear/dissection
- Ischemia
- Multi-organ failure
- Muscle hemorrhage
- Pain
- Pneumothorax
- Pseudoaneurysm
- Renal failure
- Respiratory arrest
- Sepsis
- Stent embolization
- Stent migration
- Stent occlusion
- Stroke
- Transient Ischemic Attack (TIA)
- Trauma to adjacent structures
- Worsened claudication or rest pain

Occurrence Rate: Remote, 0.002%-<0.02%

- Aneurysm
- Angina/coronary ischemia/myocardial infarction
- Arterial restenosis
- Arterial stenosis or dissection
- Arteriosclerosis
- Arteriovenous fistula
- Disseminated intravascular coagulation
- Edema, peripheral
- Embolism
- Emergent repeat hospital intervention or surgery
- Necrosis
- Restenosis of the stented segment
- Tissue necrosis
- Vascular injury, including perforation, rupture and dissection
- Vasospasm
- Vessel occlusion/thrombosis, puncture site (restenosis or recurrent stricture)

Occurrence Rate: Occasional, 0.02% to <1%
No risks

Occurrence Rate: Probable, 1% to <10%
No risks

Occurrence Rate: Frequent, >10%
No risks

*All hematoma events should be reported according to the EASY Hematoma Classification System presented in Appendix D.

The following is a list of anticipated AEs categorized by occurrence (Improbable, Remote, Occasional, Probable, Frequent), for the SABERX RADIANZ™ PTA Balloon Catheter.

Occurrence Rate: Improbable, <0.002%

- Acute Myocardial infarction
- Allergic reaction (device, contrast medium, and medications)
- Amputation
- Arrhythmias
- Arteriovenous fistula
- Bradycardia
- Death
- Hypotension/ hypertension
- Inflammation
- Infection / sepsis
- Neurological events, including peripheral nerve injury, transient ischemic attack, and/ or stroke
- Organ failure (single, multiple)
- Procedural complications: bleeding, hypotension, access site complications
- Pseudoaneurysm
- Renal failure
- Vascular complications (e.g. intimal tear, dissection, pseudoaneurysm, perforations, rupture, spasm, occlusion)

Occurrence Rate: Remote, 0.002% to <0.02%

- Abrupt vessel closure
- Access site complication
- Dissection
- Embolism
- Hematoma at puncture site
- Hemorrhage
- Ischemia
- Necrosis
- Pain
- Restenosis of the dilated vessel

Occurrence Rate: Occasional, 0.02% to <1%

- Potential for balloon burst and potential complications (rated burst pressure)

Occurrence Rate: Probable, 1% to <10%
No risks

Occurrence Rate: Frequent, >10%
No risks

*All hematoma events should be reported according to the EASY Hematoma Classification System presented in Appendix D.

13.3 Serious Adverse Events

A Serious Adverse Event (SAE) is any AE that led to any of the following:

a) death
b) serious deterioration in the health of the subject, that resulted in any of the following:
   - life-threatening illness or injury;
   - permanent impairment of a body structure or a body function;
   - hospitalization or prolongation of existing hospitalization;
   - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
   - chronic disease
c) fetal distress, fetal death or a congenital physical or mental impairment or birth defect

The Investigator must report all new SAEs or changes to previously-reported SAEs (based on any new findings), with whatever information is available at the time, to the sponsor and/or designee by any acceptable method as communicated by them, within 24 hours or one working day of first awareness of the event by any member of the site study team and provide any additional information as required by the sponsor/designee. Principally, such events may be reported through the EDC system within 24 hours or one working day of first awareness; if this is not possible, the event must still be reported in the EDC system as soon as possible. In the case of death, all available information, e.g., autopsy or other post-mortem findings, including causality/association to the investigational product, should be provided. The medical monitor of this study will decide if more follow-up information is needed in case the event is not resolved at the time of subject exit from the study.

The Investigator or Contract Research Organization (CRO) shall notify the EC of the institution at which SAEs occurred (and/or the ECs of other participating institutions) in accordance with institutional requirements.

SAEs will be recorded and followed until resolution or stabilization of the event or until the subject has exited the study.

13.4 Major Adverse Events

Certain significant SAEs are also classified as Major Adverse Events (MAE). For this study, an MAE is defined as any event which resulted in one of the following:

- Death
- Index Limb Amputation
- Target Lesion Revascularization

The Investigator must report all new MAEs or changes to previously-reported MAEs (based on any new findings), with whatever information is available at the time, to the sponsor and/or designee by any acceptable method as communicated by them, within 24 hours or one working day of first awareness of the event by the study team at the institution and provide any additional information as required by the sponsor/designee. If the event is not reported through the EDC system within this time period, it must be done so as soon as possible. In the case of death, all available information, e.g., autopsy or other post-mortem findings, including causality/association to the investigational product, should be provided. The medical monitor of this study will decide if more follow-up information is needed in case the event is not resolved at the time of subject exit from the study.

The Investigator or CRO shall notify the EC of the institution at which MAEs occurred (and/or the ECs of other participating institutions) in accordance with institutional requirements.

MAEs will be recorded and followed until resolution or stabilization of the event or until the subject has exited the study.

13.5 Unanticipated Serious Adverse Device Effects

An Unanticipated Serious Adverse Device Effect (USADE) is a serious AE (adverse effect) related to the use of a study device which by its nature, incidence, severity or outcome has not been identified in the current risk assessment or any other unanticipated serious problem associated with a study device that relates to the rights, safety, or welfare of subjects. Procedures associated with the use of a device should be addressed in the risk assessment, which makes it possible to determine whether the procedure-related SAEs are USADEs or not. SAEs related to procedures required in this study but not with the use of the device should not be considered USADEs.

The Investigator must report all potential new USADEs or changes to previously-reported USADEs (based on any new findings), with whatever information is available at the time, to the sponsor and/or designee by any acceptable method as communicated by them, within 24 hours or one working day of first awareness of the event by the study team at the institution and provide any additional information as required by the sponsor/designee. If the event is not reported through the EDC system within this time period, it must be done so as soon as possible. In the case of death, all available information, e.g., autopsy or other post-mortem findings, including causality/association to the investigational product, should be provided. The medical monitor of this study will decide if more follow-up information is needed in case the event is not resolved at the time of subject exit from the study.

The Investigator or CRO shall notify the EC of the institution at which USADEs occurred (and/or the ECs of other participating institutions) in accordance with institutional requirements.

USADEs will be recorded and followed until resolution or stabilization of the event or until the subject has exited the study.

13.6 Device Deficiencies

A device deficiency is any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including device malfunction, use errors or inadequacy in information supplied by the manufacturer.

- A device malfunction is considered a failure of a device to meet any of its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the Instructions for Use (IFU)/Investigator's Brochure (IB)/clinical study protocol.

In the event of a device deficiency, detailed information on the product, circumstances of the deficiency as well as any complications and their management will be collected and reported.

Though subjects are considered enrolled only from the time they are confirmed to qualify for study participation according to the eligibility criteria (i.e., upon completion of angiography), all device deficiencies for all enrolled subjects, including those from the "roll-in" cohort of the study, will be reported retroactive to the initial use or handling of a study device until their exit from the study (i.e., point of study completion or premature discontinuation).

The Investigator must report all new device deficiencies or changes to previously-reported device deficiencies (based on any new findings), with whatever information is available at the time, to the sponsor and/or designee by any acceptable method as communicated by them, within 24 hours or one working day of first awareness of the event by the study team at the institution and provide any additional information as required by the sponsor/designee. If the event is not reported through the EDC system within this time

period, it must be done so as soon as possible. If applicable, the Investigator must make arrangements for the safe return of any malfunctioned, damaged, and/or unused investigational devices in accordance with the instructions provided by the sponsor.

13.7 Complaints for CE Marked Product

AEs and device deficiencies that occur with approved (CE marked) product used in accordance with the Instructions for Use (i.e., within the scope of its intended use) will be considered as "complaints". In other words, complaints for CE marked product are considered the equivalent of AEs and device deficiencies for investigational product. **Therefore, the criteria used to categorize all complaints for CE marked product by type and the timeframes and methods for recording and reporting each to the sponsor will be the same as they apply for all adverse events and device deficiencies reported for investigational product, as described in sections 13.1 through 13.6 above.**

In this study, the CE marked products are:

- BRITE TIP RADIANZ
- 8 mm and smaller diameters of SABERX RADIANZ

Since all sizes of the BRITE TIP RADIANZ device and all sizes of the SABERX RADIANZ device with an 8 mm or smaller diameter are CE marked, the anticipated events associated with use of these devices are the same as those that appear in the "Complications" section within the respective IFUs, which will be provided by the sponsor.

13.8 Reportable Events

13.8.1 *Investigational Product*

The following events are considered "reportable", which require immediate reporting from the sponsor (which can be the manufacturer, the legal representative or another contact person/entity established by the sponsor, if accepted by the Member State) to the National Competent Authorities (NCA)):

a) any SAE that has a causal relationship† with the investigational devices or the investigation procedure or where such causal relationship is reasonably possible;

b) any device deficiency that might have led to an SAE if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate;

c) any new findings in relation to any event referred to in points a) and b).

Even if it is not possible to report all new SAEs, MAEs, USADEs, device deficiencies and complaints for CE marked product or changes to such previously-reported events to the sponsor by any acceptable method within 24 hours or one working day of first awareness of the event by the study team at the institution, every effort must be made to ensure all events that meet the above criteria as "reportable", are still reported to the sponsor **no later than three (3) calendar days of first awareness by the study team**.

The sponsor will follow the below timelines for notifying NCAs of all reportable events for the investigational products used in this study, unless a different timeline or modality is agreed upon between the NCAs and sponsor:

- For all reportable events which indicate an imminent risk of death, serious injury, or serious illness and that require prompt remedial action for other subjects, users or other persons or a new finding to it: Immediately, but no later than two (2) calendar days after awareness by sponsor of a new reportable event or of new information in relation with an already reported event. This includes

† Possible, probable or causal relationship assigned to the SAE by either the sponsor or Investigator

events that are of significant and unexpected nature such that they become alarming as a potential public health hazard and includes the possibility of multiple deaths occurring at short intervals. These concerns may be identified by either the NCA or the manufacturer.

- Any other reportable events or a new finding/update to it: Immediately, but no later than seven (7) calendar days following the date of awareness by the sponsor of the new reportable event or of new information in relation with an already reported event.

The period for reporting shall take into account, the severity of the event. Where necessary to ensure timely reporting, the sponsor may submit an initial report that is incomplete followed up by a complete report.

Reportable events will be reported all at the same time to all NCAs where the clinical investigation is authorized to start or has commenced.

The reporting method (i.e., use of the Summary Reporting Form) and above reporting timelines, as specified in the MDCG 2020-10/1 guidance entitled, "Safety Reporting in Clinical Investigations of Medical Devices Under the Regulation (EU) 2017/745" (October 2022) will be followed in the process for notifying the NCAs of all reportable events.

Individual countries may also require separate and similar reporting to the Ethics Committee(s) of participating institutions in those countries.

13.8.2 *CE Marked Product*

Any SAE or device deficiency that might have led to an SAE that is related to CE marked product used in this study is "reportable" if there is a causal (or reasonably possible) relationship to the device or the investigation procedure, in which case the sponsor would follow the same reporting procedures and timelines as they apply for investigational product (see **section 13.8.1**) in addition to following the normal vigilance reporting procedures for CE marked product (see **section 13.9**).

13.9 Post-Market Surveillance and Vigilance

13.9.1 *Reporting Serious Incidents and Field Safety Corrective Actions*

For the CE marked devices used in this study, the sponsor will report to the relevant NCAs, any serious incidents or potentially reportable serious incidents involving these devices and any field safety corrective actions with respect to these devices and perform a follow-up analysis of such serious incident or field safety corrective action (see **Section 13.9.3**). The period for reporting shall take into account, the severity of the event. Where necessary to ensure timely reporting, the sponsor may submit an initial report that is incomplete followed up by a complete report.

- The sponsor shall report the serious incident or potentially reportable serious incident immediately, and no later than 15 days, upon awareness of the incident and establishing the causal relationship between the incident and device or that such causal relationship is reasonably possible.
  - Additionally, the sponsor will report a serious public health threat immediately, and no later than two (2) days, upon awareness of the threat.
  - Additionally, the sponsor will report a death or unanticipated serious deterioration in a person's state of health immediately, and no later than 10 days, upon awareness of the serious incident and establishing or suspecting a causal relationship between the device and the serious incident.

- Except in urgent cases where it is necessary to undertake immediate field safety correction action, the sponsor will report the field safety correction action prior to it being undertaken.

- If agreed upon between the sponsor and NCAs, the sponsor may provide periodic summary reports in lieu of individual serious incident reports for similar serious incidents that occur with the same device or device type and for which the root cause has been identified or a field safety corrective action implemented or for which the incidents are common and well-documented.

If the sponsor considers an incident as NOT a serious incident or as an expected, undesirable side effect covered by trend reporting, it will provide an explanatory statement for review and consideration by the NCA. If the statement is not agreed to by the NCA, the sponsor may still be required to report the incident and perform a follow-up analysis.

13.9.2 *Trend Reporting*

For the CE marked devices, the sponsor will report to the NCAs, any statistically significant increase in the frequency or severity of **non-serious incidents or expected, undesirable side effects that could have a significant impact on the benefit-risk analysis** (i.e., have led or may lead to risks to the health or safety of patients, users or other persons that are unacceptable when weighed against the intended benefits), when compared to the foreseeable frequency or severity of such incidents during a specific period as per the technical documentation and product information. The management of these incidents, methods used for determining the statistically significant increase and observation period are described in the sponsor's Post-Market Surveillance Plan.

13.9.3 *Analysis of Serious Incidents and Field Safety Corrective Actions*

Following the reporting of a serious incident to the relevant NCAs, the sponsor will immediately perform the necessary investigations related to the serious incident and the CE marked devices concerned, which will include a risk assessment of the incident and field safety corrective action. Such investigations will NOT involve altering the device or a sample of the device lot/batch concerned in a way that may affect any subsequent evaluation of the causes of the incident, prior to informing the NCAs of such action. Upon request, the sponsor will provide the NCA with any documentation necessary for their conduct of a risk assessment. The sponsor will also provide a final report to the NCA with findings and conclusions from the investigation and where applicable, the corrective actions to be taken.

The sponsor will ensure that all users of the device in question are immediately notified of all information regarding the field safety corrective action taken via a field safety notice that is written in the official language(s) of the Member State/country in which the field safety correction action is taken. Except in urgent cases, the sponsor will submit the content of the draft field safety notice to the evaluating NCA (or where appropriate, the coordinating NCA) for comments. The field safety notice will clearly explain, without understating the level of risk, the reasons for the field safety corrective action with reference to the device malfunction and associated risks for patients, users or other persons, and will clearly indicate all actions to be taken by users.

13.10 Risk Assessment and Management

Risks arising during the course of this clinical study will be managed as follows:

1) Risks will be monitored against established risk acceptability thresholds.
2) When concerns have been recognized, a preliminary risk analysis will be performed and documented by the sponsor along with the Investigator and other advisors, as appropriate, and can result in one of the following outcomes:
   A. The new information is adequately reflected in the existing risk assessment and the individual and overall residual risks to subjects, users, or other persons remain acceptable.
   B. If a potential, unacceptable risk or serious health threat has been identified, the sponsor will suspend the clinical study immediately and notify all interested parties of the preliminary risk analysis while making appropriate arrangements for conducting a comprehensive risk assessment per ISO 14971. If appropriate, the Data and Safety Management Board (DSMB) (see **section 18.1**) or other expert

advisors will be requested to provide their input into the comprehensive risk assessment, which can result in one or more of the following outcomes:

i. The new information is adequately reflected in the existing risk assessment and individual and overall residual risks to subjects, users or other persons remain acceptable, in which case the sponsor will ensure a rationale is recorded in the clinical study documentation and necessary activities are performed before resuming the clinical study.
ii. Corrective actions can be applied, including the following:
    a. If the corrective actions do not affect the validity of the clinical study, the sponsor will revise the benefit-risk analysis to justify continuation of the clinical study and perform necessary activities before resuming the clinical study.
    b. If the corrective actions affect the validity of the clinical study, the sponsor will terminate the clinical study.
iii. Corrective actions cannot be applied, in which case the sponsor will terminate the clinical study.

Signals from adverse events or device deficiencies that might indicate a serious health threat can be detected by either the sponsor or investigator but are always evaluated by the sponsor.

A formal review of risks will be performed upon completion of this clinical study and incorporated into the risk analysis and clinical evaluation and an update of the benefit-risk conclusions made in both documents.

Additionally, the sponsor and/or designee, including but not limited to the clinical project manager, medical monitor and representatives from its post-market surveillance (complaint handling) groups will review information on individual, site-reported adverse events, device deficiencies and complaints and/or periodic listings of such events to assess for any trends, identify any new risks, etc. that may impact the safety of study subjects.

14 Statistics/Data Analyses

Previous clinical studies of therapeutic Iliac and femoropopliteal artery lesion stent treatments have focused on demonstrating the efficacy and safety of the stents under study. As such, the endpoints centered on how well the stent improved luminal diameter and any major adverse events associated with the stent treatment. There was little if any data captured on the stent delivery systems, or the access artery used in these studies.

The primary objective of the RADIANCY study is to evaluate acute safety and efficacy of the S.M.A.R.T. RADIANZ™ Vascular Stent System, when used with the BRITE TIP RADIANZ™ Guiding Sheath and SABERX RADIANZ™ PTA Balloon Catheter, in treating patients with obstructive iliac or femoropopliteal arterial disease via radial artery access. In other words, the focus of this study is on demonstrating the efficacy and safety of the RADIANZ delivery system when using radial artery access (as opposed to femoral artery) to deliver the S.M.A.R.T. stent to iliac and femoropopliteal artery lesions (previously approved indications for this stent). Therefore, the efficacy and safety endpoints for this study focus on access and delivery success and any adverse events associated with access and delivery. The aim of this study is to demonstrate the safety and effectiveness with which the new delivery system can access the radial artery to deliver the S.M.A.R.T. stent to obstructive iliac or femoropopliteal lesions.

14.1 Analysis Population

Analyses for the endpoints will be performed using the intent-to-treat (ITT) population. The ITT population will consist of all subjects enrolled in the study and for whom a device insertion was attempted, regardless of the treatment actually received.

The per-protocol analysis population is defined as a sub-group of the ITT population consisting of subjects without protocol deviations that could possibly affect the primary endpoints. Primary endpoint analysis using this population is supportive in nature.

14.2 Statistical Hypotheses for Endpoints

Effectiveness

The primary efficacy endpoint is technical success at the conclusion of the index procedure defined as successful insertion of the S.M.A.R.T. RADIANZ™ Vascular Stent System through the vasculature, successful deployment of the study device (S.M.A.R.T.™ stent) at the intended location, and successful withdrawal of the delivery system without conversion to femoral access.

The hypothesis being tested is:

Ho: $\pi \leq 0.93$

Vs

Ha: $\pi > 0.93$

where π is the proportion of limbs that are successfully treated with one or more S.M.A.R.T. RADIANZ™ Vascular Stent Systems.

Safety

The primary safety endpoint is the occurrence rate of device or procedure-related complications associated with transradial artery access through the time of hospital discharge.

The safety hypothesis being tested is:

Ho: $\pi \geq 0.07$

Vs

Ha: $\pi < 0.07$

where π is the proportion of subjects experiencing a radial access related complication.

14.3 Sample Size Determination

The statistical objective of this study is to assess the efficacy and safety of the primary endpoints. Approximately 129 of the 159 subjects enrolled in this study at approximately 15 sites will be included in the analyses of the primary safety and efficacy endpoints. The remaining cohort of approximately 30 subjects (consisting of the first two (2) enrolled subjects at each study site, as applicable) will define the "roll-in" cohort for the study. Such subjects will be pre-specified as "roll-in" subjects prior to their enrollment and must meet all criteria for enrollment, however, they will be followed up and evaluated to 30 days post-procedure only for safety and not included in any endpoint analyses. The intent of including a "roll-in" cohort is to enable lesser experienced investigators to gain training/experience with the study procedure and for all investigators to become better accustomed to the use of the various study devices.

The justification for this sample size is as follows:

Efficacy
It is assumed that the technical success rate will be 98%, which is derived from other studies using radial access procedures. The performance goal was also based on a literature review and was set at 93%. Using a one-sided exact 95% confidence interval calculated using the Clopper-Pearson method, a sample size of 129 limbs provides 88% power to demonstrate that the observed technical success rate is greater

than the performance goal of 93%. Given the acute, in-hospital nature of the endpoint, no adjustment for attrition was made.

Safety
It is assumed that the in-hospital device or procedure related radial artery complications will be 2% which is derived from other studies using radial access procedures. The performance goal was also based on a literature review and was set at 7%. Using a one-sided exact 95% confidence interval calculated using the Clopper-Pearson method, a sample size of 129 subjects provides 88% power to demonstrate that the observed complication rate is less than the performance goal of 7%. No adjustment for attrition was made.

To adequately assess the efficacy and safety of both iliac and femoropopliteal artery treatment under study a minimum of 30 subjects will be required for each artery treatment, i.e., a minimum of 30 iliac and minimum of 30 femoropopliteal arteries.

In order to characterize the safety and efficacy of the SABERX RADIANZ device, it is a goal of this study to collect information on 30 distinct uses of the device. This is a goal and not a minimum since use of the SABERX RADIANZ device is dictated by the attending physician. Ideally, the 30 uses will be evenly distributed between the iliac and femoropopliteal arteries.

14.4 Statistical Analysis Methods

Except where otherwise specified, the following general principles apply to the planned statistical analyses. All descriptive statistical analyses will be performed using SAS version 9.4 or higher, unless otherwise noted (SAS Institute Inc., Cary, NC) or other widely accepted statistical or graphical software as required. Derived variables will be independently verified by an independent programmer / statistician.

For categorical variables, the numerator, denominator, rate (%) and exact 95% CI will be calculated. For continuous variables, the median, mean, standard deviation, interquartile range, number of observations, minimum and maximum values, and 95% CI, as appropriate, will be presented.

For each parameter, the baseline value will be defined as the last non-missing value collected at the time closest to but before treatment with the investigational device.

Statistical tests of the primary endpoints will be performed at the one-sided 0.05 significance level.

Primary Analysis

Efficacy

A one-sided lower exact 95% CI for technical success rate will be calculated using the Clopper-Pearson method. The lower bound will be compared to the performance goal of 93%. If the lower bound is greater than the performance goal then this endpoint will have been successfully achieved. Technical success is defined in section 8.1 above.

This analysis will be done on a per limb basis since some subjects enrolled in the trial have bilateral lesions. Each lesion can be treated with up to two stents. In the case that two stents are used, success is based on successful insertion of each of the S.M.A.R.T. RADIANZ™ Vascular Stent System through the radial artery, successful deployment of both stents at the intended location and the successful withdrawal of both systems with no conversion to femoral access. While some subjects will present with bilateral lesions, the actual number of those subjects will be small. As such, each limb will be considered an independent observation for the purpose of analysis of this endpoint.

The same analysis will be completed on the per-protocol analysis population if that population is different from the ITT population.

Safety

A one-sided upper exact 95% CI for device or procedure-related radial artery complications rate will be calculated using the Clopper-Pearson method. The upper bound will be compared to the performance goal of 7%. If the upper bound is less than the performance goal, then this endpoint will have been successfully achieved. Complications related to radial access are defined in section 8.1 above.

Even though some subjects may contribute bilateral lesions, the safety analysis will be analyzed on a per subject basis.

The same analysis will be completed on the per-protocol analysis population if that population is different from the ITT population.

Trial success is defined as successful achievement of both the primary efficacy and the primary safety endpoints.

14.4.2 *Additional Analyses*

Secondary endpoints will be summarized using the statistical methods described in section 14.4. No formal hypothesis testing will be done on the secondary endpoints.

All secondary safety endpoints will be summarized on a per subject basis.

The secondary endpoint of technical success of the BRITE TIP RADIANZ™ Guiding Sheath will be summarized on a per subject basis since the guiding sheath would not be completely removed between lesion treatments of a bilateral subject.

Procedural success of the SABERX RADIANZ™ PTA Balloon Catheter will be summarized on a per limb basis. In cases where pre-dilation and post-dilatation are performed and/or more than one SABERX balloon was used to treat a lesion, each device must be successfully inserted into the peripheral vasculature through the radial artery, successfully inflated and deflated, and successful withdrawn with the achievement of a final residual diameter stenosis of < 30% for the treated lesion.

The additional data points of fluoroscopy time and procedural time, time to achieve hemostasis, time to ambulation, time to hospital discharge, time to hospital discharge eligibility, method to achieve closure and the scoring of the EQ-5D and SF-36 will be completed on a per subject basis.

Roll-in subjects will be summarized separately and are not part of any endpoint analysis.

A subgroup analysis on the primary endpoints may be performed by artery treated, i.e., iliac and femoropopliteal.

14.5 Missing Data

For both primary endpoints, a sensitivity analysis will be done where missing data is imputed using a worst-case scenario. Specifically, for the efficacy endpoint (technical success), missing data will be imputed as “unsuccessful.” Likewise, missing safety data will be imputed to indicate that the subject experienced a radial access-related AE.

For secondary endpoints, no imputation of missing data is planned since these endpoints are hypothesis-generating and not being used to expand labeling. Subjects who have ascertainment of status at a later out-of-window date (for example, subjects who are known to be free of events past discharge but missed

the discharge visit) are not considered missing as their status is known and their data will be used as noted previously.

14.6 Reporting

A final clinical summary (report) will be developed for this study upon completion of all subject follow-up visits/database lock for the last required follow-up visit in the study. This final report will be submitted to all relevant NCAs within one (1) year of end of study, as described in **section 11.11**.

A clinical investigation report will be submitted to all relevant NCAs within three (3) months of an early termination or temporary halt of the study.

This will be provided to the applicable regulatory authorities as well as all participating Investigators and eCs. Interim reports will also be developed and provided only as required.

15 Quality Control and Quality Assurance

15.1 Regulatory and Ethical Compliance

The sponsor maintains a quality management system with written Standard Operating Procedures (SOP) to ensure that clinical studies are conducted and data are generated, documented and reported in compliance with the study protocol and the requirements of ISO 14155:2020, ICH E6 R2 Good Clinical Practice, Regulation (EU) 2017/745 (including Annex XIV and Annex XV) and the requirements of all applicable regulatory authorities. The staff of Cordis is trained regularly to ensure adherence to these SOPs.

15.2 Data Quality Assurance

Study procedures to ensure the quality of all data collected and analyzed within this study include, but are not limited to, the following:

- Qualified Investigators, study sites and monitors will be selected.
- The investigational devices will be provided to Investigators/sites after being tested and released according to appropriate standards.
- Training:
    - Training will be provided to and documented for all Investigators and study team, which includes, but is not limited to, a review of the protocol, all study devices and the index procedure (via a hands-on demonstration using model devices) for the Investigators, CRFs, EDC system, GCP guidelines and study expectations. This training will be provided at or around the time of the site initiation visit and prior to the start of any study-related activities (especially the treatment/enrolment of any study subjects), and as necessary (e.g., when there are changes to the study team).
    - Training will be provided to all study monitors on the study protocol, background/therapeutic area and GCP-conforming monitoring activities. Monitors will receive project-specific monitoring conventions and all forms needed to document the monitoring activity (e.g., forms for monitoring reports, investigational product accountability).
- Approximately 30 subjects will be included in the “roll-in” cohort for the study to allow less experienced investigators to overcome the learning curve in performing the study procedure and for all investigators to become better accustomed/acclimated to the operation/use of all study devices through the first couple study subjects treated at their respective sites, but without including such subjects in endpoint analyses.
- Live case support during the study procedure may be provided for the first two (2) subjects enrolled at each study site and may be provided for any additional subjects, as deemed necessary.

- The sponsor and/or designee plans to conduct 100% source document verification, as specified in the sponsor's monitoring plan, by comparing original source documentation against the CRFs for all different types of source data. Any discrepancies identified will be resolved with the Investigator, or designee, as appropriate.
- Appropriate edit checks incorporated within the EDC system and periodic reviews of the data by Data Management will verify the completeness and accuracy of the data. Similar to the study monitor, Data Management will post queries to data points in need of further clarification and/or correction from sites and will keep the sponsor study team informed of the status of queries and completeness of the study database.
- The EDC vendor, Medrio, has policies in place governing data protection, privacy and security measures that are in compliance with regulations such as 21 CFR Part 11, Annex 11, Good Clinical Practice, General Data Protection Regulation (GDPR), CCPA, and HIPAA. It is expected that all investigational sites also have data privacy, protection and security policies and a General Data Protection Officer in place.
- Professional, independent core laboratories will be used for review and analysis of all site-submitted imaging and independent data review committees (Data Safety Monitoring Board and Clinical Events Committee) will be used to review aggregate study data and adjudicate certain events at periodic intervals.
- The laboratory analysis in this trial will be performed by routine techniques of the laboratory of the study center. Laboratory certification and normal range values will be obtained from each investigational site's laboratory.

The Investigator must produce/capture, review and maintain all study documents and data (including electronic source data) to ensure reliability, integrity, control and traceability. All documents must be identifiable, traceable and appropriately stored to provide a complete history of the study. The accuracy of all translations, if applicable, must be documented. The Investigator must also ensure accuracy, attribution, completeness, legibility and timeliness of all study data reported in the CRFs and in all required reports. If copies of the original source documents are on file, they must be certified via dated signature by a member of the study team or generated through a validated process.

The Investigator must ensure all trained study site team members are recorded and tracked via a Delegation of Authority log, which will include their names, initials, signatures and roles (functions).

15.3 Clinical Data

The case report form (CRF) for each subject is a record of their eligibility to enter the study, medical history, pre-procedure/baseline assessments, concomitant medications, all study devices used during the index procedure, all procedural complications, and adverse events as well as data from discharge, follow-up and any unscheduled visits. It is the obligation of each Investigator (or designee) to ensure that all source documents (e.g., medical files, clinic charts, diagnostic films, nursing files), are available to support all data points collected within the CRF for every screened and/or enrolled subject for verification by the study monitor(s). All information obtained during and between all protocol-required procedures needs to be clearly documented within the subject's source documentation and CRF. A printout of the CRFs **CANNOT** be used as source documentation.

Qualified study site team members trained to the protocol, CRFs and EDC system will perform primary data collection and data entry into the CRFs in a timely manner following subject enrollment and the completion of study-required assessments/follow-up visit at 30 days post-procedure. Data will be collected from subject'' hospital charts, imaging films, and/or other medical records, which the Investigator is responsible to ensure are adequate to support all CRF entries. Corrections to CRFs will be performed by the Investigator or other authorized study site personnel. A record of study site team members authorized to perform CRF data entry and/or corrections will be maintained by the site and provided to the sponsor.

The Investigator must sign and da”e th’ specified section(s) within the CRF to confirm that s/he has reviewed the data and that the data are complete and accurate.

15.4 Monitoring

The sponsor (and/or designee) will oversee the conduct and progress of the study at each investigational site. In addition to regular communications with the site, the sponsor will conduct on-site and/or remote interim monitoring visits (IMV) at periodic intervals to verify the following:

- The rights and well-being of the subjects are protected;
- The study is conducted according to International Council of Harmonization (ICH), applicable international standards and Good Clinical Practices (GCP) (ICH E6), the Declaration of Helsinki (1964) amended in Brazil 2013 and all national, state and local laws of the pertinent regulatory authorities;
- The study is conducted in compliance with all requirements identified within the approved protocol/ amendment(s);
- The data reported in the CRFs/EDC system are accurate, complete and verifiable from source documentation.

The study monitor will complete verification of the above primarily from review and assessment of regulatory documents; signed informed consent forms; accountability, records and storage of investigational product; and CRF/EDC system entries against all source documents. As mentioned in **section 15.2**, the sponsor and/or designee plans to conduct 100% source document verification, as specified in the sponsor’s monitoring plan, by comparing original source documentation against the CRFs for all different types of source data. Additionally, the sponsor/designee will review/screen source documents to ensure any new adverse events or changes to previously-reported adverse events have been reported appropriately by the study site or otherwise, request they be promptly reported.
The monitor will also post and address queries within the EDC system and discuss the conduct of the study with the Investigator and study team. CRFs would need to be completed in a timely manner, within 5 working days or 1 week, to ensure availability for IMVs. Complete details regarding the monitoring procedures followed for the study are described in the sponsor’s Monitoring Plan.

The Investigator must agree to provide study monitors with direct access to the office/clinic/facilities, medical records/source data/source documents for all enrolled subjects, regulatory documents and any/all other applicable study-related documents to enable the proper completion of IMVs.

IMVs will be conducted throughout the course of this study according to the sponsor’s Monitoring Plan. The IMV frequency is planned to be one IMV conducted approximately every 6-8 weeks during both the enrollment phase and acute follow-up period, however, will also be based on factors including, but not limited to, the rate and volume of enrollment, the timing of subjects completing follow-up visits and overall compliance by the investigational site.

Routine, on-site and/or remote closeout visits (COV) will be scheduled after completion of clinical site participation (i.e., all enrolled subjects completed final follow-up assessments as required per the protocol), premature discontinuation/termination of a study or site or deemed otherwise appropriate. They will be conducted to ensure that the Investigator’s records are complete, all documents needed for the sponsor’s files are retrieved, all remaining clinical investigation materials are disposed of, previously identified issues have been resolved, Investigator’s responsibilities and obligations have been addressed and all parties are notified.

Complete details regarding the monitoring procedures followed for the study are described in the sponsor’s Monitoring Plan.

15.5 Protocol Modifications

15.5.1 *Protocol Amendments*

Changes to the research covered by this protocol must be implemented through a formal protocol amendment. Change(s) to only logistical or administrative aspects of the study will be reflected in the study protocol if/when it is next amended to address any changes to the research. Protocol amendments may be initiated by the sponsor or at the request of the Investigator. In either case, however, all protocol amendments must be approved by the sponsor, signed and dated by the Investigator and approved by the respective NCA and EC prior to implementation. Depending on the nature of the changes reflected in the amended protocol, amendments to the ICF, CRF and/or IB, etc. may also be required with all applicable approvals obtained prior to implementation.

15.5.2 *Protocol Deviations/Noncompliance*

A protocol deviation is defined as a divergence from a specific element of the study protocol (e.g., missed assessment, visit out of window, violation of inclusion/exclusion criteria). Sites must comply with all requirements of the study protocol to control the number of protocol deviations to the extent possible. This does not include circumstances where necessary to eliminate an immediate hazard to study subjects (see section below) or that involve only logistical or administrative aspects of the study.

The study monitor will verify the conduct of the study is in compliance with the currently approved protocol at each site and will identify any deviations from the protocol. The study monitor will also determine if there are any other issues of noncompliance (e.g., with EC requirements, regulations from applicable regulatory authorities). If any protocol deviations or other areas of noncompliance are noted, the Investigator, site staff and/or study monitor will ensure corrective actions are implemented and evaluate the effectiveness of those corrective actions. Recurrence of noncompliance may require development of a formal corrective action plan that includes a suspension in enrollment and/or other actions. All protocol deviations and other issues of noncompliance at a site will be monitored closely by the sponsor and/or designee(s) and will be reported to the applicable regulatory authorities and/or the EC, as required.

No protocol waivers will be issued by the sponsor for this study.

15.5.3 *Emergency Deviations*

Emergency deviations would occur only in cases where the change is necessary to eliminate an immediate apparent hazard and protect the life or physical well-being of a study subject. Such cases must be reported to the sponsor/Medical Monitor and the EC in writing within five (5) working days of the occurrence and will still be entered as protocol deviations in the CRF.

15.6 Audits

The sponsor and/or designee and the FDA may contact the participating institution to inform the Investigator of an upcoming audit and/or inspection, which may be routine or “for cause”. In the event the Investigator receives notification from FDA of an audit/inspection for this study, the Investigator should immediately notify the sponsor.

The Investigator must agree to provide direct access to the office/clinic/facilities, medical records/source documents for all enrolled subjects, regulatory documents and any/all other applicable study-related documents to all representatives of the sponsor and/or designee and all regulatory authorities to enable proper completion of the audit/inspection.

15.7 Subject Confidentiality and Data Privacy

Subject confidentiality will be maintained throughout the clinical study. A unique subject identification number will be assigned to every enrolled study subject, which will identify all data reported for that subject and ensure the data can be traced back to their source records.

The Institution and Investigator will conduct the study and test the study devices in accordance with all applicable data protection laws, in particular GDPR, to ensure that all legal data protection requirements are met in relation to the processing of personal data of study participants. In particular, the Institution and Investigator will provide all study participants with data protection information in accordance with applicable data protection law and to obtain data protection-compliant informed consent from the study participants.

Data relating to the study may be made available to all representatives of the sponsor and/or designee and third parties (e.g., in the case of an audit performed by regulatory authorities), provided the data are treated confidentially and that the subject's privacy is guaranteed in accordance with all applicable data protection laws, in particular GDPR.

The EDC system used in this study will capture data reported by sites and other entities that will be sent outside of the geographic region (Europe) in which the study is being conducted.

The results of the study may be published in a medical book or journal or presented at meetings, however, neither subject names nor any other personal health information that specifically identifies them will be used in those publications or presentations.

15.8 Ethics Committee (EC)

Prior to study initiation, the protocol, informed consent form and all other applicable study-related documents, including any written materials to be provided to subjects must be submitted for review by a certified EC. Written approval or favorable opinion of these documents must be obtained and submitted to the sponsor prior to screening and enrolling any subjects and initiating any study-related activities.

The Investigator will prepare the draft informed consent form (ICF) and provide to the sponsor and/or designee for approval prior to submission to the EC. If the sponsor requires any changes, a revised draft of the ICF incorporating these changes must be approved by the sponsor prior to EC submission. If the EC requires additional changes, these must be reviewed and approved by the sponsor prior to resubmission to the EC. Copies of the final, EC-approved ICF and all other EC-approved study documents must be submitted to sponsor or designee.

The Investigator or authorized designee will promptly report all changes in research activity and all unanticipated events/issues involving risks to human subjects to the EC. All sponsor-approved amendments to the study protocol, ICF, etc. must be approved by the EC prior to implementation. All other changes to research activities must be approved by the sponsor and EC prior to implementing, except when necessary to eliminate an immediate apparent hazard to the subject.

If applicable, at least annually, or more frequently if required by EC policy, the Investigator or authorized designee must submit a study progress report to their EC to obtain continuing review approval for the study prior to the expiration of the most recent approval. Additionally, the Investigator must provide notification to their EC, within three (3) months following the completion, termination, or discontinuation of the study at the specific site and provide the acknowledgement letter from the EC to the sponsor.

16 Record Keeping/Publication Policy

16.1 Record Retention

All study records (e.g. correspondence, regulatory documents, CRFs and all source documents, informed consent forms, laboratory reports, progress notes, medical histories, physical and diagnostic findings, diagnoses, procedure/assessment dates and investigational product disposition records, etc. that support the CRFs) must be retained in the files of the responsible Investigator at the study institution for the retention period required by applicable local laws.

All study records must be accessible upon request by the applicable regulatory authorities, the sponsor and/or designee until destruction is possible. **The sponsor will notify each Investigator in the study as to when records destruction is possible according to the applicable local laws, unless a longer retention period is required per institutional requirements.**

If the Investigator retires, relocates, or for other reasons, withdraws from assuming primary responsibility for keeping the study records, written notice (transfer of obligation) must be submitted to the sponsor and EC indicating the name and address of the new custodian accepting primary responsibility.

16.2 Use of Information and Publications

All information concerning the sponsor (Cordis US Corp.), the study devices, patent application, manufacturing processes, and scientific data supplied by the sponsor to the Investigator and not previously published, is considered confidential and remains the sole property of the sponsor. The Investigator understands the information developed in the clinical study will be used by the sponsor to prepare a clinical study report (CSR)/clinical investigational report in connection with a regulatory submission and thus may be disclosed as required to other Investigators or government regulatory authorities.

At the conclusion of the study, a manuscript may be prepared for publication of results across multiple study centers in a reputable scientific journal. The publication of the principal results from any single study center is not allowed until the preparation and publication of the multi-center results. Exceptions to this rule require prior approval of the sponsor. The analysis of pre-specified and non-pre-specified endpoints will be performed by the sponsor and/or designated entity(-ies) for data management and/or statistics. Secondary analyses as well as other proposed investigations will require the approval of the sponsor. For purposes of timely abstract presentation and publication, secondary publications will be delegated to the appropriate principal authors.

17 Product Accountability

17.1 Product Accountability

Both investigational and CE marked products will be used in this clinical study.

- All sizes of the S.M.A.R.T. RADIANZ device and all SABERX RADIANZ units with 9 and 10 mm diameters are investigational in nature and will be labeled as “Exclusively for Investigational Use”.
- All other sizes (8 mm and smaller diameters) of the SABERX RADIANZ device and all sizes of the BRITE TIP RADIANZ device are CE marked and will therefore not have the investigational use label. Both CE marked products, however, are currently NOT commercially available in Europe and are being made available exclusively for use in this clinical study.

All product for this clinical study must be kept in a secure location with restricted access to authorized members of the study team and stored according to the conditions outlined in the Instructions for Use (IFU)

and/or Investigator Brochure (IB) for each product. All product is intended solely for use by the Investigator or Sub-Investigator(s) and in subjects of this clinical study.

Accountability for all products will include tracking of all units from point of shipment to the investigational sites through point of final disposition and verifying the presence and completeness of all documentation supporting product accountability and inventory of product. Documentation is to be maintained for all investigational and CE-marked product supplied for this study and includes, but is not limited to, the following:

- Packing slips provided with each product shipment.
- An up-to-date, complete and accurate product accountability log, separately maintained for each product, (or equivalent) showing receipt, use and final disposition of every unit shipped to the site.
- Copies of product malfunction forms (or equivalent) for the return of devices for which there was a malfunction reported.
- Copies of product return forms (or equivalent) for the return of unused or expired devices.
- All other device accountability records including source documents and/or package labels of product used in study subjects, shipping labels, delivery confirmations, etc.

The Investigator and/or authorized designee will maintain adequate records of the receipt, use, and final disposition of all products as required by protocol and applicable country, local and federal regulations.

All product in this clinical study may be inventoried during on-site visits to ensure there is an adequate supply available for use at each site throughout the study.

All product that is opened/used will be accounted for in the CRFs. All AEs, device deficiencies and other product issues must also be recorded in the CRFs.

17.2 Instructions for Return of Investigational Products

The sponsor will provide instructions to all sites on the re-package and return of all products not used in subjects in this clinical study, the appropriate form(s) (or equivalent) that must be completed and the address(es) to which the product must be returned based on whether it is opened/unopened and unused, expired, damaged, mislabeled, a product complaint or malfunction has occurred or study enrollment has been completed.

18 Committees

18.1 Data and Safety Monitoring Board

The DSMB is a body of professionals (primarily comprised of physicians, a biostatistician, and/or a medical ethicist) which reviews overall study data at intervals pre-determined before the start of the study and/or based on subject enrollment accrual and/or event accrual to assess progress and identify any safety concerns or other issues. The DSMB is independent of the sponsor, the investigational sites or anyone otherwise involved in the conduct of the study. Members will not have any scientific, financial or other conflict of interest related to the sponsor or the study Investigators.

Information in safety reports provided to the DSMB will include, but not be limited to, all serious, major and reportable adverse events; unanticipated serious adverse device effects, device deficiencies and events related to the primary safety endpoint.

The DSMB will be responsible for providing to the sponsor, minutes of their meetings and any recommendations regarding early termination, suspension or modifications to the study, if the safety and well-being of the subjects is in jeopardy. Any formal statistical rules for terminating or recommending

termination of the study will be determined by the DSMB, as applicable. A memo summarizing the outcomes and/or any recommendations from the DSMB will be provided to all investigational sites after each DSMB meeting.

The structure and function of the DSMB will be documented in the DSMB Charter.

18.2 Clinical Events Committee

The Clinical Events Committee (CEC) is responsible for the review and final adjudication of a specific list of adverse events using source documents provided by sites, upon request, against a set of criteria to categorize clinical events and clinical endpoints in the study. The CEC will establish study-related guidelines for the requisite source data and the algorithm followed in order to classify a clinical event (according to the study definition). The sponsor will review the definitions prior to the start of the adjudication process.

The CEC will consist of qualified physicians with the appropriate expertise for the type of investigational product or condition under study. Similar to the DSMB, the CEC is also an independent body, functioning separately from the sponsor, the investigational sites or anyone otherwise involved in the conduct of the study or the clinical care of study subjects. Members will not have any scientific, financial or other conflict of interest related to the sponsor or the study Investigators. As appropriate, members of the CEC will be blinded to the primary results of the trial.

The CEC will be responsible for providing adjudication results and minutes of their meetings to the sponsor for internal review.

The structure and function of the CEC will be documented in the CEC Charter.

18.3 Early Study Termination or Suspension

The sponsor, DSMB, regulatory authorities or the Investigator may choose to temporarily suspend or prematurely terminate the study if the safety and well-being of the subjects is in jeopardy (e.g., if there is an unacceptable risk or serious health threat).

The sponsor reserves the right to temporarily suspend or prematurely terminate this study either at a single site, multiple sites or across all sites at any time for reasons including, but not limited to:

- Safety or ethical issues – e.g., if in the opinion of the Investigator, the incidence and/or severity of device deficiencies or adverse events in the study caused by treatment with the investigational product indicates a potential health hazard
- Inaccurate or incomplete reporting of data
- Non-compliance
- Unsatisfactory enrollment with respect to quality or quantity
- Technical reasons (e.g., change in personnel)

If the sponsor prematurely terminates or temporarily suspends the study, they will promptly notify the applicable Investigator(s)/institution(s) and the regulatory authority(ies) of the termination or suspension and the reason(s) for such, in accordance with applicable regulatory requirement(s). The applicable EC(s) should also be informed and provided with the reason(s) for termination or suspension by the sponsor or by the Investigator(s)/institution(s), in accordance with applicable regulatory requirement(s). In addition, the sponsor will provide direction on the return of all unused investigational product and other study materials.

The sponsor will inform the Member State in which the clinical study was conducted within 15 days of the date of early termination or temporary suspension (or within 24 hours if done for safety reasons).

If the Investigator terminates or suspends the study without prior agreement with the sponsor, he/she will promptly provide all details to the institution, the sponsor, and the EC.

If the EC terminates or suspends the study, the Investigator will promptly inform the sponsor with written explanation.

In all cases, the investigator(s)/institution(s) must arrange for any continued safety monitoring, treatment and/or follow-up of subjects as per standard-of-care/best clinical judgement, unless it has been determined by the Investigator that the continued follow-up may jeopardize the rights, safety, and/or welfare of the subject.Subject enrollment may be paused or terminated early if the sponsor or DSMB determines that the potential benefits of the investigational product/procedure are unlikely to outweigh the risks. For example, if the probability of achieving the target primary endpoint falls below a certain threshold, the study will be stopped or paused for re-evaluation.

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Appendix A. Definitions

Adverse Event (AE): An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device.

Allergic reaction: The hypersensitive response of the immune system of an allergic individual to a substance.

Angiography: A procedure performed to view blood vessels after injecting them with a radiopaque dye that outlines them on x-ray. This technique can be usefully used to look at arteries in many areas of the body, including the brain, neck (carotids), heart, aorta, chest, pulmonary circuit, kidneys, gastrointestinal tract, and limbs.

Arteriosclerosis: Hardening and thickening of the walls of the arteries. Arteriosclerosis can occur because of fatty deposits on the inner lining of arteries (atherosclerosis), calcification of the wall of the arteries, or thickening of the muscular wall of the arteries from chronically elevated blood pressure (hypertension).

Artery: A vessel that carries blood high in oxygen content away from the heart to the farthest reaches of the body. Since blood in arteries is usually full of oxygen, the hemoglobin in the red blood cells is oxygenated.

Asymptomatic: Without symptoms. For example, an asymptomatic infection is an infection with no symptoms.

Blood clot: Blood that has been converted from a liquid to a solid state. Also called a thrombus.

Blood pressure: The pressure of the blood within the arteries. It is produced primarily by the contraction of the heart muscle. Its measurement is recorded by two numbers. The first (systolic pressure) is measured after the heart contracts and is highest. The second (diastolic pressure) is measured before the heart contracts and lowest.

Complication: In medicine, an additional problem that arises following a procedure, treatment or illness and is secondary to it.

Device related complication - complication attributed to the device (e.g. graft migration, graft infection, etc.).
Procedure-related complications - complication not attributed to device but arises following the procedure (e.g., cardiac issue, renal insufficiency, etc.).

Computerized tomography scan (CT scan): Pictures of structures within the body created by a computer that takes the data from multiple X-ray images and turns them into pictures on a screen. CT stands for computerized tomography.

Death: All-cause mortality.

Delivery System Failure: Delivery system did not perform as intended during the stent placement procedure.

Device deficiency: Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Includes malfunctions, use errors, and inadequate labelling.

Device malfunction: The failure of a device to meet any of its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the IFU/IB.

Dilation: The process of enlargement, stretching, or expansion. The word "dilatation" means the same thing. Both come from the Latin "dilatare" meaning "to enlarge or expand."

Dissection:

0	None
A	Small radiolucent area within lumen of the vessel
B	Linear, non-persistent extravasation of contrast
C	Extraluminal, persisting extravasation of contrast
D	Spiral shaped filling defect
E	Persistent lumen defect with delayed anterograde flow
F	Filling defect accompanied by total occlusion

Duplex ultrasound Success: The presence of a triphasic waveform, or biphasic doppler waveform in a patient whose post-procedural CFA doppler waveform was biphasic. The duplex ultrasound scan must be taken at a 60° angle to the direction of the blood flow.

Duplex ultrasound Failure: The presence of a monophasic waveform, or a biphasic doppler waveform in a patient whose post procedural common femoral artery doppler waveform was triphasic. The duplex ultrasound scan must be taken at a 60° angle to the direction of the blood flow.

Embolization: A treatment that clogs small blood vessels and blocks the flow of blood.

Hematoma: A mass of usually clotted blood that forms in a tissue, organ, or body space as a result of a broken blood vessel.

Hemostasis: Absence of any signs of arterial pulsatile bleeding or signs of expanding or developing hematoma.

High blood pressure: Also known as hypertension, high blood pressure is, by definition, a repeatedly elevated blood pressure exceeding 140 over 90 mmHg

Immunodeficiency: Inability to mount a normal immune response. Immunodeficiency can be due to a genetic disease or acquired as in AIDS due to HIV.

Inflammation: A basic way in which the body reacts to infection, irritation or other injury, the key feature being redness, warmth, swelling and pain. Inflammation is now recognized as a type of nonspecific immune response.

Low blood pressure: Any blood pressure that is below the normal expected for an individual in a given environment. Low blood pressure is also referred to as hypotension.

Magnetic Resonance Angiogram (MRA): A noninvasive test that has demonstrated usefulness in defining the anatomy of blood vessels of certain size in the head and neck. MRA serves as a complement to traditional MRI scanning in evaluation of the brain and neck.

Magnetic Resonance Imaging (MRI): A special radiology technique designed to image internal structures of the body using magnetism, radio waves, and a computer to produce the images of body structures. For more information, see: Magnetic Resonance Imaging; Paul C. Lauterbur; Peter Mansfield.

Major Adverse Event (MAE): For this study, an MAE is any AE/SAE which resulted in one or more of the following: death, index limb amputation or target lesion revascularization.

Myocardial infarction: Q-wave MI with CK/MB fraction > 3 times the upper limit of normal.

Occlusion: A complete absence of flow within a blood vessel.

Operation: Although there are many meanings to the word "operation", in medicine it refers to a surgical procedure.

Peripheral: Situated away from the center, as opposed to centrally located.

Procedural Success: Absence of device malfunctions during the index procedure.

Pseudoaneurysm: An encapsulated hematoma in communication with an artery.

Rupture: A break or tear in any organ or soft tissue

Rutherford/Becker Classification:

Grade	*Category*	*Clinical Description*	*Objective Criteria*
0	0	Asymptomatic, no hemodynamic significant occlusive disease	Normal results of treadmill test (five minutes at 2 mph on 12° incline.
I	1	Mild claudication	Treadmill exercise completed, post-exercise AP is greater than 50 mm Hg but more than 25 mm Hg less than normal
	2	Moderate claudication	Symptoms between those of categories 1 and 3
	3	Severe claudication	Treadmill exercise cannot be completed, post-exercise AP is <50 mm Hg
II	4	Ischemic rest pain	Resting AP of ≤40 mm Hg, flat or barely pulsatile ankle or metatarsal plethysmographic tracing; toe pressure <30 mmHg
I–I	5	Minor tissue loss - non-healing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP ≤60 mm Hg, ankle or metatarsal plethysmographic tracing flat or barely pulsatile; toe pressure less than 40 mm Hg–
	6	Major tissue loss - extending above transmetatarsal level, functional foot no longer salvageable	Same as for category 5

Scan: The data or image obtained from the examination of organs or regions of the body by gathering information with a sensing device.

Serious Adverse Event (SAE): Any AE that led to any of the following:

a) death
b) serious deterioration in the health of the subject, that resulted in any of the following:
   - life-threatening illness or injury;

- permanent impairment of a body structure or a body function;
- hospitalization or prolongation of existing hospitalization;
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
- chronic disease

c) fetal distress, fetal death or a congenital physical or mental impairment or birth defect

Stent: A tube designed to be inserted into a vessel or passageway to keep it open.

Stent Thrombosis: Formation of thrombus within the AAA stent graft (aortic bifurcate or one or both iliac limbs) leading to significant limitation of blood flow, requiring secondary intervention to restore blood flow (e.g. thrombolysis, thrombectomy, PTA …).

Surgery: The branch of medicine concerned with diseases and conditions which require or are amenable to operative procedures. Surgery is the work done by a surgeon.

Stroke: Any acute, new, persistent, documented neurological deficit ending in death or lasting greater than 24 hours and classified by a physician as a stroke.

Symptom: Any subjective evidence of disease.

Target lesion: The site of stenosis/restenosis.

Target lesion revascularization: Revascularization of the target lesion using either bypass surgery or percutaneous (i.e., angioplasty) techniques.

Technical Success: Successful insertion of the S.M.A.R.T. RADIANZ™ Vascular Stent System through the vasculature, successful deployment of the study device (S.M.A.R.T.™ stent) at the intended location, and successful withdrawal of the delivery system without conversion to femoral access.

Thrombosis – Formation of thrombus within a blood vessel leading to significant limitation of blood flow, requiring secondary intervention to restore blood flow (e.g., thrombolysis, thrombectomy, PTA)

Thrombus: Discrete, mobile intraluminal filling defect with defined borders with or without associated contrast staining.

Ultrasound: High-frequency sound waves used to bounce off of tissues using special devices. The echoes are then converted into a picture called a sonogram.

Unanticipated Serious Adverse Device Effect (USADE): A serious adverse effect related to the use of a study device which by its nature, incidence, severity or outcome has not been identified in the current risk assessment or any other unanticipated serious problem associated with a study device that relates to the rights, safety, or welfare of subjects.

Vessel: A tube in the body that carries fluids: blood vessels or lymph vessels.

Appendix B. Acronyms and Abbreviations

Acronym / Abbreviation	Term
ACM	All-cause mortality
AE	Adverse Event
AP	Anterior/Posterior
BID	Twice Daily
BP	Blood Pressure
CEC	Clinical Events Committee
CFA	Common Femoral Artery
CFR	Code of Federal Regulations
CI	Confidence Interval
Cm	Centimeter
COV	Closeout Visit
CRF	Case Report Form
CRO	Contract Research Organization
CSR	Clinical Study Report
CT	Computerized Axial Tomography Scan
DSMB	Data and Safety Monitoring Board
ECeCRF	Ethics Committee Electronic Case Report Form
EDC	Electronic Data Capture
EQ-5D	EuroQOL-5 Dimension
EU	European Union
FDA	Food and Drug Administration
Fr	French (sizing unit for devices)
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GFR	Glomerular Filtration Rate
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Council on Harmonization
IFU	Instructions for Use
IMV	Interim Monitoring Visits
ISO	International Organization for Standardization
ITT	Intent-to-treat
MAE	Major Adverse Event
mm	Millimeter
mmHg	Millimeters of mercury (unit of pressure)
mSv	Millisievert
NCA	National Competent Authorities
PPA	Proximal popliteal artery
PTA	Percutaneous transluminal angioplasty
PAD	Peripheral Arterial Disease
QD	Once Daily
RVD	Reference Vessel Diameter
SAE	Serious adverse event
SF-36	Short-Form 36
SFA	Superficial femoral artery
SOP	Standard Operating Procedures
TFA	Transfemoral Artery
TFATIA	Transfemoral Arterial

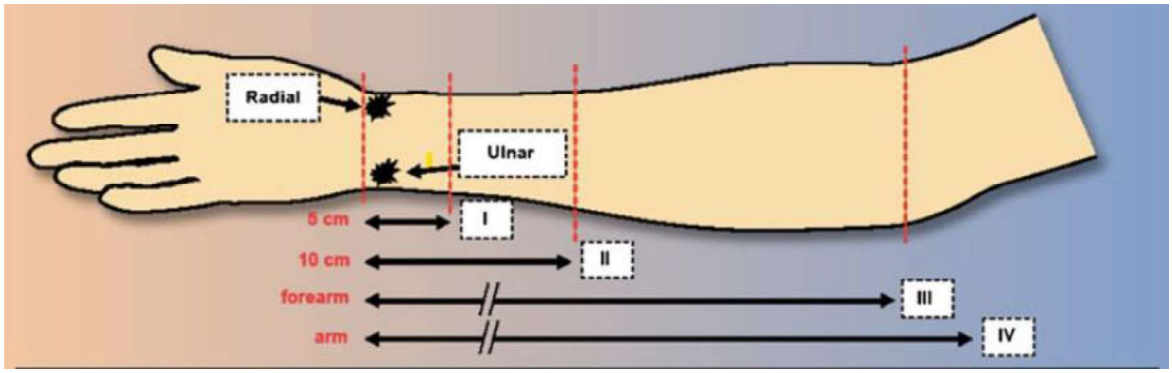
Acronym / Abbreviation	Term
TIA	Transient Ischemic Attack
TLR	Target lesion(s) revascularization
TRA	Transradial Arterial
USADE	Unanticipated Serious Adverse Device Effect

Appendix C. Participating Investigators and Sites

Site Investigator Name	Site Name	Site Address	Site Country
Dr. Koen Deloose	ID3 Medical CVBA (A.Z. Sint-Blasius Hospital-Dendermonde)	Kroonveldlaan 50 9200 Dendermonde	Belgium
Prof. Andrea Kahlberg	IRCCS San Raffaele Scientific Institute	Via Olgettina 60 20132 Milan	Italy
Dr. Luca Bertoglio	University of Brescia/ASST Spedali Civili Hospital	Piazzale Spedali Civili 1, 25123 Brescia	Italy
Dr. Paolo Sbarzaglia	Maria Cecilia Hospital Via Corriera	1 Cotignola Ravenna 48033	Italy
Dr. Giovanni Balestriero	Belluno General Hospital	Viale Europa 22, 32100 Belluno BL	Italy
Prof. Marianne Brodmann	Medical University Graz	Auenbruggerplatz 27, Graz	Austria
Dr. Martin Werner	Hanusch Krankenhaus	Henirich Collin Strasse 30 1140 Vienna	Austria
Prof. Dr. Klaus A. Hausegger	KABEG Klinikum Klagenfurt am Wörthersee	Dept. of Diagnostic and Interventional Radiaology Feschnigstraße 11 Klagenfurt Kärnten 9020	Austria
Prof. Oliver Schlager	Medical University of Vienna	Spitalgasse 23, 1090, Vienna	Austria
Dr. Christoph Binkert	Kantonsspital Winterthur	Brauerstrasse 15 Winterthur 840	Switzerland
Prof. Raphael Coscas	CHU Ambroise Paré	CHU Ambroise Paré AP-HP 9 Ave Charles de Gaulle Boulogne-Billancourt 92100	France
Dr. Antoine Sauguet	Pasteur Clinic	SCP des Médecins Cardiologues 45 Ave de Lombrez BP	France
Prof. Yann Gouëffic	Groupe Hôpital Paris St Joseph	Vascular and Endovascular Surgical Center 185 rue Raymond Losserand Paris 75014	France

Site Investigator Name	Site Name	Site Address	Site Country
Dr. Gilles Goyault	Cardiovascular Institute Strasbourg - Clinque Rhena	10 rue Francois Epailly, Strasbourg, 67000 Alsace	France
Dr. Gerd Groezinger	University Hospital Tubingen	Hoppe-Seyler-Straße 3 72076 Tübingen	Germany
Dr. Arne Schwindt	St. Franziskus Hospital Muenster	Hohenzollernring 70 Munster NRW, 48145	Germany
Dr. Mercedes Guerra	University Hospital of Guadalajara	Donante de sangre s/n 19002 Guadalajara Secretaría del Servicio de Angiología,Cirugía Vascular y Endovascular	Spain

Appendix D. EASY Hematoma Classification System



The table below should be used to classify hematomas[94]:

Grade	I	II	III	IV	V
Incidence	≤5%	<3%	<2%	≤0.1%	<0.01%
Definition	Local hematoma, superficial	Hematoma with moderate muscular infiltration	Forearm Hematoma and muscular infiltration, below the elbow	Hematoma and muscular infiltration extending above the elbow	Ischemic threat (compartment syndrome)
Treatment	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice Inflated BP cuff	Analgesia Additional bracelet Local ice Inflated BP cuff	Consider surgery
Notes		Inform physician	Inform physician	Inform physician	Stat call to physician
Remarks	- Control blood pressure (BP) (importance of pain management) - Consider interruption of any anticoagulation and/or antiplatelet infusion - Follow forearm and arm diameters to evaluate requirement for additional bracelet and/or BP cuff inflation - Additional bracelet(s) can be placed alongside artery anatomy - Ice cubes in a plastic bag or washcloth are placed on the hematoma - Finger O_2 saturation can be monitored during inflated blood pressure cuff - To inflate blood pressure cuff, select a pressure of 20 mmHg < systolic pressure and deflate every 15 minutes - After bracelet removal, use "Velpeau bandage" around forearm/arm for a few hours to maintain mild positive pressure				

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