# NCT03480685

**The SCAN Trial**

**Protocol Number: P0986**

A Post-market, Multi-vessel Evaluation of the Imaging of Peripheral Arteries for Diagnostic Purpose**S** Comparing Optical **C**oherence TomogrA**A**phy and I**N**travascular Ultrasound Imaging

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# 1. INTRODUCTION

Intravascular imaging provides clinicians with information essential to the development of treatment strategy and avoidance of procedure-associated injuries to the vessel walls. Two primary modalities of such imaging are intravascular ultrasound (IVUS) and optical coherence tompography (OCT). Both have advantages and challenges for use in assessing occlusions and structures in peripheral arteries.

As the name denotes, IVUS uses high-frequency sound waves that rebound off vessel walls and are collected by a processing system. The intensity of the waves vary depending on the tissue encountered and the system electronics process those signals to create a cross-sectional image.[1] It is used to measure plaque extent, morphology and distribution, but has low resolution and calcium deposits in the vessel walls can reduce penetration of the sound waves.[2,3] OCT imaging uses near-infrared light to optimize intravascular visualization of tissue. OCT images have higher resolution and faster imaging acquisition than IVUS,[4] but imaging requires management of blood flow, which can interfere with light transmission.[5]

# 2. DEVICE AND TECHNOLOGY DESCRIPTION

The devices that will be used in this study are the Pantheris (Avinger, Inc.) and the Visions (Royal Philips Corp.) catheters. Both devices have been reviewed by the United States's Food and Drug Administration (FDA) and have marketing clearance for commercial use and use in diagnostic imaging in peripheral vessels. Neither device is considered investigational or experimental and in this study they will be used in accordance with their FDA-cleared indications for use.

## 2.1. Pantheris System and Catheter

The Pantheris system is comprised of the Pantheris catheter (Figure 1), Lightbox Imaging Sled (Sled), and the Lightbox HS Imaging Console (Lightbox). The catheter is connected to the Lightbox via the Sled and it is the Lightbox Console that displays the OCT images captured by the catheter's rotating laser. The Sled provides optical and rotational power to the Pantheris catheter.

The Pantheris catheter is a monorail (rapid exchange) device with a working length of 110 cm and is compatible with a 0.014" guidewire. The Pantheris is designed for treatment of lesions in vessels with a diameter of 3 mm to 7 mm. The catheter is provided sterile and is for single use only.

OCT imaging can differentiate neointimal morphology and its capability of determining stent malapposition, tissue protrusion around and through stent structure, and stent edge dissection allows the clinican to make decisions about treatment strategy (Figure 2). The system also has the capability to measure the diameter of the lumen of the vessel.

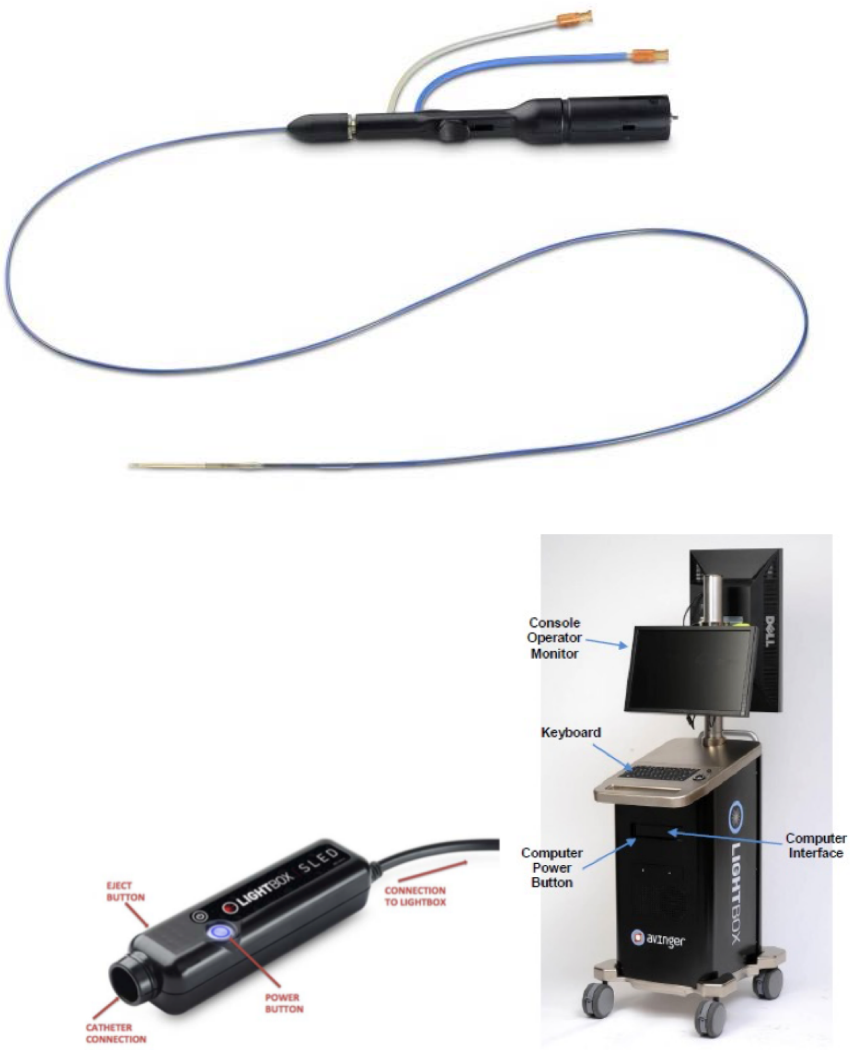


**FIGURE 1: PANTHERIS SYSTEM ELEMENTS; THE CATHETER (TOP), THE SLED (LOWER LEFT) AND THE LIGHTBOX (LOWER RIGHT).**

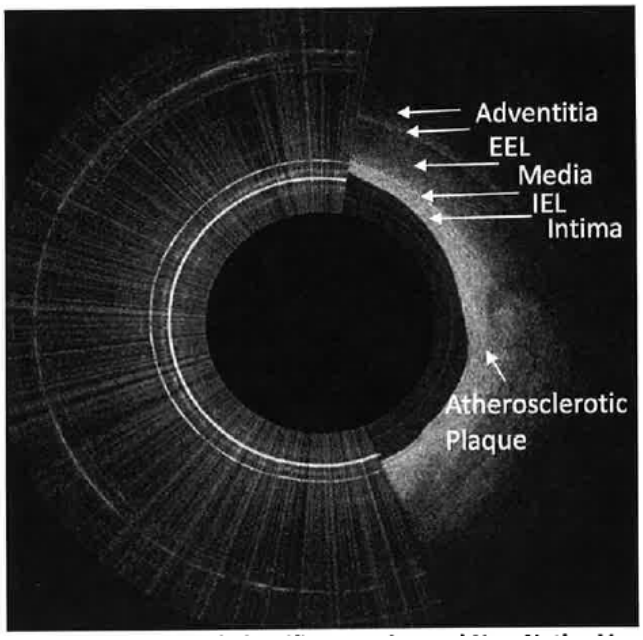


**FIGURE 2: VESSEL ANATOMY VISIBLE WITH OCT IMAGING BY THE PANTHERIS CATHETER.**

## 2.2. VISIONS IVUS catheter

The Visions PV 0.014P IVUS catheter (Visions catheter) has a working length of 150 cm and is advanced through an indwelling vascular sheath, following an 0.014" guide wire. The catheter is connected with an imaging system that displays the images (Figure 3). The IVUS catheter permits the clinician to assess disease markers, such as plaque burden and lesion location and morphology, as well as provide measurements of the lumen of the vessel. It is provided sterile and for single use only.

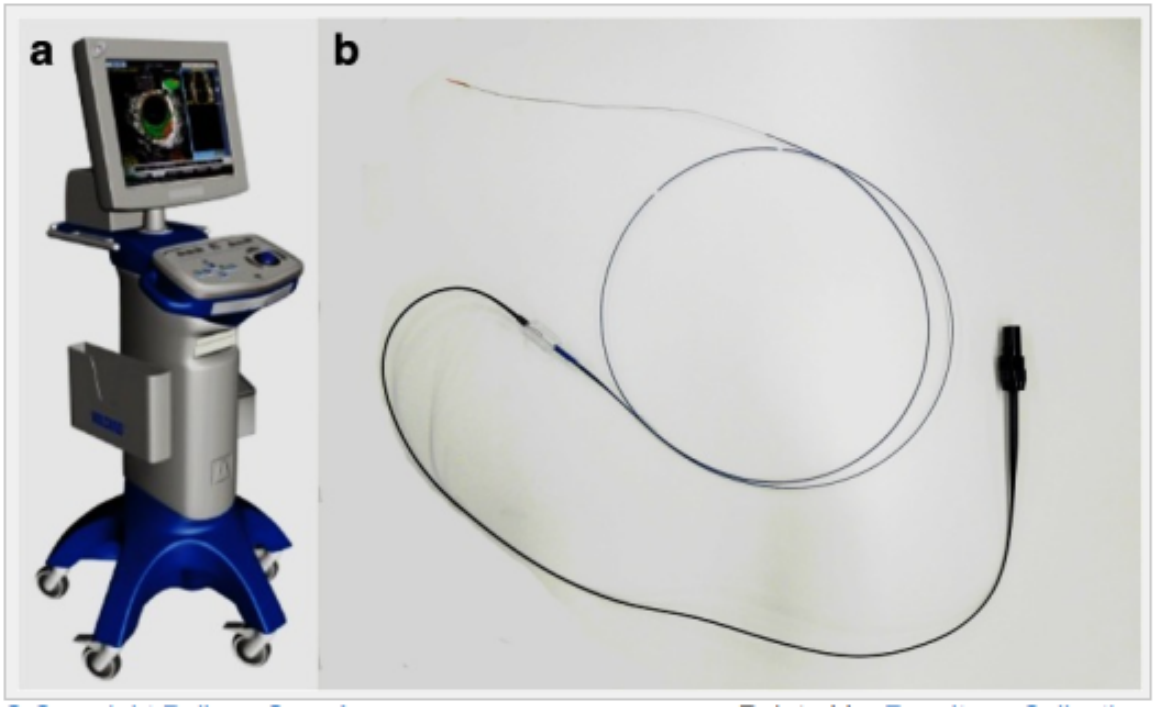


**FIGURE 3: THE VISIONS IVUS IMAGING SYSTEM AND CONSOLE (A), AND VISIONS IVUS CATHETER (B).**

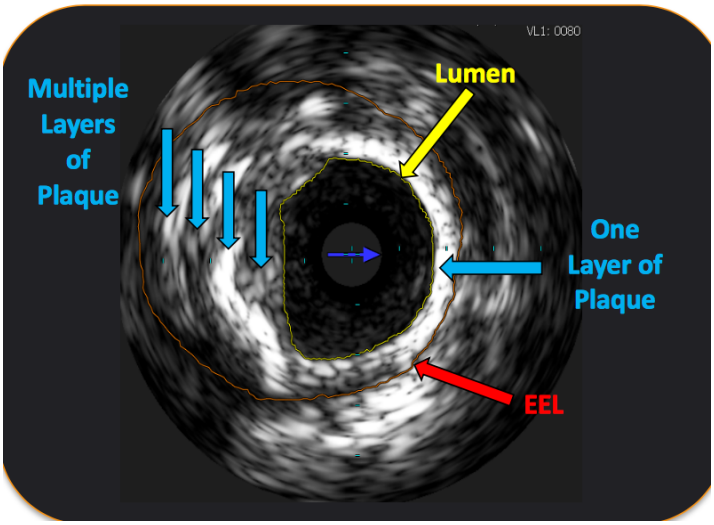


**FIGURE 4: VESSEL MORPHOLOGY AS IMAGED BY AN IVUS CATHETER.**

## 3. RISK/BENEFIT ASSESSMENT

### 3.1. Risks

Introduction of either the Pantheris or Visions catheter into a peripheral artery carries some known risks.

Adverse effects possible with the use of the Pantheris OCT and Visions IVUS catheters include, but are not limited to, the following events:

- Vessel dissection, perforation, rupture or injury;
- Restenosis;
- Hemorrhage or hematoma;
- Infection;
- Vessel spasm;
- Embolism;
- Entry puncture site bleeding;
- Vessel thrombosis;
- Renal failure;
- Vessel trauma requiring surgical repair or intervention; and
- Death.

The patients involve in this study diagnostic imaging and the possible risks for diagnostic include, but are not limited to, the following events:

- Entry site complications
- Entry site pain
- Acute vessel closure
- Arterial rupture
- Arterial spasm
- Bleeding complications
- Infection

There are risks associated with the use of medical equipment connected to an energy source. These risks have been mitigated through in-house testing and compliance.

Risk will be mitigated by working with an Investigator who is experienced and skilled in endovascular diagnostic techniques. Additionally, only Investigators with experience of proper device operation will participate in this study.

### 3.2. Benefits

Knowledge gained in this study on the use of OCT or IVUS systems to assist in diagnosis and treatment planning may provide physicians with an additional option that is as good or better than what is available currently for visualization of vessel morphology during the procedure.

# 4. CURRENT INDICATIONS FOR USE FOR THE TWO DEVICES

## 4.1. Pantheris System's Current Indications for Use

The Pantheris System's OCT imaging system being used in this study was originally cleared under K152275 in October of 2015, with device iterations being reviewed in subsequent regulatory submissions. The device has been commercially available since 2016.

The Indications for Use statement for the Pantheris system is:

> "The Pantheris System is intended to remove plaque (atherectomy) from partially occluded vessels in the peripheral vasculature with a reference diameter of 3.0 mm to 7.0 mm, using OCT-assisted orientation and imaging. The system is an adjunct to fluoroscopy by providing images of vessel lumen, wall structures and vessel morphologies. The Pantheris System is NOT intended for use in the iliac, coronary, cerebral, renal or carotid vasculature."

The Pantheris catheter was cleared for diagnostic use under K162326.

## 4.2. VISIONS PV 0.014P's Current Indications for Use

The Visions 0.014P device being used in this study was originally cleared by the FDA under K152829 in November 2015. The device is available commercially.

The Indications for Use statement for the Visions PV 0.014 IVUS catheter system is:

> "The Visions PV 0.014 IVUS catheter is designed for use in the evaluation of vascular morphology in blood vessels of the coronary and peripheral vasculature by providing a cross-sectional image of such vessels. This device is not currently indicated for use in cerebral vessels. It is designed for use as an adjunct to conventional angiographic procedures to provide an image of the vessel lumen and wall structures."

# 5. INVESTIGATIONAL PLAN

## 5.1. Study Design Overview

The purpose of this is a study to collect images of the same vessel segments using both the IVUS and OCT systems so that a comparison can be made of the two imaging modalities. IVUS and OCT images will be captured at identical positions within vessel segments. Continuous imaging will occur as the catheters are moved from distal to proximal endpoints established with a radiopaque marking tape attached to the subject's leg.

The trial will enroll up to 25 subjects diagnosed with peripheral arterial disease of the lower extremities, with the goal to acquire at least 115 matched images for analysis.

The images will be anonymized and given a unique identification prior to assessment by three radiologists (readers) for review. The readers will review the images and rank each for image clarity (using a visual analogue scale or VAS) and identification of vessel morphology and disease pre- and post-procedure.

The inclusion criteria for subjects are:

1. Subject is an adult ( $\geq$18 years old); and
2. With suspected vascular disease that might be a candidate for IVUS; and
3. Reference vessel lumen is acceptable for use of the Pantheris and IVUS catheters as per visual angiographic estimation.
4. Successful diagnostic imaging and removal of the IVUS catheter with no adverse events.

The exclusion criteria are:

1. Subject, if female, is pregnant or breast feeding; or
2. Subject is unwilling to give informed consent.

## 5.2. Sample Size Estimate

When the sample size is 108 images of both the OCT and IVUS catheters, a two group 0.05 one-sided matched t-test will have 90% power to reject the null hypothesis that the test (OCT) and standard (IVUS) are not equivalent in favor of the alternative hypothesis that the two groups are equivalent. To obtain 108 vessel segment images at five images per subject, 22 subjects would be needed; however, recognizing that some images (~ 5%) may be of poor quality and illegible, 25 subjects should be enrolled and 115 images evaluated.

## 5.3. Study Endpoints

Primary efficacy endpoint is met when OCT imaging has the equivalent or higher ranking of IVUS imaging of the visualization of vessel morphology and disease for:

- Layered structure – intima, media, external elastic lamina, and adventitia;
- Non-layered structure—presence of disease in the vessel structure;
- Abnormal physiology—dissection/tissue flap/false lumen, thrombus, calcium;
- Bifurcation of the vessel; and
- Frequency of artifacts.

Secondary efficacy endpoint is met when OCT imaging has the equivalent dimensions of vessel diameter and total luminal area as that determined with IVUS imaging.

Primary safety endpoint is freedom from diagnostic imaging procedure-related and device-associated adverse events, as reported by the physician.

### 5.4. Enrollment and Study Duration

Subjects will be enrolled at 3 clinical sites in the USA.

Subjects will be considered enrolled into the study once the consent form is signed and the Pantheris catheter is introduced into the vasculature. Subjects will be considered exited from the study once the Pantheris catheter (OCT device) diagnostic imaging and vessel measurements have been completed. Enrollment is expected to start in Q1 2018, and conclude by the end of Q2 2018.

Subjects may withdraw at any time from the study without prejudice or detriment to their medical care. If a subject prematurely terminates from the study, the reason for the termination will be recorded. Subjects who actively withdraw from the trial will be considered "withdrawals." If termination is a result of an adverse event or death, an Adverse Event Case Report Form will also be completed.

### 5.5. Duration of Subject Participation

Participation lasts the duration of the diagnostic imaging procedure. No follow-up imaging or patient data will be collected.

## 6. STUDY PROCEDURE

### 6.1 Gathering OCT and IVUS Images

After providing informed consent, the subject will be prepared for the diagnostic procedure according to the institution's and investigator's standard procedures. Demographic information will be recorded for each subject.

A radiopaque ruler will be attached to the subject's leg to provide reference marks for starting and stopping points of the "target segment" that will be used for image acquisition by the two devices.

Subjects will undergo diagnostic angiographic images to identify the target segment starting poing (distal end) and ending point (proximal end) which will be between 5 cm and 10 cm within the vessel.

A 7 Fr vascular sheath will be advanced up-and-over the aortic bifurcation and to the region of interest of the artery.

A 0.014 inch guide wire will be advanced distal to the target segment under angiographic imaging.

An IVUS catheter will be loaded onto the wire and advanced until its imaging transducer resides at the distal end of the target segment (starting point). Using the radiopaque ruler as a reference of the starting point (distal end) and stopping point (proximal end) of the target segment, the IVUS catheter will be energized for imaging and retracted through the target segment (between 5 cm and 10 cm within the vessel) capturing images within the target segment.

The diameter of the lumen of the vessel at the starting, mid, and ending points of the target segment will measured using the IVUS system software. Mean diameter and luminal area will be calculated for each target segment imaged.

After all images and measurments of the target segment have been captured on the IVUS system, the IVUS catheter will be removed.

Using the radiopaque ruler as a reference, an OCT catheter will be advanced over the 0.014 guide wire until its imaging window is at the exact same starting point (distal end) of the target segment. Once the OCT catheter is inserted, the subject is enrolled in the study. With the device energized, the OCT catheter will be retracted through the exact same target segment of the vessel and the OCT images captured on the Lightbox system.

The diameter of the lumen of the vessel at the starting, mid, and ending points of the target segment will measured using the OCT system software. Mean diameter and luminal area will be calculated for each target segment imaged.

After all images and measurments of the target segment have been captured on the OCT system, the subject is exited from the study. Once the subject is exited from the study, the investigator can choose to remove the OCT catheter or use it to perform atherectomy.

IVUS images will be collected either on DICOM and stored on a hard drive or saved to an S-VHS and then transferred to a PC hard-drive for processing, per the clinic's standard protocol. OCT images will be captured on the Lightbox and downloaded to a memory stick or external hard drive or DVD.

## 6.2 **Analysis of Images**

The trial will acquire at least 115 matched images for analysis by three independent readers who are experienced radiologists and were not involved in the cases during which these images were captured. Sample images of IVUS and OCT will be reviewed prior to the image assessment to create a consistent nomenclature for the readers when identifying different tissue types with both imaging modalities and standardize the image review process. The images will be anonymized and given a unique identification number prior to assessment by the readers. Since the presentation of IVUS and OCT images are visibly different, the readers cannot be blinded as to which imaging device used to generate the image, but the images will

be provided in a random sequence so that the reader cannot match a specific IVUS image to a specific OCT image at the time of the review.

The readers will view the images and rank each for clarity (using a visual analogue scale or VAS) and identification of vessel morphology and disease pre- and post-procedure.

Qualitative interpretation of OCT and IVUS images will be ranked as follows:
on) for:

- Layered structure – intima, media, external elastic lamina and adventitia (ranked as 1- clear differentiation of the vessel wall layers, 2- differentiation of at least three vessel wall layers, 3- differentiation of at least two vessel wall layers, and 4- no differentiation of any vessel wall layer);
- Non-layered structure—presence of disease in the vessel structure (a 5-point VAS of 1- excellent histology-like image quality to 5- unacceptably poor image quality);
- Abnormal physiology—dissection/tissue flap/false lumen, thrombus, calcium (a 5-point VAS of 1- excellent histology-like image quality to 5- unacceptably poor image quality);
- Bifurcation of the vessel (1- excellent image, 2- acceptable image, 3- unacceptably poor image quality); and
- Frequency of artifacts (ranked as 1- no artifacts, 2- tolerable/not limiting diagnostic image quality, 3- intense and limits diagnostic image quality).

The results of all readings of both imaging modalities will be used for intrareader and interreader comparison to evaluate the reproducibility and reliability of the respective imaging modality.

## 6.3 Statistical Analyses

Statistical analyses will be carried out using StatView software (SAS Institute, Cary, NC). A $p$ value $< 0.05$ will be considered statistically significant. Matched Pairs *t*-Test will be performed to compare means and on paired samples to compare procedural data and complications associated with the imaging techniques. The mean values of the results of all readings of all readers will be calculated for comparison of image quality. Fisher's Exact Test will be used to compare proportions. The Mann-Whitney-Wilcoxon test will be applied for statistical comparison of the results for OCT and IVUS imaging. Interreader and intrareader reproducibility will be calculated by intraclass correlation (ICC) analysis in a two-way mixed model. Correlation of the mean values of the results of the quantitative measurements of all readers with both imaging modalities will be calculated as Pearson correlation coefficient.

# 7. SAFETY AND DEVICE MALFUNCTION REPORTING

## 7.1. Safety Reporting

Incidence and severity of procedure-related and device-related adverse events (*e.g*., vessel spasm, thrombosis, distal embolism, *etc*.) will be evaluated following each scan and documented over the course of the study. All adverse events (AEs) will be are required to be completely documented through Avinger's complaint handling process..

The following events will be considered to be serious adverse events (SAEs) and must be reported to the Sponsor by telephone, fax and/or email. These events must be reported whether or not the Investigator believes they are related to study procedures, activities or device:

- Death;
- Life-threatening event;
- Disability – significant, persistent, or permanent change, impairment, or damage or disruption in the subject's body function/structure, physical activities or quality of life;
- Necessitate immediate medical or surgical intervention to:
  - Preclude permanent impairment of a body function or permanent damage to a body structure
  - Relieve unanticipated temporary impairment or damage; or
- Prolongation of a hospitalization.

It is the responsibility of the Investigator to inform their Institutional Review Board (IRB) of serious adverse events as required by their IRB's procedures and in conformance with local regulatory requirements.

## 7.2. Device Malfunction and/or Device Failure Reporting

All reported device malfunctions or failures of the Pantheris Catheter, Imaging Sled, or Lightbox Console are required to be completely documented through Avinger's complaint handling process. All malfunctions or suspected failures of the Pantheris catheter shall be returned to Avinger for analysis with instructions provided by Avinger. Any malfunctions or suspected failures of the IVUS device should be reported to its manufacturer.

NOTE: Device failures or malfunctions are **NOT** to be reported as adverse events. However, if there is an adverse event associated with a device failure or malfunction, the specific event should be recorded on the adverse event report form.

## 8. DEVICE AVAILABILITY

IVUS devices will be drawn from the institution's inventory. Avinger will provide sterile units of the Pantheris catheter for use in this study at no charge to the institution.

## 9. GOOD CLINICAL PRACTICES (GCP)

The trial will be performed in accordance with the relevant parts of ISO 14155-1/14155-2.1; the ICH Guidelines for Good Clinical Practices (E6), the Declaration of Helsinki, and any regional and/or national regulations.

### 9.1. Institutional Review Board (IRB) Approval

Prior to study initiation, this protocol and the informed consent document must be submitted to an IRB for written approval. The IRBs written notification of approval will be provided to Avinger prior to study commencement. Any changes to the protocol that may increase study risks or present new risks to the subject or may adversely affect the outcome of the study must be approved in writing by the study Sponsor and the site IRB before the change is made.

### 9.2. Informed Consent

Prior to participation in the clinical trial, each subject must give written Informed Consent after the study has been fully explained to the subject in language that is easily understood by the subject. The subjects must also be given the opportunity to ask questions and have those questions answered to their satisfaction. The subject will receive a copy of the Informed Consent form.

The Informed Consent document provided to subjects will be in accordance with the current guidelines as outlined by the Good Clinical Practices (GCP) guidelines, Declaration of Helsinki and the International Conference on Harmonization (ICH).

### 9.3. Amending the Protocol

An Investigator may not make protocol changes without prior approval by Avinger and other oversight bodies.

Any requested change to this protocol must be submitted to Avinger for review and agreement, followed by approval by the IRB. The investigative sites must send Avinger a copy of the IRB approval letter for a protocol amendment.

### 9.4. Subject Confidentiality

All information concerning subjects or their participation in this trial will be considered confidential. Only authorized Avinger personnel and designated consultants will have access to these confidential files. Enrolled subjects will be assigned a unique identifier that will be used to maintain confidentiality of subjects' medical information. Subject names and other protected health information will not be captured on the case report forms. In addition, angiographic, IVUS, and OCT

images submitted from the participating site to the Sponsor should be redacted of all subject identifiers.

### 9.5. Coverage of Expenses

The treated subjects will not be compensated for participating in the study.

### 9.6. Compensation in the Event of Injury

Both devices are being used as intended and following FDA-reviewed and cleared instructions for use. The cost of any treatment for any injury sustained during this study will be the obligation of the subject and/or the subject's insurance.

### 9.7. Data Monitoring and Quality Control

All collected data will be verified for accuracy with source documents including, but not limited to, medical records, office/clinic notes, procedure reports, laboratory results, physician and nursing progress notes. Verification and quality of data, monitoring of clinical study progress and Investigator compliance with the approved protocol will be conducted by Avinger or its designated representative.

Telephone and/or e-mail contact will be conducted by Avinger on a regular basis with the Investigator and the site staff to ensure that the protocol is being followed and to address any issues that may occur during the course of the trial.

If a deficiency is noted during the course of the trial, the site's clinical monitor is required to bring this to the attention of Avinger to discuss the situation and (if required) to secure compliance.

## 10. QUALITY CONTROL AND QUALITY ASSURANCE

### 10.1. Site Training

To ensure accurate, complete, and reliable data, the Sponsor or its representatives will provide instructional material to the trial sites, as appropriate, and:

- Instruct the Investigators and trial personnel on the protocol and the completion of the CRF;
- Communicate regularly with site personnel via mail, email, telephone, and/or fax; and
- Make periodic visits to the trial sites (if applicable).

During those visits, the Sponsor or its representatives will monitor the subject data recorded in the CRF against source documents at the trial site.

### 10.2. Physician Training

Prior to enrolling subjects in the trial, Investigators will be trained on the data required for completion of the CRF.

### 10.3. Audits and Inspections

The Principal Investigator for the site will allow representatives of the governing IRB, the United States Food and Drug Administration (FDA), and other applicable regulatory agencies to inspect all study records. These inspections are for the purpose of verifying adherence to the protocol, completeness and exactness of the data being reported and compliance with FDA regulations.

The Principal Investigator for the site will inform the Sponsor or the Sponsor's designee in advance if they are to be audited or inspected by any regulatory agencies. The Sponsor or the Sponsor's designee will also inform the site if they are made aware of a pending audit or inspection by a regulatory agency.

## 11. STUDY MONITORING AND ADMINISTRATION

Avinger will make necessary efforts to ensure that this study is conducted in compliance with GCPs and all applicable regulatory requirements.

### 11.1. Source Documentation

The Investigator must maintain detailed source documents on all trial subjects who are enrolled in the trial. Source documents include subject medical records, hospital charts, clinic charts, Investigator's subject trial files, as well as the results of diagnostic tests (*e.g.*, laboratory tests).

The following minimum information should be recorded in the subject's medical records:

- The date the subject entered the trial and the subject number;
- The trial protocol number and the name of the Sponsor;
- The date that informed consent was obtained;
- Evidence that the subject meets trial eligibility requirements (*e.g.*, medical history, trial procedures and/or evaluations);
- The dates of all trial-related subject visits;
- Evidence that required procedures and/or evaluations were completed;
- Use of any concurrent medications;
- Documentation of specific device used;
- Occurrence and status of any Adverse Events; and
- The date the subject exited the trial, and a notation as to whether the subject completed the trial or was discontinued, including the reason for discontinuation.

### 11.2. Criteria for Terminating the Study

Avinger reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons related to protection of subjects. Investigators and associated IRBs will be notified in writing in the event of termination.

### 11.3. Criteria for Suspending/Terminating a Study Center

Avinger reserves the right to stop enrollment of subjects at a particular study center at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/terminating a study center include:

- Repeated failure to complete case report forms prior to scheduled monitoring visits;
- Failure to obtain written Informed Consent;
- Failure to report SAEs/UADEs to Avinger; or
- Loss of (or unaccounted for) product inventory.

### 11.4. Sponsor Responsibilities

As the study Sponsor, Avinger, Inc. of Redwood City, California, is committed to the following:

- Obtaining Institutional Review Board approval for the Protocol and Informed Consent Form (ICF) from the central IRB (WIRB) prior to enrolling subjects;
- Selecting qualified Investigators;
- Ensuring proper Investigator training;
- Ensuring proper clinical site support and monitoring;
- Ensuring that the central IRB is informed of any significant new information about the study;
- Maintaining accurate and complete study records and submitting required reports;
- Obtaining signed Investigator Protocol Signature pages;
- Providing case report forms and ensuring that completed forms match source documentation;
- Ensuring protocol compliance; and
- Ensuring proper reporting of all AEs.

### 11.5. Investigator Responsibilities

All Investigators involved in this trial will sign an Investigator's Agreement affirming that they will adhere to the following activities:

- Submitting the site specific ICF to the central IRB and securing approval;
- Ensuring that enrolled subjects comply with the inclusion/exclusion criteria;
- Obtaining written IRB approval prior to subject enrollment;
- Obtaining written informed consent from each subject prior to enrollment;
- Performing the study evaluations as described in this protocol;
- Maintaining source documentation in the subject's medical files;
- Completing case report forms corroborated by source documentation;
- Submitting required reports to the study Sponsor and IRB, if necessary;
- Complying with the study protocol and reporting any deviations in advance of their occurrence;
- Maintaining study related records; and
- Maintaining accurate records related to device accountability.

### 11.6. Protocol Deviations

A protocol deviation is defined as an event where the Investigator or site personnel did not conduct the study according to the protocol.

Investigators shall be required to obtain prior approval from Avinger clinical study management before initiating deviations from the protocol, except where necessary to protect the life or physical well-being of a subject in an emergency. Such approval shall be documented in writing and maintained in clinical study management and Investigator files. Prior approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's control, (*e.g.*, subject was not available for scheduled follow-up office visit, blood sample lost by laboratory, *etc*.); however, the event is still considered a deviation and will be reported via the CRF.

Deviations must be reported to Avinger regardless of whether medically justifiable, pre-approved by Avinger or taken to protect the subject in an emergency. Subject specific deviations will be reported on the CRF. Non-subject specific deviations, (*e.g.*, unauthorized use of an study device outside the study, unauthorized use of an study device by a physician who is not a participating investigator or not been trained in the use of the device, *etc*.), will be reported to Avinger via the CRF. Investigators will also adhere to procedures for reporting study deviations to the IRB in accordance with the central IRB reporting policies and procedures.

Regulations require that Investigators maintain accurate, complete and current records, including documents showing the dates of and reasons for each deviation from the protocol.

## 12. Literature Cited


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3. Kashyap VS, *et al. In vivo* assessment of endothelial function in human lower extremity arteries. *J Vasc Surg* 2013; 58(5): 1259-1266.
4. Eberhardt KM *et al*. Prospective evaluation of optical coherence tomography in lower limb arteries compared with intravascular ultrasound *JVIR* 2013; 24: 1499-1508.
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## APPENDIX A – Protocol Signature Page

### The SCAN Trial

### Protocol Number: P0986

I have read the protocol and agree to comply with all the contents contained herein. I will make a reasonable effort to conduct the study in a timely and efficient manner and will ensure that all participating staff members are adequately trained to carry out the tasks for which they have been assigned.

I will provide access to the study Sponsor and/or its designated representative as well as any regulatory agency personnel. I further understand that the study may be terminated or enrollment suspended at any time by the study Sponsor, regulatory authorities or the IRB in the event the subjects' best interests may be compromised or the results of ongoing Investigators deem the study Sponsor's product to be unsafe.

**INVESTIGATOR'S SIGNATURE:**

_____

Investigator's Printed Name

_____

Investigator's Signature Date

**SPONSOR'S SIGNATURE:**

_____

Thomas Lawson, PhD Date
VP, Clinical and Regulatory Affairs
Avinger, Inc.