NCT03848650

The Drift-Reduction for Improved FFR using Fiberoptic Technology (DRIFT) study

Version 4.1
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1. Protocol Summary

Study Title	The Drift-Reduction for Improved FFR using Fiberoptic Technology (DRIFT) study
Device Description	OpSens Medical OptoWire Duex Pressure Wire
Study Design	Prospective, observational, multi-center, single-arm, clinical registry
Objectives	The primary objective of this study is to assess the accuracy, efficacy and durability of the OpSens Medical OptoWire Deux Pressure Wire in the assessment of angiographically intermediate proximal left anterior descending (LAD) stenosis in clinical practice.
Subject Population	Subjects with stable angina, unstable angina, or non–ST segment elevation myocardial infarction (if the LAD lesion is the non-culprit lesion) who are referred to coronary angiography and have an angiographically intermediate proximal LAD stenosis with anatomy amenable to percutaneous intervention. Patients meeting enrollment criteria and had fractional flow reserve (FFR) with the OpSens FFR system and optical coherence tomography (OCT) of the LAD as part of their routine care using a standard of care technique will be eligible for enrollment in this study.
Number of Subjects and Sites	This study will enroll a total of 60 patients at Columbia University Medical Center and St. Francis Hospital.
Primary Endpoint	The primary endpoint is the rate of significant drift, defined as Pd/Pa <0.97 or >1.03 in the pre-percutaneous coronary intervention (PCI) FFR recording.
Secondary Endpoint	*Secondary efficacy endpoints:* 1. The rate of pre-PCI positive FFR (≤0.80) in angiographically intermediate proximal LAD lesions. 2. The rate of pre-PCI resting Pd/Pa (≤0.92) in angiographically intermediate proximal LAD lesions. 3. The rate of significant drift defined as Pd/Pa <0.97 or >1.03 with post-PCI FFR recording. 4. Pre-PCI OCT correlation (minimum lumen area [MLA]<2.5 mm^2) with FFR (≤0.80). 5. Pre-PCI OCT correlation with the pullback for distinguishing focal (step-up ≥0.03) versus diffuse disease defined by pre-PCI resting Pd/Pa pullback. 6. Post-PCI OCT correlation (edge dissection [lumen area within the dissection ≤4.5 mm^2], stent underexpansion [≤4.5

	mm^2 in 3 mm vessel or ≤ distal reference lumen area], residual disease outside of stent [minimum lumen area <4.5 mm^2]) with the pullback for distinguishing focal (step-up ≥0.03) versus diffuse disease defined by post-PCI resting Pd/Pa pullback. 7. The rate of discrepancy between FFR and resting physiology indices and its correlation with an OCT derived MLA. *Secondary economic endpoints:* 8. Total number of OptoWires used during the procedure. 9. Frequency of use of alternative guidewire (workhorse wire) for the procedure. 10. Total duration of the procedure. 11. Duration of FFR procedure.
Procedural Protocol	Patients with an angiographically intermediate proximal LAD lesion, who meet the inclusion and exclusion criteria will be eligible for enrollment in this observational study post-procedure.
Inclusion Criteria	1. Male or female subjects, > 18 years of age. 2. Patients with stable angina, unstable angina or non-ST segment elevation myocardial infarction (if the LAD lesion is the non-culprit lesion) and in whom an intermediate proximal LAD stenosis (30-80%) with TIMI flow 3 has been identified on angiography. **NOTE:** Patients with multi-vessel disease can be enrolled. 3. Patients have had FFR and OCT of the LAD with the OpSens FFR system as part of their routine evaluation as standard of care procedure. 4. Provides written, informed consent and HIPPA consent to use data in a clinical study.
Exclusion Criteria	*General exclusion criteria:* 1. Patients presented with non-ST segment elevation myocardial infarction (NSTEMI) with the LAD involved as the culprit lesion 2. ST-elevation myocardial infarction within the past 30 days. 3. Hemodynamic instability requiring vasopressor or mechanical circulatory support. 4. Prior heart transplant. 5. Known left ventricular ejection fraction ≤40%

	6. LAD supplying akinetic or severely hypokinetic territories if already known based on prior imaging. 7. Patients is enrolled in another clinical study that may impact the results of this study. 8. FFR not acquired per the instructions for use (IFU) for the OpSens wire. 9. LAD Lesion not assessed with OCT. *Angiographic exclusion criteria:* 1. TIMI grade 2 or lower at baseline angiography. 2. Target lesion involves left main (>50% by visual estimation). 3. Presence of a chronic total occlusion in any vessel. 4. Presence of a side branch ≥2.75 mm with ≥70% stenosis in the LAD. 5. Bifurcation lesion that resulted in the stent implantation of a side branch.
Expected Start Date	February 2018
Enrollment	The enrollment duration is expected to last 5 months.
Follow-up	There is no clinical follow-up.
Regulatory Status	OpSens Pressure Wire received 510(k) clearance from U.S. Food and Drug Administration in March 2016.

2. Additional Summary Information

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3. Background

3.1. Fractional flow reserve

Fractional flow reserve (FFR) is an index that quantifies the hemodynamic significance of coronary artery stenosis. FFR is obtained by measuring the ratio between pressure distal to a stenosis and proximally using specialized pressure-measuring guidewires during maximal hyperemia.[1-3] FFR is considered the standard of reference for clinical decision-making. Clinical outcome studies have shown that medical therapy is preferred for non-hemodynamically significant lesions (FFR >0.80), while coronary revascularization should be considered in cases of significant functional stenosis (FFR ≤0.80).[4-11] Society guidelines reflect the importance of physiology-guided revascularization, with the ACCF/AHA/SCAI guidelines recommending that FFR is used to guide the treatment strategy in stable coronary lesions.[12] Furthermore, the most recent appropriate use criteria advocates for expanded use of intracoronary physiologic testing.[13,14]

Nevertheless, for a variety of practical reasons, FFR measurements remain underutilized. Conventional pressure guidewires are limited by three main factors. First, pressure-measuring guidewires have a more complex design than standard guidewires used in percutaneous coronary interventions (PCI). Consequently, traditional pressure guidewires have handling, torquability and lesion crossing characteristics that are suboptimal compared to the mechanical performance of workhorse guidewires. In the FFR cohort in the DEFINE-FLAIR study, only 30.7% of PCI procedures were performed with a pressure wire.[15] A pressure wire with improved handling characteristics to permit use as a workhorse guidewire during interventions fills an important void and improves the likelihood an operator assesses post-intervention FFR by avoiding the need to cross with an additional wire.

Secondly, pressure drift can lead to unreliable FFR values and is a prominent limitation with conventional pressure wires. Drift can occur when air bubbles become trapped in the cavity of the pressure sensor coupled with the inherent thermal and electrical instability of pressure sensors.[16] Signal drift has been reported to occur in as many as 17.5% of FFR cases.[17] Lastly, contrast agents and blood can affect connectivity with conventional pressure wires, reducing its reliability post-stenting.

Therefore, the ability to derive accurate FFR values reliably with minimal drift and with durability to work throughout an entire intervention coupled with the mechanical performance of a workhorse guidewire could have an important impact on daily clinical practice by increasing utilization of FFR both pre- and post-PCI.

The introduction of fiber optic wires can address these issues and improve the performance of FFR wires. The design of the OpSens Medical OptoWire Deux pressure wire combines optimal guidewire performance with the ability to perform FFR measurements. Fiber optic pressure wires may reduce drift, decreasing the number of repeat FFR recordings as well as reducing the number of wire changes. Using the FFR pressure wire for the PCI, thereby avoiding multiple wire exchanges, may have both economic and clinical benefits.

3.2. Rationale for study endpoints and cutoff values

3.2.1. Angiographically intermediate LAD lesions

Lesions in the intermediate range involving the LAD are often undertreated.

Physiologic assessment of these lesions can ensure that the treatment of these lesions is selected and deferred appropriately.

3.2.2. Correlation of Pre-PCI OCT MLA with Pre-PCI FFR

OCT provides accurate and reproducible quantitative assessment of coronary lesions.[18] Prior to revascularization, an OCT MLA <2.5 mm^2 can be used to predict FFR ≤0.80 in the proximal LAD location.[19-21] Correlation of MLA with a positive FFR value is associated with improved accuracy in the proximal LAD region compared to other coronary segments.[20]

3.2.3. Resting gradient

Resting gradients can be used to predict physiologic significance, however a large discrepancy exists between FFR and resting gradients in locations which supply a large myocardial territory including the left main coronary artery and proximal left anterior descending artery. A resting Pd/Pa ≤0.92 can be used to predict a significant FFR based on results from the RESOLVE study with a positive predictive value of 89.2% and overall accuracy of 81.5%.[22]

3.2.4. Pullback measurements

Repetitive pullback recordings are a safe and effective method to localize lesions for revascularization.[23, 24] A pullback recording with a pressure wire can also help distinguish the presence of a focal lesion versus diffuse disease. A gradual change in the recording indicates diffuse disease, whereas an abrupt change indicates a focal lesion, and the stenosis can be localized with angiography. A pressure step-up of 0.03 or greater on resting Pd/Pa pullback represents a significant and focal stenosis.[25] Sparse data exists correlating changes in coronary pressure pullback with intravascular ultrasound (IVUS) or OCT lesion assessment.[26]

3.2.5. Post-PCI OCT Assessment

Use of post-PCI MSA as a predictor for future events has been validated in the CLI-OPCI II study. Suboptimal stent deployment based on specific OCT criteria is associated with increased risk for future events. OCT assessment post-PCI with an MSA <4.5 mm^2 is an independent predictor of major adverse cardiac events. Edge dissection >200 μm at the distal stent edge and reference lumen area <4.5 mm^2 at either the distal or proximal stent edge is also an independent predictor of worse outcomes.[27]

3.2.6. Post-PCI FFR

Post-PCI FFR may be a useful indicator of optimal PCI, with post-PCI FFR ≥0.9 associated with a lower risk of repeat PCI and major adverse cardiac events.[28] Data regarding the correlation between post-PCT FFR and intravascular imaging is limited.[29]

3.2.7. Discrepancy between FFR and resting physiology indices

Discordance exists between FFR and resting indices such as iFR is related to lesion location. This discordance is most evident in areas of highest flow, including the proximal LAD.[30] Deferring revascularization in the LAD based on

iFR values is associated with significantly decreased events compared with FFR.[31] The correlation between OCT derived MLA and physiologic measurements, in lesions with discordant FFR and resting gradients, has not been previously investigated.

3.3. Study Device: OpSens Medical OptoWire Deux Pressure Wire

The OptoWire Deux pressure wire (OpSens Medical, Quebec, Canada) is a novel technology utilizing optical coherence technology to enhance FFR assessment of the coronaries. The OptoWire and OptoMonitor system design allows for simultaneous acquisition of distal pressure from the fiber optic sensor embedded in the OptoWire and aortic pressure from an external pressure transducer to determine an FFR value. The concentric guidewire construction allows for high fidelity pressure measurements during the entire procedure with good steerability and torquability. It is the first hybrid nitinol and stainless steel-based FFR wire designed to improve support for PCI tool delivery and resist kinks. The design of the guidewire allows the OptoWire to function as a workhorse guidewire (Figure 1. Guidewire construction). The optical contact is not affected by blood and allows immediate and reliable signal transmission for FFR measurements. The pressure wire calculates a lesion specific physiological index to determine the hemodynamic severity of an intracoronary lesion.

The OptoWire is FDA approved to measure pressure in coronary vessels during diagnostic angiography and coronary interventions. Anecdotal data suggest fiber optic pressure wires are associated with a significant reduction in signal drift; however, this has yet to be thoroughly validated in clinical practice.[16]

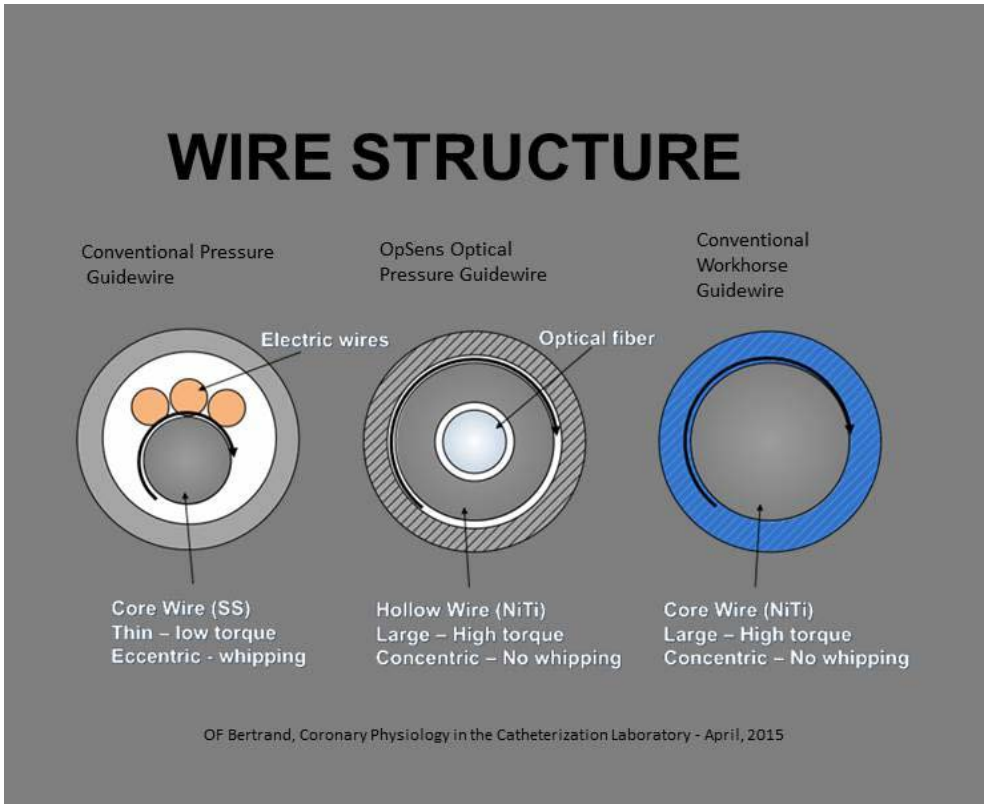

Figure 1. Guidewire construction.

4. Study Objectives

4.1. Study Objectives

The primary objective of this study is to assess the accuracy, efficacy, and durability of the OpSens Medical OptoWire Deux pressure wire in the assessment of angiographically intermediate proximal left anterior descending coronary artery (LAD) stenoses in clinical practice.

4.2. Primary Endpoint

The primary endpoint is the rate of significant drift, defined as Pd/Pa <0.97 or >1.03 with the pre-PCI FFR recording.

4.3. Secondary Endpoints

Secondary efficacy endpoints:

1. The rate of pre-PCI positive FFR (≤0.80) in angiographically intermediate proximal LAD lesions.
2. The rate of pre-PCI resting Pd/Pa (≤0.92) in angiographically intermediate proximal LAD lesions.
3. The rate of significant drift defined as Pd/Pa <0.97 or >1.03 with post-PCI FFR recording.
4. Pre-PCI OCT correlation (MLA <2.5 mm^2) with FFR (≤0.80).
5. Pre-PCI OCT correlation with the pullback for distinguishing focal (step-up ≥0.03) versus diffuse disease defined by pre-PCI resting Pd/Pa pullback.
6. Post-PCI OCT correlation (edge dissection [lumen area within the dissection ≤4.5 mm^2], stent underexpansion [≤4.5 mm^2 in 3-mm vessel or ≤ distal reference lumen area], residual disease outside of stent [minimum lumen area <4.5 mm^2]) with the pullback for distinguishing focal (step-up ≥0.03) versus diffuse disease defined by post-PCI resting Pd/Pa pullback.
7. The rate of discrepancy between FFR and resting physiology indices and its correlation with an OCT derived MLA.

Secondary economic endpoints:

8. Total number of OptoWires used during the procedure.
9. Frequency of use of alternative guidewire (workhorse wire) for the procedure.
10. Total duration of the procedure

11. Duration of the FFR procedure

5. Study Design and Population

This study is designed as a prospective, observational, multi-center, single-arm, clinical registry to estimate the ischemic burden of angiographically intermediate proximal LAD stenosis in clinical practice using the OpSens Medical OptoWire Deux FFR system. Subjects with stable angina or unstable angina who are found to have an intermediate proximal LAD stenosis on coronary angiography with anatomy amenable to PCI and underwent physiological lesion assessment with the OptoWire Deux pressure wire and OCT as part of their routine procedures using standard of care techniques will be enrolled. Patients meeting enrollment criteria will be offered the opportunity to enroll in this observational registry post-procedure. All patients enrolled in this study are expected to be evaluated and treated using a standard of care technique. This study will enroll a total of 60 patients at Columbia University Medical Center and St. Francis Hospital.

5.1. Determination of Study Eligibility

Subjects eligible for initial study screening are patients with stable angina, unstable angina or NSTEMI (if the LAD lesions is the non-culprit lesion), who are referred to coronary angiography and have had an invasive FFR measurement and OCT in the LAD artery. Subjects will need to read and sign the required informed consent document and fulfill the necessary eligibility criteria, as described below, to be enrolled in the study.

5.2. Inclusion Criteria

1. Male or female subjects, >18 years of age.
2. Patients with stable angina, unstable angina or non-ST segment elevation myocardial infarction (if the LAD lesion is the non-culprit lesion) and in whom an intermediate proximal LAD stenosis (30-80%) with TIMI flow 3 has been identified on angiography.

   NOTE: Patients with multi-vessel disease can be enrolled.
3. Patients have had FFR and OCT of the LAD with the OpSens FFR system as part of their routine evaluation as standard of care procedure
4. Provides written, informed consent and HIPAA consent to use the data in a clinical study.

5.3. Exclusion Criteria

General exclusion criteria

1. Patients presented with NSTEMI with the LAD involved as the culprit lesion
2. Any ST-elevation myocardial infarction within the past 30 days.
3. Hemodynamic instability requiring vasopressor or mechanical circulatory support.
4. Prior heart transplant.
5. Known left ventricular ejection fraction ≤40%.
6. LAD supplying akinetic or severely hypokinetic territories if already known based on prior imaging.

7. Patient is enrolled in another clinical study that may impact the results of this study.
8. FFR not acquired per the IFU for the OpSens Wire.
9. LAD Lesion not assessed with OCT

Angiographic exclusion criteria

1. TIMI grade 2 or lower at baseline angiography.
2. Target lesion involves left main (stenosis >50%).
3. Presence of chronic total occlusion in any vessel.
4. Presence of a side branch≥2.75 mm with ≥70% stenosis in the LAD.
5. Bifurcation lesion that resulted in the stent implantation of a side branch.

5.4. Subject Screening and Informed Consent

At the investigational centers (Columbia University Medical Center and St. Francis Hospital), a qualified Investigator or his designee will approach individual patients who are potential candidates for participation after the patient has fully recovered from the procedure and will explain the purpose, procedures, risks, benefits, and intent of the study to each. Interested subjects will be invited to join the study and asked to provide written informed consent as well as HIPAA consent to use the data for research purposes.

The informed consent form used must be approved by the IRB/EC and other local regulatory bodies (as appropriate). The approved consent form should clearly reflect the IRB/EC approval date.

Failure to obtain a signed and hand-dated informed consent form will preclude enrollment in this registry.

All subjects who begin the study screening process will be tracked by utilizing a study screening log. The screening log documents the screening effort to enroll consecutively eligible subjects in this study.

5.5. Subject Enrollment

Subjects will be recruited consecutively at Columbia University Medical Center and St. Francis Hospital. This is intended to ensure that the range of FFR values in the sample will represent that of the intended use population. Subjects who fail to meet the clinical inclusion and exclusion criteria will not be included in this study. Subjects will only be formally enrolled in the study after all clinical and angiographic criteria are met and the subject provides informed consent and HIPAA consent.

5.6. Subject Withdrawal

Subjects have the right to withdraw from the study at any time and for any reason without prejudice to their future medical care by the study personnel or institution.

6. Procedures and Assessments

6.1. Schedule of Events

Table 1: Schedule of Events

Study Requirement	Post-procedure
Informed consent and HIPAA consent to use data	X
Demographics	X
Medical history and baseline medication	X
Collection of procedural information	X

6.2. Baseline Procedures

The following data must be collected for all patients post-procedure, unless otherwise specified:

- Subject demographics
- Medical history
- Baseline medications
- Clinical assessment
- Procedural information

6.3. Procedural Protocol

In patients with an angiographically intermediate proximal LAD lesion, eligible for enrollment in the study whom an OptoWire Deux was used for physiologic lesion assessment in addition to OCT as standard of care, will be offered consent for enrolling in this observational study post-procedure.

6.4. Procedural Information

The following procedural information will be collected:

- Number of OptoWire Deux used
- Number of workhorse wires used
- Total duration of procedure
- Duration of FFR measurement
- Coronary angiogram (DICOM)
- OCT images
- Cine marking the position of the FFR wire pressure sensor (DICOM)
- Physiology tracing (resting Pd/Pa, FFR, pullback)

6.5. Shipment of Materials to the Core Lab

The following documentation should be forwarded to the Core Lab:

- Coronary angiogram (saved on a CD labeled with patient ID)
- FFR tracings
- OCT images
- Study worksheet (Appendix B)
- Catheterization report

Cardiovascular Research Foundation Core Lab
Trial Identifier: OpSens FFR Trial
1700 Broadway, 9th Floor
New York, NY 10019
USA

7. Study Risk Determination

Participation in this study presents no medical risk to the patient (data collection only).

8. Statistical Considerations

This is a prospective, observational, multi-center, clinical study designed to estimate the ischemic burden of angiographically intermediate proximal LAD stenosis using FFR. Efficacy will be measured using the OpSens FFR system.

The study's primary endpoint is the rate of significant drift, defined as FFR <0.97 or >1.03 with the pre-PCI FFR recording using the OpSens OptoWire Deux pressure wire system.

8.1. Statistical Analysis and Analysis Sets

All statistical analyses will be performed using SAS (SAS Institute Inc., Cary, NC). Patient data listings and tabular presentations of results will be provided listing the mean, standard deviation, median, minimum, maximum, and number of subjects for continuous data, or in tables listing count and percentage for categorical data, where appropriate.

8.2. Analysis of Baseline Demographics and Procedural Characteristics

All clinically relevant baseline variables will be tabulated using descriptive statistics. Descriptive statistics for categorical variables will include the number and percentage of subjects, with 2-sided 95% confidence intervals of the percentage of subjects.

9. Definitions

REFERENCE VESSEL DIAMETER

Defined as the average of normal segments within 10 mm proximal and distal to the target lesion from 2 orthogonal views using quantitative coronary angiography.

TIMI CLASSIFICATION

TIMI 0: No perfusion.

TIMI 1: Penetration with minimal perfusion. Contrast fails to opacify the entire bed distal to the stenosis for the duration of the cine run.

TIMI 2: Partial perfusion. Contrast opacifies the entire coronary bed distal to the stenosis; however, the rate of entry and/or clearance is slower in the coronary bed distal to the obstruction than in comparable areas not perfused by the dilated vessel.

TIMI 3: Complete perfusion. Filling and clearance of contrast equally rapid in the coronary bed distal to stenosis as in other coronary beds.

10. Reporting Responsibilities

Table 2: Investigator Reporting Responsibilities

Type of Report	Prepared For	Time Frame
Withdrawal of IRB/EC approval or other action on part of the IRB/EC that affects the study	Sponsor	**Written** – Within 5 working days of IRB/EC decision.
Progress Reports	IRB/EC	At regular intervals.
Final Report	Sponsor and IRB/EC	Within 3 months after termination or completion of study or termination of site's participation.

Table 3: Sponsor Reporting Responsibilities

Type of Report	Prepared For	Time Frame
Withdrawal of IRB/EC Approval.	Investigators, all other reviewing IRBs/ECs and appropriate regulatory bodies	**Written** – Within 5 working days.

11. Data Submission Requirements

11.1. Required Data

All required data for this study will be collected via case report form.

11.2. Data Collection

Case Report Form Development, Modification, and Maintenance:

The final set of case report form is designed to accommodate the specific features of the trial design. Modification of case report form will only be made if deemed necessary by the sponsor. All core lab raw data will be sent to the core labs at the Cardiovascular Research Foundation at the address listed in Section 2: Additional Summary Information. This information is documented and the data are transmitted to the data center at Cardiovascular Research Foundation for integration into the study database.

Components of the case report form:

1. Enrollment screening and subject eligibility
2. Baseline demographics, medical history, and clinical presentation
3. Procedural and lesion data

11.3. Data Collection and Tracking

Research coordinators at each clinical site will perform primary data collection from source document (e.g., hospital chart, office record) reviews. Data will be entered by the site personnel into case report forms. The Sponsor or its designee will provide clinical monitoring, including review of case report form with verification to the source documentation. This will include case report documentation and hospital charts/office records.

11.4. Time Windows for Expected Completion of Case Report Forms

The case report form data submission detailed in the following table should be completed as follows:

Table 4. Responsibilities and Guidance for Submitting Reports and Other Data

Type of Notification/Report/Other Data	Submitted to	Time Window for Submission
Coronary angiogram	Angiographic Core Lab	Monthly
FFR	FFR Core Lab	Monthly
Withdrawal of IRB approval	Notify sponsor	Within 5 working days of withdrawal
Final report	Sponsor, IRB/EC	Within 3 months of study completion or termination

12. Study Steering Committees

The Steering Committee is composed of the PIs, several other leading physician experts, and a Sponsor representative. The Steering Committee participates in regularly scheduled meetings to review study progress and conduct and to provide feedback to the Sponsor on an ad hoc basis. Steering Committee membership will be decided by the sponsor.

13. Ethical and Regulatory Considerations

This study will be conducted in accordance with the principles outlined in the Declaration of Helsinki and all local Good Clinical Practice requirements.

13.1. Subject Confidentiality

Subject confidentiality will be maintained throughout the clinical study in a way that assures that data can always be tracked back to the source data. For this purpose, a unique subject identification code (ID number and subject name code) will be used that allows identification of all data reported for each subject.

Data relating to the study might be made available to third parties (for example in case of an audit performed by regulatory authorities) provided the data are treated confidential and that the subject's privacy is guaranteed.

"Protected Health Information" will be treated and maintained in compliance with the HIPAA Privacy rule with regard to the processing of personal data and on the free movement of such data.

The duration of the storage time of the personal data at the investigational sites, will be in accordance with the national regulations.

13.2. Selection of Investigators

The sponsor and its designees will select qualified investigators, obtain signed study agreements, and provide the investigators with the information necessary to conduct the study.

13.3. Initiation of Study Sites

Prior to subject enrollment, a study initiation visit will be completed at the investigational site to ensure the following: IRB/EC approval has been obtained and documented prior to subject screening, the investigators and study personnel are appropriately trained and clearly understand the study, the investigators and study personnel accept the obligations incurred in undertaking this clinical investigation.

13.4. Study Closeout Visit

Upon completion of the clinical study, all data have been entered into the case report form, all queries have been resolved, and final signatures have been obtained), a study closeout visit will be performed. The study monitor will ensure that the Investigator's regulatory files are current and complete, and that any outstanding issues from previous visits have been resolved. Other issues that will be reviewed with site personnel at this visit include: discussing retention of study files, the possibility of site audits, publication policy, and to ensure that the Investigator will notify the site's IRB/EC regarding study closure.

13.5. Maintaining Records

The sponsor and/or its designees will maintain copies to include all trial-related correspondence, regulatory documents, data, and other records related to the clinical trial. The sponsor and/or its designees will maintain records related to the signed Investigator Agreements.

13.6. Submitting Reports

The sponsor reporting responsibilities are detailed in Table 3.

The site will notify the ponsor within 24 hours of the time the Investigator becomes aware of withdrawal of IRB/EC approval. The Investigator reporting responsibilities are detailed in Table 2.

13.7. Site Record Retention Policy

All core laboratories and the clinical sites will maintain study records until the sponsor notifies them and the reviewing regulatory authorities that research is completed or terminated under the clinical investigation in compliance with United States Food and Drug regulations.

14. Risks to the Subjects

14.1. Human Subjects Involvement and Characteristics

This study will enroll a total of 60 subjects. The inclusion and exclusion criteria are described above in Sections 5.2. and 5.3. Vulnerable populations, specifically prisoners, and institutionalized individuals will not be targeted for recruitment.

14.2. Sources of Materials

Research material obtained from study participants includes health information obtained through medical history, physical and angiographic examination.

Copies of data obtained as part of the study will be retained by the sites, with appropriate source documentation, on all subjects that sign informed consent. The data utilized in this study are described above and consist of information from subject interview and examination, medical records, or study-specified measures and interventions.

14.3. Potential Risks

There are no medical risks associated with this study (data collection only).

14.4. Confidentiality of Subject Medical Information

Confidentiality of subject medical information will be ensured by providing unique identifiers for data transmitted from the enrolling centers. The sponsor and the core laboratories will not receive identifiable subject information. The sponsor and the core laboratories will receive case report forms that are already encoded with study identifiers, thus preventing knowledge of any subject-identifying information. All diagnostic tests performed at the core labs will be labeled to obscure subject-identifying information and provide specific fields in which to encode subject identifiers (using the same set of subject initials and numbers encoded on the case report forms). This process ensures that the core lab data is eventually incorporated with the main subject file held by the sponsor, Dr. Manish Parikh. All direct subject contact (informed consent, subject screening and study procedures) and relevant confidentiality protections are the responsibility of the sponsor.

Table 6: List of Acronyms

Acronym	Term
CFR	Code of Federal Regulations
EC	Ethics committee
EDC	Electronic data capture
FFR	Fractional flow reserve
HIPAA	Health Insurance Portability and Accountability Act
iFR	Instantaneous wave-free ratio
IFU	Instructions for use
IRB	Institutional review board
IVUS	Intravascular ultrasound
LAD	Left anterior descending coronary artery
MLA	Minimum lumen area
OCT	Optical coherence tomography
PCI	Percutaneous coronary intervention
PI	Principal investigator
TIMI	Thrombolysis in Myocardial Infarction

15. References

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