Study Protocol:
Cardiac Cath Lab **St**A**F**f Radiation **E**xposure During Chronic **T**otal Occlusion PCI:
CorPath®GRX vs. Manual

Sponsored By:

Corindus Vascular Robotics, Inc.
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REVISION HISTORY			
Author	**Version**	**Date**	**Summary of Changes**
Tina Ridgeway	A	April 4, 2019	Initial Release

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Protocol Signature Page

I have read and understand the contents of this protocol. I agree to follow and abide by the guidelines set forth in this document.

_____

Investigator Name (print)

_____ _____

Investigator Signature Date

Synopsis

STUDY TITLE	Cardiac Cath Lab Staff Radiation Exposure During Chronic Total Occlusion PCI: CorPath®GRX vs. Manual
SHORT TITLE	SAFE-T Study
PRINCIPAL INVESTIGATOR	William Nicholson, MD WellSpan York Hospital, York, PA
STUDY SPONSOR	Corindus Vascular Robotics, Waltham, MA
RATIONALE	The PRECISE pivotal trial showed that operators sitting at the CorPath' s shielded cockpit had a median 92.5% reduction in radiation exposure when compared to published results. To date there have been no direct randomized comparisons of patient safety and staff radiation exposure comparing robotic-assisted (CorPath GRX) CTO PCI to conventional manual CTO PCI. This study will be a randomized evaluation comparing patient outcomes and radiation exposure of Cardiac Catheterization Laboratory staff in similarly matched coronary CTO PCI procedures.
REGULATORY STATUS	The CorPath GRX System was granted 510(k) clearance (K160121) on October 27, 2016.
FDA CLEARED INDICATION FOR USE	The CorPath GRX is intended for use in the remote delivery and manipulation of guidewires and rapid exchange catheters, and remote manipulation of guide catheters during percutaneous coronary and vascular procedures.
STUDY OBJECTIVE	The objective of this randomized safety and observational study is to demonstrate CorPath GRX CTO PCI is safe, and that Cardiac Catheterization Laboratory staff have no additional exposure to radiation when compared to conventional manual CTO PCI procedures without added procedure time.
STUDY DESIGN	This is prospective, dual-arm, randomized, multi-center, observational study comparing patient outcomes and staff radiation exposure in CTO PCI procedures through 48 hours post procedure or hospital discharge, whichever occurs first.
SUBJECT POPULATION	Subjects >18 years of age with symptoms suggestive of ischemic heart disease, with TIMI grade 0 flow and a lesion that is thought to be present for more than 3 months.

NUMBER/LOCATION OF SITES	This safety and observational study will be conducted at up to no less than three (3) centers.
STUDY DURATION	All subjects will be followed through 48 hours post CTO PCI procedure or hospital discharge, whichever occurs first.
SAMPLE SIZE	At least 90 CTO PCI procedures (45 CorPath GRX (robotic-assisted) / 45 Manual)
EFFECTIVENESS PERFORMANCE MEASURE	**Clinical Success** Defined as successful CTO PCI revascularization with achievement of <30% residual diameter stenosis (visual estimate) within the treated segment and restoration of antegrade TIMI grade 3 flow, without in-hospital major adverse events (MAE).
SAFETY MEASURE	**In-hospital MAE** MAE that occurs within 48 hours of the CTO PCI procedure or hospital discharge, whichever occurs first.
OTHER MEASURES	**Operator Radiation Exposure** Cumulative dose the physician receives as recorded from electronic pocket dosemeter during procedure. **Staff Radiation Exposure** Cumulative dose the staff receives as recorded from electronic pocket dosemeter during procedure. **Patient Radiation Exposure** DAP (dose-area-product) and cumulative dose/air kerma as recorded during the procedure **Overall Procedure Time** Defined as the time measured from the placement of the first guide catheter to last guide catheter removal. **Fluoroscopy Time** Total fluoroscopy (min.) utilized during the procedure as recorded by an Imaging System. **Contrast Fluid Volume** Total contrast (mL) used during the procedure.

INCLUSION CRITERIA	For a CTO PCI procedure to qualify for this study, the procedure must meet the following inclusion criteria: 1. Age ≥ 18 years; 2. CTO lesion, successfully crossed with conventional manual techniques; 3. The Investigator deems the procedure appropriate for robotic-assisted CTO PCI with the CorPath GRX System; 4. Individual monitoring of radiation dose, using the pocket dosimeter, was initiated at start of procedure; 5. The subject has been informed of the nature of the study, agrees to its provisions and has provided written informed consent.
EXCLUSION CRITERIA	If any of the following criteria are met, the procedure cannot be included in this study: 1. Failure/inability/unwillingness to provide informed consent, or 2. Cardiogenic Shock; or 3. Perforation which requires treatment (e.g. covered stent, coil and other embolization techniques, or pericardiocentesis).
RANDOMIZATION	The randomization scheme will utilize random block sizes of 4 or 6. Once the investigator has determined that the procedure is eligible based on inclusion/exclusion criteria, the procedure will be randomized in a 1:1 fashion to either CorPath GRX robotic-assisted CTO PCI or conventional manual CTO PCI. To randomize the procedure, a member of the study staff will select the next sequential number from the electronic data capture (EDC) system and declare the procedure's assignment. The assignment will be logged in the EDC.
INVESTIGATIONAL DEVICE	N/A: CorPath GRX will be used with accordance to the indication cleared by FDA.

1 INTRODUCTION

1.1 Device Name

CorPath® GRX System

1.2 BACKGROUND

As interventional cardiology moves to more cases and more complex procedures, reduction in radiation exposure for both patients and catheterization laboratory staff has become a primary concern.[1–3] Interventional cardiologists have increased incidences of cataracts and posterior lens opacities than do other medical professionals[2,4,5] and have, in an observational report, been reported to have a possible association between radiation exposure and left-sided brain tumors.[6] At the Latin American Society of Interventional Cardiology (SOLACI) 2014 conference, Ariel Rogiun reported on 36 physicians with head and neck tumors; 28 were interventional cardiologists. Eighty-six percent of the tumors with reported sidedness, were on the left side; the side closest to the ionizing radiation source.[7]

Percutaneous coronary intervention on chronic total occlusion causes 2- to 10-fold higher radiation burden on patients and operators compared to standard PCI.[8] In the PRECISE study, the use of remote robotic-PCI system resulted in a significant decrease in operator radiation exposure, with a median reduction of 95.2% when compared to previously published results.[9] The lesions were relatively simple lesions that could be covered with a single stent. The safety of robotic assisted PCI in non-CTO lesions has been demonstrated in previous studies [10,11]. However, the effect of radiation exposure and procedure time in robotic assisted CTO PCI has not been previously reported.

This study is being conducted as a randomized comparison evaluating the safety of robotic-assisted CTO PCI and Cardiac Catheterization Laboratory staff radiation exposure when compared to conventional manual CTO PCI.

2 INTENDED DEVICE AND DEVICE DESCRIPTION

2.1 Intended Use

The CorPath GRX System is intended for use in the remote delivery and manipulation of guidewires and rapid exchange catheters, and remote manipulation of guide catheters during percutaneous coronary and vascular procedures.

2.2 Device Description

The CorPath GRX System is intended to allow physicians to deliver and manipulate commercially available guidewires, rapid exchange catheters and guide catheters during percutaneous coronary and vascular procedures. During the use of the CorPath GRX System, the physician maneuvers interventional devices using intuitive controls under independent angiographic fluoroscopy visual guidance using computer controlled movements while in a seated position away from the radiation source.

The CorPath GRX System is composed of the following two functional sub-units:

1. Bedside Unit – Which consists of the Extended Reach Arm, Robotic Drive and Single-use Cassette
2. Remote Workspace (also known as robotic cockpit) – Which consists of the Control Console, angiographic monitor(s), hemodynamic monitors and X-ray foot pedal..

Commercially available guidewires, rapid exchange catheters, and guide catheters are loaded into the Single-use Cassette. By using the joysticks or the Control Console touch screen, the physician can control the Robotic Drive to advance, retract, and rotate the guidewire, advance and retract the rapid exchange catheter, and advance, retrace, and rotate the guide catheter. The Robotic Drive and Control Console communicate via a single communication cable.

***Note**: For a more detailed description of the CorPath GRX please refer to the CorPath GRX System Operator's Manual.*

3 OBJECTIVE

The objective of this randomized safety and observational study is to demonstrate CorPath GRX robotic-assisted CTO PCI is safe and that Cardiac Catheterization Laboratory staff and physicians have no additional exposure to radiation when compared to conventional manual CTO PCI procedures without added procedure time.

3.1 Effectiveness Performance Measures

The following study measures will be evaluated in patients enrolled in the SAFE-T Study:

3.1.1 Clinical Success

Defined as successful CTO PCI revascularization with achievement of <30% residual diameter stenosis (visual estimate) within the treated segment and restoration of antegrade TIMI grade 3 flow, without in-hospital major adverse events (MAE).

In-hospital major adverse events (MAE) is defined as composite of in-hospital death, myocardial infarction (MI), clinical perforation, vessel dissection, septal hematoma, new arrhythmia, stroke and pericardial effusion.

3.2 Safety Measures

Several safety-based measures will also be utilized to confirm the overall safety of CTO PCI procedures. These include:

3.2.1 In-hospital MAE

Defined as MAE that occurs within 48 hours post-CTO PCI procedure or hospital discharge, whichever occurs first.

3.3 Other Measures

3.3.1 Operator Radiation Exposure

Cumulative dose the physician receives as recorded from electronic pocket dosemeter during procedure measured in µSv.

3.3.2 Staff Radiation Exposure

Cumulative dose the staff receives as recorded from electronic pocket dosemeter during procedure measured in µSv.

3.3.3 Patient Radiation Exposure

DAP (dose-area-product) and cumulative dose/air kerma as recorded during procedure.

3.3.4 Procedure Time

Defined as the time measured from the placement of the first guide catheter to last guide catheter removal.

3.3.5 Cockpit Time

Defined as the time the physician operator enters the cockpit to the last guide catheter removal.

3.3.6 Fluoroscopy Time

Total fluoroscopy utilized during the procedure as recorded by an Imaging System.

3.3.7 Contrast Fluid Volume

Total contrast used during the procedure.

4 METHODOLOGY

4.1 Study Summary

This is prospective, dual-arm, randomized, multi-center, observational study comparing patient outcomes and staff radiation exposure during CTO PCI procedures through 48 hours post procedure or hospital discharge, whichever occurs first.

4.2 Institutional Review Board Waiver or Approval

Prior to any data collection for the SAFE-T Study, the protocol and informed consent forms must be sent to the applicable institutional review board (IRB) for review and approval.

4.3 Informed Consent Process

If the IRB determines patient informed consent is required, consent, using the IRB-approved ICF, must be obtained prior to randomization. The patient's consent to participate will be documented on the IRB-approved ICF and the clinical investigator or their designate will witness the patient's signature. The original signed consent form will be retained in study records at the investigational site, and a copy of the consent form will be provided to the patient.

4.4 Cath Lab Staff Training

4.4.1 Study (protocol) Training

Prior to staff participation in this study, staff members will be trained by either the PI or Sponsor representative on study objectives and procedures, pocket dosimeter and participant involvement. Once training is complete, the individual staff member will have an opportunity to opt-in to the study by signing a document acknowledging their willingness to voluntarily participate (if required by the IRB).

4.4.2 Procedural Training

- Prior to study start, training on key principles of radiation safety will be provided to staff members by either the PI or Sponsor.
- The following protection principles will be discussed:
  - Time - less imaging equals less exposure.
  - Distance - as distance doubles, exposure decreased by a factor of four.
  - Extension Tubing - a disposable 40-48 inch extension tubing will be utilized. It will be connected between the guiding catheter and manifold. This will allow for further distance from the radiation source during hand injections.
  - Shielding - lead aprons and shields absorb 90% of radiation

  - Transparent ceiling mounted shielding - the operating physician and scrub technician will optimize the position of the movable transparent shield prior to fluoroscopy and cine imaging. Also, they will utilize the fixed lead shielding located below the patient table that protects legs and feet, if available.
- Dosimetry Training
  - Pocket dosimeter - on a routine basis during the study period, in addition to the hospital required radiation badges, the *operating physician and scrub technician* will wear a pocket dosimeter. The dosimeter will be clipped to the left pocket of lead apron. The dosimeter will be worn for the duration of the procedure.
  - A pocket dosimeter will also be added as a control, to be placed on Catheterization Lab x-ray table where the primary physician would stand for all enrolled cases.
  - Dosimeter must have a current calibration date.
- Cockpit Time
  - Cockpit time is defined as the time the physician operator enters the robotic cockpit to the last guide catheter removal.
  - Manual interruption time is defined as the cockpit time minus any manual interruption time (a timer should start when the operator sits in the robotic cockpit and stop if the operator leaves the cockpit for the tableside, and resume when he/she returns to the cockpit).

4.5 Study Entrance Criteria

Procedures included for analysis in this study must meet the following inclusion criteria below.

4.5.1 Inclusion Criteria

For a CTO PCI procedure to qualify for this study, the procedure must meet the following inclusion criteria:

1. Age ≥ 18 years;
2. CTO lesion; successfully crossed with conventional manual techniques;
3. The investigator deems the CTO PCI procedure appropriate for robotic-assisted PCI with the CorPath GRX System;
4. Individual monitoring of radiation dose, using the pocket dosimeter, was initiated at the start of the procedure;
5. The subject has been informed of the nature of the study, agrees to its provisions and has provided written informed consent.

4.5.2 Exclusion Criteria

If any of the following criteria are met, the procedure cannot be included in this quality improvement study:

1. Failure/inability/unwillingness to provide informed consent; or
2. Cardiogenic shock; or
3. Perforation which requires treatment (e.g. covered stent, coil and other embolization techniques, or pericardiocentesis).

4.6 Procedure Enrollment

An interventional procedure is enrolled in this study when:

- All inclusion and exclusion criteria are met,
- The patient has signed the approved informed consent form, and
- All staff have volunteered to participate.

4.7 Randomization

The randomization scheme will utilize random block sizes of 4 or 6. Once the investigator has determined that the procedure is eligible based on inclusion/exclusion criteria, the procedure will be randomized in a 1:1 fashion to either robotic-assisted CTO PCI or conventional manual CTO PCI. Qualified subjects will be randomized to treatment using an Interactive Web-based Randomization System (IWRS). The IWRS will assign treatment arm and will be recorded in the eCRF.

4.8 Screen Failure

A patient who signs an informed consent form (ICF), staff who have volunteered to participate, and the procedure is enrolled in the study, but one or more of the conditions below are not met prior to initiation of the CTO PCI procedure, will be considered a screening failure and excluded from the analyses.

- Procedure does not meet eligibility criteria;
- Patient or Staff withdraws their consent.

4.9 Procedure and Data Collected

Additionally, the operating physician and scrub technician (or second physician) will be equipped with pocket dosimeters. They will wear the dosimeters for the duration of the study, while in the "study" room.
Cockpit time is defined as the time the primary operator enters robotic cockpit until the procedure is complete (procedure end time).

Procedural Steps:

1. Qualified subjects will be randomized to treatment using an Interactive Web-based Randomization System (IWRS).
2. The operating physician and scrub technician will wear a pocket dosimeter. The dosimeter will be clipped to the thyroid collar or pocket of the lead apron.
3. Control pocket dosimeter will be turned on and clipped to the Cardiac Catheterization Laboratory X-ray table near where the primary physician will stand.
4. Document initial guide catheter in time.
5. Perform CTO PCI based on randomization.
6. Document cockpit start, stop time and interruption time.
7. Document the procedure end time (guide catheter removal time).
8. Record fluoroscopy time.
9. Record DAP and AK is available
10. Remove all pocket dosimeters and record doses displayed; return dosimeters to designated area.

Procedure data collected will include:

- Radiation dose via the pocket dosimeter, for operating physician and scrub technician recorded during the CTO PCI procedure.
- Procedure data:
    - Vessel(s) treated
    - Total PCI procedure fluoroscopy time
    - Total PCI procedure time (sheath in to guide catheter out times)
    - DAP & AK
    - Contrast amount
    - Cockpit time
    - Manual interruption time (start and stop times when the physician is not in the cockpit)
    - Manual interruption reason

Follow standard operator and institutional routines for recommended anticoagulation and anti-platelet regimens.

4.10 Patient Enrollment

The patients will be followed for 48 hours post-procedure or hospital discharge, whichever occurs first. No additional patient contact is required for this study. Data collection must be completed on all subjects at the time of end of study.

4.11 Data Entry

Authorized personnel at each investigative site will enter data directly into the EDC system. During data entry, each field is automatically subjected to data type verification and range checking. If an error occurs, the system ensures that the error is addressed before moving to the next entry field.

5 DATA AND QUALITY MANAGEMENT

5.1 Study Data Collection

5.1.1 Study Data Requirements

To ensure data quality and completeness, all required data will be recorded on standardized electronic case report forms (eCRFs).

5.1.2 Completion and Collection of Case Report Forms

Electronic Case Report Forms (eCRFs) must be completed for each subject and, once complete, signed by the Investigator. The Investigator, or their authorized designee, is responsible for recording all study data in the eCRFs.

5.2 Protocol Deviations

A protocol deviation is defined as a circumstance in which the Investigator or other site personnel did not conduct the study according to the protocol. Protocol deviations will be documented in the EDC by using associated Narrative form. All protocol deviations must have an associated explanation of events.

5.3 Clinical Event Handling

This study will collect data on subjects undergoing standard treatments and procedures. Sites will be asked to provide documentation of events on the eCRFs related to specific procedural events. The Sponsor will identify events associated with the study endpoints and additional event review may be performed, as described below. Clinical sites will follow their routine hospital procedures for major adverse event handling, as necessary.

6 STATISTICAL METHODS AND DATA ANALYSIS

6.1 All Outcome Measures

6.1.1 Parameter of Interest

This is prospective, dual-arm, randomized, multi-center, observational study comparing patient safety and staff radiation exposure during CTO PCI procedures. The analysis of data collected

as part of the SAFE-T Study will include but may not be limited to the Objectives and Measures outlined in Section 2.0 of this protocol.

6.1.2 Analysis Methods

The analysis will include all randomized patients under the principle of the protocol. That is, all procedures that fulfill the protocol in the terms of the eligibility, interventions, and outcome assessment will be analyzed.

Due to potential imbalance in the number of lesions treated in each procedure group, an appropriate regression model will be used to adjust for number of lesions treated. Radiation exposure will be the response variable and both treatment and number of lesions will be fixed effect covariates. If radiation exposures are not normally distributed, transformations on the radiation exposure may be employed. The adjusted 95% confidence intervals and adjusted p-value will be the primary endpoint measure.

6.2 General Statistical Methods

Descriptive statistics will be provided for both observational study arms, see table below. This will include the mean, median, standard deviation, minimum, and maximum for continuous variables, and numbers and percentages for ordinal or categorical variables. For statistical tests not described in detail above, the following tests will be used at the 0.05 level. T-tests will be used to compare normally distributed continuous variables; non-parametric tests will be used for continuous variables that are found to be non-normally distributed. Fisher's exact test will be used to compare the randomized groups for categorical variables.

	Manual N=45	**Robotic N=45**
Total Fluoroscopy Time	X	Y
Average Fluoroscopy Time per case	X/45	Y/45
Total Physician Radiation Exposure	A	B
Mean Physician Radiation Exposure	A/45	B/45
Total Staff Radiation Exposure	α	B
Mean Staff Radiation Exposure	α/45	β/45
Physician Radiation Exposure Normalized for Fluoroscopy Time	M	N
Staff Radiation Exposure Normalized for Fluoroscopy Time	Φ	R

7 MONITORING PROCEDURES

The study site will be monitored to ensure that the study is conducted in full compliance with the study protocol, Good Clinical Practices, and Corindus policy and procedures. A summary of these procedures follows.

7.1 Required Documentation

Enrollment may not begin until the following documents are received by Corindus:

- Documentation of waiver of IRB review or IRB approval
- Fully Executed Clinical Study Agreement
- Signed Financial Disclosure for the Principal Investigator
- Curricula vitae for the Principal Investigator
- Records of protocol training

7.2 Monitoring responsibilities

Monitoring responsibilities performed by Corindus or its designees include but are not limited to, the following:

- Site initiation visits;
- Interim monitoring visits to:
  - Assess protocol compliance;
  - Conduct source document verification;
  - Assess case report form accuracy and completeness;
- Telephone contacts with site;
- Maintenance of records of investigator/monitor contacts;
- Final site close-out visit.

At the monitoring visits, trial progress will be discussed with the investigator and completed CRFs will be reviewed for accuracy during these visits.

7.3 Monitoring Staff

Corindus or its designees will conduct the monitoring of the SAFE-T Study. The name and address of the Study Director is:

Tina Ridgeway
Corindus Vascular Robotics
309 Waverley Oaks Road, Suite 105
Waltham, MA 02452

8 RECORDS AND REPORTS

8.1 Investigator Records

The investigator is responsible for the preparation of the following documentation:

- Signed Investigator Agreement and recent curriculum vitae, both of which also must be submitted to Corindus
- Documentation of IRB waiver of review. A copy must be submitted to Corindus.

8.2 Sponsor Records

Corindus will maintain the following records:

- All correspondence which pertains to the investigation
- Signed investigator agreement and curriculum vitae
- All electronic case report forms submitted by the investigator
- Investigational plan
- Hospital staff training
- Corindus will own and store the clinical data generated under this protocol.

9 PUBLICATION POLICY

It is the intent of the Investigator(s) and Sponsor that the results of this observational study will be submitted for publication.

The Principal Investigator(s) has the right, consistent with academic standards, to publish his study results provided such publication does not constitute a violation of the Clinical Study Agreement. The Principal Investigator agrees to submit any proposed submission for publication to Corindus for review and approval 60 days prior to any submission. Consent cannot be denied without a sensible reason.

10 SPONSOR CONTACT INFORMATION

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12 APPENDIX A – DEFINITIONS

Major Adverse Events (MAE): is defined as composite of in-hospital death, myocardial infarction (MI), clinical perforation, vessel dissection, septal hematoma, new arrhythmia, stroke and pericardial effusion.

Cardiac Death: Death due to cardiac causes. If the cause of death cannot be determined, it will be categorized as cardiac.

Coronary Perforation - Coronary perforation occurs when a dissection or intimal tear propagates outward enough to completely penetrate the arterial wall. This may be caused by pre/post balloon dilatation or post stent deployment where the stent edge causes an edge perforation. Stent edge perforation will range in severity. Ellis classification of coronary perforation:

- Type I - Focal extraluminal crater without extravasation
- Type II - Pericardial or myocardial 'blush' without contrast agent
- Type III - Contrast agent 'jetting' through a frank (>1 mm) perforation

Clinically relevant MI after coronary revascularization is defined as:

- Patients with normal baseline cardiac biomarkers
    - CK-MB >10x ULN or cTn (I or T) >70x ULN, or
    - CK-MB >5x ULN or cTn >35x ULN plus new Q-waves in >2 contiguous leads or LBBB
- Patients with elevated baseline cardiac biomarkers
    - Baseline biomarkers are stable or falling:
    - CK-MB >10x ULN or cTn (I or T) >70x ULN of most recent pre-procedure level, or
    - CK-MB >5x ULN or cTn >35x ULN of most recent pre-procedure level plus new Q-waves in >2 contiguous leads or LBBB
- Baseline biomarkers have not been shown to be stable or falling: CK-MB (or cTn) rises by an absolute increment equal to those recommended above plus new ST-segment elevation or depression plus signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension.

Septal Hematoma: defined as the dissection between the spiral planes of the ventricular septum.

In-Hospital MAE: MAE that occurs within 48 hours of the procedure or prior to hospital discharge, whichever occurs first.

Pericardial Effusion: abnormal accumulation of fluid in the pericardial cavity. Because of the limited amount of space in the pericardial cavity, fluid accumulation leads to an increased intrapericardial pressure which can negatively affect heart function.

Other Definitions

Adverse Event Classification: An adverse event is defined as any adverse change in health or undesirable clinical occurrence from the subject's baseline whether it is considered device related or not.

An adverse event is considered serious if it results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is an important medical event which may jeopardize the subject and may require medical or surgical intervention to prevent one of the above outcomes.

Coronary Dissection - Refers to a split or a tear in the wall of the artery which compresses or compromises the lumen of the artery reducing blood flow.

Coronary Guidewire Dissection - A coronary dissection where a coronary guidewire is inadvertently positioned in a subintimal position or when stiff-tipped or hydrophilic-tipped guidewires are used to cross highly stenosed or totally occluded arteries.

TIMI FLOW:

- TIMI 0: Dye fails to enter the microvasculature. There is either minimal or no ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit artery indicating lack of tissue level perfusion.
- TIMI I: Dye slowly enters but fails to exit the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that fails to clear from the microvasculature, and dye staining is present on the next injection (approximately thirty (30) seconds between injections).
- TIMI II: There is delayed entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that is strongly persistent at the end of the washout phase (i.e. dye is strongly persistent after three (3) cardiac cycles of the washout phase and either does not or only minimally diminishes in intensity during washout).
- TIMI III: There is normal entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that clears normally, and is either gone or only mildly/moderately persistent at the end of the washout phase (i.e. dye is gone or is mild/moderately persistent after three (3) cardiac cycles of the washout phase and noticeably diminishes in intensity during the washout phase), similar to that in an uninvolved artery. Blush that is of only mild intensity throughout the washout phase but fades minimally is also classified as grade III.

Total Occlusion: True total occlusion is a lesion with TIMI 0 antegrade intraluminal flow and 100% diameter stenosis. A functional total occlusion is a lesion with TIMI I antegrade

intraluminal flow and 99% diameter stenosis (functional TO). A chronic total occlusion is either of the above that has been present for at least 3 months.

Vessel Characteristics:

- Angulation: Vessel angle formed by the centerline through the lumen proximal to the stenosis and extending beyond it, and a second centerline in the straight portion of the artery distal to the stenosis measured in a non-foreshortened view.
- Spasm: Transient narrowing >50% diameter in a region where a <25% diameter stenosis had previously been.
- Tortuosity: Number of bends that must be traversed by a device to reach the target lesion.
- Haziness: Presence of radiolucencies within the arterial lumen not satisfying the criteria for thrombosis.

Lesion Characteristics:

- Anastomotic: Lesion located at the junction of a bypass graft and native vessel.
- Aneurysm: An expansion of the lumen in the region of maximum stenosis that ex-tends with a wide or narrow mouth beyond the apparent normal contour.
- Aorto-ostial: Lesion which begins within 3-5 mm of the origin of a major epicardial artery. Ostial lesions represent a challenge to the interventional cardiologist because they often involve the wall of the aorta, they are often calcified, they may not fully di-late, and they are prone to restenosis.
- Bifurcation: Lesion located at the origin, immediately after, or branch that has a diameter ≥ 2mm.
- Medina Classification: Bifurcation (Medina) is classified when 50% lumen narrowing occurs within 3 mm of the bifurcation point.
- Eccentricity: A stenosis that has one of its luminal edges in the outer one-quarter of the apparent normal lumen.
- Calcification: Readily apparent densities noted within the apparent vascular wall at the site of the stenosis. Calcification is classified as none/mild, moderate when densities noted only during the cardiac cycle prior to contrast injection, and severe when densities noted without cardiac motion prior to contrast injection generally involving both sides of the arterial wall.
- Intimal Flap: Extrusion of tissue extending from the arterial surface into the lumen.
- Irregularity: Lesion borders with abnormal margins based on the presence of an ulceration, aneurysm, or intimal flap.
- Length: “Shoulder to shoulder” distance, which is measured from the proximal shoulder to the distal shoulder of a lesion in the projection that shows the most elongated view of the stenosis.
- Discrete: Lesion length <10.0 mm.
- Tubular/Focal: Lesion length >10.0 mm and <20.0 mm.
- Diffuse: Lesion length >20.0 mm.
- Location: Designated as ostial, proximal, mid and distal.
- Ostial: Lesions that begin within 3.0 mm of the origin of the artery.

- Ulceration: A small crater or flap in a lesion.

ACC/AHA Lesion Characteristics (Type A, B and C):

- Type A Lesions (high success, >85%; low risk): Discrete (<10mm length), concentric, readily accessible, non-angulated segment ,45o, smooth contour, little or no calcification, less than totally occlusive, non-ostial in location, no major branch involvement and absence of thrombus.
- Type B (B1 and B2) Lesions (moderate success, 60 - 85%; moderate risk): Tubular (10-20 mm length), eccentric, moderate tortuosity of proximal segment, moderately angulated, 45 - 90o , irregular contour, moderate or heavy calcification, ostial in location, bifurcation lesions requiring double guidewires, some thrombus present and total occlusion < 3 months old. Type B2 lesion classification has more than one characteristic above.
- Type C Lesions (low success, < 60%; high risk): Diffuse (>2 cm length), excessive tortuosity of proximal segment, extremely angulated, > 90o, inability to protect major side branch, degenerated vein grafts with friable lesions and total occlusions > 3 months old.

13 APPENDIX B – CASE REPORT FORMS (CRFs)