2025 Summary of Safety and Clinical Performance (SSCP) – Makoto® Intravascular Imaging System

CONTROLLED

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i) and Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42).
The SSCP is not intended to replace the Instructions For Use (IFU) as the main document to ensure the safe use of the Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i) and Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42), nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals. A supplemental SSCP with information for patients is not provided since the Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i) and Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42) are not intended to be used directly by patients.

Activity	**Name/Title**
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Abbreviations

ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
BVS	Bioresorbable Vascular Scaffold
CABG	Coronary Artery Bypass Graft Surgery
CAV	Coronary Allograft Vasculopathy
CI	Confidence Interval
CRP	C-Reactive Protein
CTCA	Computed Tomography Coronary Angiography
DEB	Drug-Eluting Balloon
EMC	Electromagnetic Compatibility
ESC	European Society of Cardiology
ESD	Electrostatic Discharge
FCT	Fibrous Cap Thickness
FSCA	Field Safety Corrective Action
GDMT	Guideline-Directed Medical Therapy
HF	High Frequency
HR	Hazard Ratio
IFU	Instructions For Use
IRA	Infarct Related Artery

IVUS	Intravascular Ultrasound
LCBI	Lipid Core Burden Index
LCP	Lipid Core-containing Plaques
LDL	Low-Density Lipoprotein
LRP	Lipid-Rich Plaque
MACE	Major Adverse Cardiovascular Event
MLA	Minimum Lumen Area
MVD	Multivessel Disease
NC-MACE	Non-Culprit Major Adverse Cardiovascular Event
NB	Notified Body
NIR	Near Infrared
NIRS	Near Infrared Spectroscopy
OCT	Optical Coherence Tomography
PAV	Percent Atheroma Volume
PMCF	Post-market Clinical Follow-up
PTCA	Percutaneous Transluminal Coronary Angioplasty
RF	Radio Frequency
SRN	Single Registration Number
STEMI	ST-segment Elevation Myocardial Infarction
TAVI	Transcatheter Aortic Valve Implantation
TVC	True Vessel Characterization
UDI	Unique Device Identifier

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Contents

1. DEVICE IDENTIFICATION AND GENERAL INFORMATION

1.1. DEVICE TRADE NAME(S)

Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i)

Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42)

1.2. MANUFACTURER'S NAME AND ADDRESS

Infraredx, Inc.

28 Crosby Drive, Suite 100

Bedford, MA 01730

1.3. MANUFACTURER'S SINGLE REGISTRATION NUMBER (SRN)

US-MF-000002341

1.4. BASIC UDI-DI

0857595006CNUC8 (TVC-C195-42)
0857595006SNUEQ (TVC-MC10/TVC-MC10i)

1.5. MEDICAL DEVICE NOMENCLATURE DESCRIPTION / TEXT

Product	EMDN Code	Category Description
TVC-C195-42	C0104010102	CARDIAC AND INTRACORONARY ULTRASOUND CATHETERS
TVC-MC10/TVC-MC10i	C019004	CARDIOVASCULAR MONITORING SYSTEMS

1.6. CLASS OF DEVICE

Device: Dualpro® IVUS+NIRS Imaging Catheter, TVC-C195-42

Device Classification and Rule: Class III, Rule 6

Device: Makoto® Intravascular Imaging System, TVC-MC10/TVC-MC10i

Device Classification and Rule: Class IIb, Rule 11

1.7. YEAR WHEN THE FIRST CERTIFICATE (CE) WAS ISSUED COVERING THE DEVICE

The TVC-MC10 system and corresponding TVC-C195-42 catheter were first CE marked under the MDD in August of 2017 (CE 670602, CE 670605). The system and catheter later received MDR certification (MDR 766209 (EU) 2017/745 Annex IX, Chapter I and III, MDR 766211 (EU) 2017/745 Annex IX, Chapter II) in December, 2022.

1.8. AUTHORISED REPRESENTATIVE IF APPLICABLE; NAME AND THE SRN

Name: Emergo Europe B.V.

SRN: NL-AR-000000116

1.9. NB'S NAME (THE NB THAT WILL VALIDATE THE SSCP) AND THE NB'S SINGLE IDENTIFICATION NUMBER

Name: BSI Group The Netherlands B.V

SRN: 2797

2. INTENDED USE OF THE DEVICE

2.1. INTENDED PURPOSE/USE

Invasive imaging of coronary arteries by near-infrared light and ultrasound.

2.2. INDICATIONS FOR USE AND TARGET POPULATION(S)

1. The Makoto® Intravascular Imaging System is intended for the near-infrared examination of coronary arteries in patients undergoing invasive coronary angiography.
    a. The System is intended for the detection of lipid-core-containing plaques of interest.
    b. The System is intended for the assessment of coronary artery lipid core burden.
    c. The System is intended for the identification of patients and plaques at increased risk of major adverse cardiac events.

2. The System is intended for ultrasound examination of coronary intravascular pathology.
    a. Intravascular ultrasound imaging is indicated in patients who are candidates for transluminal coronary interventional procedures.

2.3. CONTRAINDICATIONS AND/OR LIMITATIONS

Use of the Dualpro® IVUS+NIRS Imaging Catheter is contraindicated where introduction of any catheter would constitute a threat to patient safety. Contraindications include:

- Bacteremia or sepsis
- Major coagulation system abnormalities
- Severe hemodynamic instability or shock
- Patients diagnosed with coronary artery spasm
- Patients disqualified for CABG surgery
- Total occlusion
- Patients disqualified for PTCA
- Patients who are not suitable for IVUS procedures

3. DEVICE DESCRIPTION

3.1. DESCRIPTION OF THE DEVICE

Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i)

The Makoto® Intravascular Imaging System is an intravascular imaging device with the ability to simultaneously assess vessel composition and structure using near-infrared spectroscopy (NIRS) and intravascular ultrasound (IVUS). This dual-modality instrument performs near-infrared spectroscopic analysis of the vessel to detect lipid core-containing plaques of interest (LCP) displayed in a map called a Chemogram, and simultaneously generates high resolution IVUS images that display structural details of the vessel and plaque in transverse and longitudinal views.

Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42)

The Dualpro® IVUS+NIRS Imaging Catheter is a single use disposable catheter comprised of an outer sheath, an inner core, and a hub assembly for use only with the Makoto® Intravascular Imaging System. In an intravascular procedure, the Catheter is guided into the target vessel where the sheath remains in place during scanning and the inner core rotates and pulls back to generate NIRS and IVUS images of the vessel. The Catheter has a proximal shaft profile of 3.6F, an imaging window crossing profile of 3.2F, and a tip crossing profile of 2.4F. In addition, the Catheter has a useable length of 160 cm and an imaging window length of 155 mm. Fiducial markers on the proximal shaft at 90 cm and 100 cm from the distal end of the Catheter, as well as a radiopaque marker at the distal extremity help guide the placement of the Catheter in the vessel and region of interest.

3.2. A REFERENCE TO PREVIOUS GENERATION(S) OR VARIANTS IF SUCH EXIST, AND A DESCRIPTION OF THE DIFFERENCES

The first generation NIRS-IVUS dual modality imaging system was cleared for the U.S. market in 2010 (K093993) and branded as the LipiScan™ IVUS Coronary Imaging System. LipiScan IVUS was re-branded in November, 2011 to the TVC Imaging System™. (TVC-MC7). This model is obsolete and has been removed from the market.

TVC-MC8 was introduced with the TVC Insight Catheter Hydrophilic (TVC-C195-22), which added a hydrophilic coating to the catheter sheath. These models were cleared for the U.S. market in 2013 (K130719). The TVC-MC8 console and TVC-C195-22 catheter were CE marked in 2014.

The TVC Insight XB Catheter (TVC-C195-32) and associated TVC-MC9 console were cleared for the U.S. market in 2014 (K133897 & K141682, respectively). This iteration introduced a 50 MHz high resolution IVUS transducer to the catheter. The MC9 and Insight XB were first CE marked for the EU market in 2017.

The TVC-MC8 and TVC-MC9 consoles and their corresponding catheters, TVC-C195-22 and TVC-C195-32, respectively, are no longer manufactured and no longer in service.

3.3. DESCRIPTION OF ANY ACCESSORIES WHICH ARE INTENDED TO BE USED IN COMBINATION WITH THE DEVICE

Accessory: Makoto® Controller Sterile Barrier (packaged with catheter)

Description: Individually packaged sterile Makoto Controller Sterile Barrier for TVC-MC10

Accessory: Dualpro® Catheter Priming Syringes (3 mL, 10 mL) (packaged with catheter)

Description: Syringes used to flush the catheter lumen or prime the hydrophilic coating part by injecting saline solution.

3.4. DESCRIPTION OF ANY OTHER DEVICES AND PRODUCTS WHICH ARE INTENDED TO BE USED IN COMBINATION WITH THE DEVICE

Coronary angiography provides visualization of the coronary arteries and the catheter and is intended to be used in combination with the NIRS-IVUS Imaging System.

4. RISKS AND WARNINGS

4.1. RESIDUAL RISKS AND UNDESIRABLE EFFECTS

Infraredx strives through the use of its Risk Management and associated procedures for its products to be designed, manufactured, and used with the highest consideration to the elimination, reduction, control, and monitoring of risks to patients, operators (and other persons), other equipment and the environment. Per MDR 2017/745 Annex I (3), Risk Management is a continuous iterative process throughout the entire lifecycle of a device that requires regular systematic updating. Critical aspects of this process include:

- Identifying and analyzing known and foreseeable hazards associated with the device;
- Estimating and evaluating the risks (severity and probability of occurrence of harm) associated with, and occurring during, the intended use and during reasonably foreseeable misuse of the device; and
- Eliminating or controlling the risks

Risk controls are implemented using one or more of the following options (in decreasing priority order);

1. Inherently safe design and manufacture to eliminate or reduce risks as far as possible.
2. Protective measures in the device or in the manufacturing process.
3. Information for safety (labeling) and, where appropriate, training to users

Design and Usability Failure Modes and Effects Analyses (DFMEA and UFMEA, respectively) were performed for the TVC-MC10/TVC-MC10i system and associated TVC-C195-42 catheter to determine residual risks. The main categories of harm identified through this process and their estimated probabilities of occurrence are listed in Table 1 below.

Table 1: TVC-MC10/TVC-MC10i and TVC-C195-42 Main Harm Categories and their Maximum Estimated Probability of Occurrence

Harm Category	Estimated Probability of Occurrence
Incorrect diagnosis results in additional treatment	< 1%
Patient or operator injury	< 1% *
Patient harm requiring physician intervention	< 0.1%
Patient infection	< 0.1%
Patient death	< 0.01%

* Excluding tripping hazard. The umbilical and electrical cord (mobile console) present a potential tripping hazard that could lead to operator injury. The probability of this occurrence is estimated at <10% for the purpose of risk analysis; however, the actual occurrence is likely much lower (no tripping incidents have been reported to Infraredx to date).

Based on a careful evaluation of the FMEAs, the benefit of using this device outweighs the individual and overall residual risks, including the risk of device failure or potential harm to the patient, user, environment, or other equipment.

Potential complications/adverse events/side effects associated with intravascular examination include:

- Allergic reaction
- Angina
- Cardiac arrest
- Cardiac arrhythmias including, but not limited to ventricular tachycardia, atrial/ventricular fibrillation and complete heart block.
- Cardiac tamponade/Pericardial effusion
- Death
- Device entrapment requiring surgical intervention
- Embolism (air, foreign body, tissue, or thrombus)
- Hemorrhage/hematoma
- Hypotension
- Infection
- Myocardial infarction
- Myocardial ischemia
- Stroke and transient ischemic attack
- Thrombosis
- Vessel occlusion and abrupt closure
- Vessel trauma including, but not limited to dissection and perforation

Adverse event rates for intravascular imaging were estimated from clinical investigations as well as the clinical literature.

Seven Infraredx-sponsored clinical investigations using the NIRS/IVUS imaging systems have been completed and published to date. Among these six studies, adverse events during imaging were reported in <2.5% of patients, including chest pain (angina), dissection, arrhythmia, air embolism, spasm and periprocedural myocardial infarction. These are known potential complications associated with intracoronary imaging and percutaneous coronary intervention (PCI) and the rates reported are well within reported rates for patients undergoing PCI. The five most recently completed clinical investigations, LRP (2018), Prospect II (2020), PACMAN-AMI (2022), DeBUT-LRP (2024)), and PREVENT (2024) confirmed the safety of the NIRS-IVUS system. The LRP Study reported a device-related adverse event rate of only 0.4% (6 of 1,563 patients); the Prospect II study reported device-related major complications requiring treatment occurring in 0.2% (2 of 902 patients); the PACMAN-AMI study reported complications related to the intracoronary imaging procedure in 2.3% of patients (7 of 300 patients), all of which were transient and without clinical sequelae; the DEBuT-LRP study reported three procedural complications, however no IVUS-NIRS-related complications occured; the PREVENT study reported no device-related events.

A review of the clinical literature included over 20,000 patients who underwent examination of the coronary arteries using the Infraredx imaging devices. Of the 154 published studies included in the review, only four (4) of the studies reported adverse events related to the use of the subject among a total of 24 patients.

4.2. WARNINGS AND PRECAUTIONS

The IFUs (IFU0158, IFU0163, and IFU0169) list the following Warnings & Caution statements.

TVC-MC10/TVC-TVC-MC10I, IFU0163/IFU0169

- USA Only: The effectiveness of NIRS in the peripheral vasculature has not been established.
- Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.
- Failure to heed written cautions can result in damage to the Makoto® (Integrated) Intravascular Imaging System or may result in degradation of system performance.
- Adherence to the precautions discussed in this section must be observed when installing, operating, moving, or servicing the system to avoid potentially hazardous situations.

- Tampering with or any attempt to modify the Makoto® (Integrated) Intravascular Imaging System will void the product warranty and may also result in improper operation of the system. Device degradation or product failure may result.
- Product contains a Class 1M laser product that emits invisible laser radiation. Do not view directly with optical instruments.
- Never look directly into the laser beam coming from the system or reflected from a surface.
- Do not look into the laser beam through lenses, binoculars, magnifiers, camera viewfinders, telescopes, or any optical element or instrument that may focus the light into the eye.
- Never permit reflective objects such as jewelry, watches, metal instruments, or mirrors to intercept and reflect the laser beam.
- Failure to follow the information in this section may cause equipment damage, bodily injury, even death.
- Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.
- Medical electrical equipment needs special precautions regarding EMC and needs to be installed according to the EMC information provided in Appendix H: Electromagnetic Compliance.
- DO NOT position the Makoto® (Integrated) Intravascular Imaging System close to other equipment as electrical interference may result.
- A Live IVUS or pullback scan may be interrupted if the system is exposed to an Electrostatic Discharge (ESD). If a Live IVUS or pullback scan is interrupted, the scan may be restarted immediately.
- The Makoto® system is not intended for use with high frequency (HF) / radio frequency (RF) surgical equipment.
- Radiated or conducted RF emissions may cause image distortion or artefacts on the Makoto® (Integrated) Intravascular Imaging System display.
- (TVC-MC10 Only) DO NOT position Makoto® Intravascular Imaging System mobile console operator between the Makoto® system console and other moving equipment in the catheterization lab due to the risk of bodily injury.
- The procedure table should be kept level during use of the Makoto® system or at any time when the Makoto® Controller is in the sterile field. DO NOT utilize table pitch or roll controls, if available.
- (TVC-MC10 Only) DO NOT position the Makoto® Intravascular Imaging System within the range of motion of pieces of the X-ray system.
- Ensure that cables originating from or connecting to the Makoto® (Integrated) Intravascular Imaging System lay flat on the floor.
- This equipment is not intended for use with flammable anesthetics or liquids, or oxygen rich (>25%) environments.
- STATE OF CALIFORNIA (USA ONLY)
  This product contains bisphenol-A (BPA), a chemical known to the state of California to cause birth defects, or other reproductive harm.

For information go to www.P65warnings.ca.gov

- STATE OF CALIFORNIA (USA ONLY)

  The compatible disposable products and its packaging have been sterilized with ethylene oxide. The packaging may expose you to ethylene oxide, a chemical known to the State of California to cause cancer or birth defects or other reproductive harm.
- Catheter accessories (Makoto® Controller Sterile Barrier, Priming Accessories, and compatible catheters) are supplied sterile and are designed for single patient use only. For single use only. Do not reuse, reprocess, or resterilize. Reuse, reprocessing, or resterilization may compromise the structural integrity and result in poor image quality or patient injury, illness, or death. Reuse, reprocessing, or resterilization may also contaminate the device and result in patient infection which may lead to patient illness or death. Infraredx makes no performance claim for product that is reused, reprocessed, or resterilized.
- DO NOT use the catheter if the inner package is open or damaged.
- When connected to the Makoto® Controller, DO NOT stare at the distal tip of the catheter or view directly with optical instruments.
- Medical waste can cause infection and/or disease. After use, dispose of product and packaging in accordance with hospital, administrative, and/or local government policy.
- Care should be taken when a guidewire is exposed in a stented vessel. Catheters that do not encapsulate the guidewire may engage the stent between the junction of the catheter and guidewire.
- Care should be taken when advancing a guidewire after stent deployment. When crossing a stent, the wire may exit between stent struts that are not fully apposed. Subsequent advancement of the catheter could cause entanglement between the catheter and the deployed stent.
- If resistance is met upon withdrawal of the catheter, verify resistance using fluoroscopy, and then remove the entire system simulataneously if appropriate.
- DO NOT kink or sharply bend (>45 degrees) the catheter at any time. This can result in drive cable failure.
- Use of unapproved accessories may result in noncompliance of the Makoto® (Integrated) Intravascular Imaging System with one or more of the standards listed in this section of the manual.
- The Makoto® (Integrated) Intravascular Imaging System is designed to be used exclusively by trained physicians and catheterization laboratory personnel.
- It is NOT recommended that the Makoto® (Integrated) Intravascular Imaging System be utilized as a permanent data archive location. Scan data should be archived to other media and removed from the system hard drive.
- Care should be taken when entering patient information to ensure accuracy.
- The sterile catheter must be primed in accordance with the instructions for use document that is included in the catheter package.
- Use of the supplemental on-screen priming guidance is not a substitute for training in the operation of the Makoto® (Integrated) Intravascular Imaging System.

- Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.
- Controller linear motion will stop when excessive force is encountered. Check catheter for kinks, sharp bends, or damage and resolve before continuing. Press the STOP button on the Makoto® Controller and follow on screen prompts to resolve.
  DO NOT use single step translation functions to overcome the kink or bend. Catheter sheath damage or patient injury may result.
- If at any time the STOP button on the Makoto® Controller does not halt catheter motion, immediately unplug the Makoto® Intravascular (Integrated) Imaging System.
- The user should review and assess the performance of the assistive measurement functions prior to diagnosis and selection of therapy.
- Where possible, the assistive measurement system will alert the user to segments that may require additional interpretation or editing by the user.
- (TVC-MC10 Only) DO NOT position Makoto® Intravascular Imaging System mobile console operator between the System and other moving equipment in the catheterization lab.
- (TVC-MC10 Only) DO NOT position the Makoto® Intravascular Imaging System with caster locks engaged within the normal range of motion of pieces of the X-ray system or other catheterization lab equipment during typical use.
- (TVC-MC10 Only) DO NOT reposition the Makoto® Intravascular Imaging System in a way that would obstruct access to the power plug.
- (TVC-MC10i Only) DO NOT reposition the Makoto® Integrated Imaging System components after installation by a certified technician.
- These instructions are NOT for long term storage of the Makoto® (Integrated) Intravascular Imaging System. Please contact Infraredx Customer Service or your local service provider for guidance on how to prepare the system for long term storage.
- (TVC-MC10 Only) Ensure that cables originating from or connecting to the Makoto® Intravascular Imaging System lay flat on the floor.
- (TVC-MC10 Only) If the power cable plug appropriate for the region of use does not contain a ground, then attach a grounding cable to the equipotential ground stud located on the rear of the Makoto® Intravascular Imaging System at the bottom.
- During the system start up sequence the Makoto® Controller catheter connection socket will rotate automatically. If a catheter is attached during startup of the system ensure that the catheter has been withdrawn from the patient.
- If at any time the STOP button on the Makoto® Controller does not halt catheter motion, immediately unplug the Makoto® (Integrated) Intravascular Imaging System.
- If at any time a momentary press and release of the power button does not shut the system down, then press and hold (~5 seconds) the power button until the system shuts down.
- Ensure correct entry of patient information to avoid mislabeled data or misplacement of procedure data.

- The sterile catheter must be primed and prepared in accordance with the instructions for use document that is included inside the catheter package.
- If the Makoto® Controller Sterile Barrier is damaged at any time, immediately replace with a new sterile barrier.
- Keep the sterile operator's hand outside of the blue cover on the sterile barrier.
- Position the Makoto® Controller in a stable location on the procedure table. DO NOT place the controller near the edges of the table.
- Procedure table should be kept level during Makoto® System operation or at any time when the Makoto® Controller is in the sterile field. DO NOT utilize table pitch, tilt, or roll controls, if available.
- Ensure that umbilical slack is provided within the sterile field to accommodate motion of the table, console, or patient to minimize risk of unintended Makoto® Controller motion.
- DO NOT allow sterile items to contact Makoto® Controller through the catheter socket opening of the Makoto® Controller Sterile Barrier.
- DO NOT allow the side of the sterile barrier gasket cover that has come in direct contact with the Makoto® Controller socket to come in contact with the sterile operator.
- Ensure the white gasket is securely attached to the socket of the Makoto® Controller. The barrier material should not obstruct the opening. There will be a small gap between the white gasket and the front surface of the controller when properly applied.
- The sterile catheter must be handled and prepared in accordance with the instructions for use document that is included in the catheter package.
- Do not touch the underside of the blue cover as it may have been in contact with the Makoto® Controller socket which is not sterile.
- The Makoto® Controller should be positioned on the patient table such that adequate space for the catheter connection is available and the Makoto® Controller catheter socket is free of obstructions.
- Do not contaminate the fiber faces of the catheter or Makoto® Controller socket during the connection process.
- See catheter Instructions for Use document for guidance on loading the catheter onto the guidewire, the catheter into the guiding catheter, and advancing the catheter into the artery.
- Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.
- Controller linear motion will stop when excessive force is encountered.
  Check catheter for kinks, sharp bends, or damage and resolve before continuing.
  Press the STOP button on the Makoto® Controller and follow on screen prompts to resolve.
  DO NOT use single step translation functions to overcome the kink or bend. Catheter sheath damage or patient injury may result.
- Imaging within the guiding catheter should be minimized for optimum chemogram results.
- In case of emergency use the STOP button on the Makoto® Controller.

- See catheter Instructions For Use document for guidance on preparing the catheter for additional scans.
- Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.
- Controller linear motion will stop when excessive force is encountered. Check catheter for kinks, sharp bends, or damage and resolve before continuing. Press the STOP button on the Makoto® Controller and follow on-screen prompts to resolve.
  DO NOT use single step translation functions to overcome the kink or bend. Catheter sheath damage or patient injury may result.
- Imaging within the guiding catheter should be minimized for optimum chemogram results.
- Once confirmed by user, the deletion of a scan cannot be undone.
- Connecting the Makoto® system to a network increases the risk that the equipment may be affected by network-based cybersecurity attacks. The System is designed to secure network connections and communications. However, the risks associated with a network-based cybersecurity attack cannot be entirely mitigated.
  See Manufacturer Disclosure Statement for Medical Device Security (MDS2) to manage cybersecurity risks and to ensure the safe and effective use of the device in its intended use environment. Contact Service Provider to request additional copies of the statement as required.
- Using removable media with the Makoto® system may expose the system to software-based risks on that media. The System is designed to secure these media ports and interact only with recognized files. However, the risks associated with software- based threats cannot be entirely mitigated.
- Ensure that cables originating from or connecting to the Makoto® (Integrated) Intravascular Imaging System lay flat on the floor.
- Connecting to IT networks, including other equipment, could result in previously unidentified risks to patients, operators or third parties.
- Changes to the IT network could introduce new risks that require additional analysis. Changes to the IT network include:
  - Changes in network configuration
  - Connection of additional items
  - Disconnection of items
  - Updates of equipment
  - Upgrades of equipment
- The customer should identify, analyze, evaluate and control the risks associated with connecting the Makoto® Intravascular Imaging System to an IT network. See Manufacturer Disclosure Statement for Medical Device Security (MDS2) to manage cybersecurity risks and to ensure the safe and effective use of the device in its intended use environment. Contact Service Provider to request additional copies of the statement as required.
- Identifying information contained within the text of annotations on frames or scans will not be modified.
- Deletion of data from the system is permanent and CANNOT be undone.

- The Makoto® (Integrated) Intravascular Imaging System is not intended as a permanent data storage or archive location.
- Connecting the Makoto® system to a network increases the risk that the equipment may be affected by network-based cybersecurity attacks. The System is designed to secure network connections and communications. However, the risks associated with a network-based cybersecurity attack cannot be entirely mitigated.
  See Manufacturer Disclosure Statement for Medical Device Security (MDS2) to manage cybersecurity risks and to ensure the safe and effective use of the device in its intended use environment. Contact Service Provider to request additional copies of the statement as required.
- Using removable media with the Makoto® system may expose the system to software-based risks on that media. The System is designed to secure these media ports and interact only with recognized files. However, the risks associated with software- based threats cannot be entirely mitigated.
- It is strongly recommended that the Makoto® Administrator implement and enforce password strength requirements that conform to their institution's security policies for this type of medical equipment.
- Connecting the Makoto® system to a network increases the risk that the equipment may be affected by network-based cybersecurity attacks. The System is designed to secure network connections and communications. However, the risks associated with a network-based cybersecurity attack cannot be entirely mitigated.
  See Manufacturer Disclosure Statement for Medical Device Security (MDS2) to manage cybersecurity risks and to ensure the safe and effective use of the device in its intended use environment. Contact Service Provider to request additional copies of the statement as required.
- Ensure that cables originating from or connecting to the Makoto® (Integrated) Intravascular Imaging System lay flat on the floor.
- (TVC-TVC-MC10i Only) If the power cable plug appropriate for the region of use does not contain a ground:
  Attach a grounding cable to the equipotential ground stud located on the rear of the Makoto® Stationary Console. If a grounding connection cannot be made at this location, a grounding cable can be attached to the equipotential ground stud located on the Makoto® Local Junction Box.
- (TVC-MC10i Only) DO NOT obstruct access to the power plug of the installed Makoto® Stationary Console.
- Hospitals and healthcare facilities should follow their protocol for handling blood borne risks.
- Care should be taken to prevent cleaning fluids, saline, or other liquids from entering into the Makoto® Controller or Console.
- Care should be taken to avoid contamination of the optical connectors of the Makoto® Controller. In the event that the controller optical fiber connectors cannot be cleaned, please contact your local service provider or Infraredx for further instructions.

- Do not dispose of any parts of this product as industrial or domestic waste. The product contains hazardous materials which require special disposal. Incorrect disposal of any of these materials may lead to serious environmental pollution.

TVC-C195-42, IFU0158

- After use, dispose of the product and packaging in accordance with hospital and/or local government policy.
- For single use only. Do not reuse, reprocess, or resterilize. Reuse, reprocessing, or resterilization may compromise the structural integrity and result in poor image quality or patient injury, illness, or death. Reuse, reprocessing, or resterilization may also contaminate the device and result in patient infection which may lead to patient illness or death. Infraredx makes no performance claim for product that is reused, reprocessed, or resterilized.
- If Catheter Sterile Packaging is damaged, unintentionally opened before use, or exposed to environmental conditions outside of the specified limits, immediately dispose of the Packaging and its Contents and replace with a new Catheter Sterile Package
- DO NOT use any type of contrast media either in replacement of or in combination with the saline as priming medium.
- If Controller Sterile Barrier is contaminated or damaged at any time, immediately replace with a new Controller Sterile Barrier.
- Do not contaminate the fiber faces of the catheter or Makoto Controller during the connection process.
- When connected to the Makoto IVUS+NIRS Imaging System, laser radiation is emitted from the distal end of the catheter. Do not stare into beam or view directly with optical instruments
- Retracting the imaging core of a primed catheter outside the body may introduce air into the catheter sheath. Flush the catheter using the 3 mL priming syringe then advance the catheter imaging core to the fully distal position using the distal motion controls.
- Never advance the Dualpro catheter without guidewire support.
- Never advance the Dualpro catheter sheath without the imaging core advanced to its most distal or READY position.
- Never advance or withdraw the Dualpro catheter without direct fluoroscopic visualization.
- If resistance is encountered anytime during Dualpro imaging catheter sheath positioning, DO NOT pull, push, or rotate with excessive force.
- Never advance the distal tip of the Dualpro catheter near the unsupportive end of the guidewire due to the risk of guidewire entanglement.
- Guidewires that supply more stiffness near the distal tip are recommended.
- An excessively tightened hemostasis valve may distort the IVUS image or cause permanent damage to the imaging core during rotation.
- Inspect the guidewire exit port and imaging window prior to re-insertion to verify that no damage has occurred during withdrawal.

- Do not advance the imaging core into a kinked sheath.
- Care should be taken when a guidewire is exposed in a stented vessel. Catheters that do not encapsulate the guidewire may engage the stent between the junction of the catheter and guidewire.
- Care should be taken when re-advancing a guidewire after stent deployment. A guidewire may exit between stent struts when re-crossing a stent that is not fully apposed. Subsequent advancement of the Dualpro catheter could cause entanglement between the catheter and the mal-apposed stent.
- If resistance is met upon withdrawal of the catheter, verify source of resistance using fluoroscopy and ensure the catheter is not entangled in a stent or other interventional device then apply an appropriate catheter removal strategy.
- If a Dualpro catheter sheath breach occurs during the procedure, do not advance the catheter core. Immediately remove the entire system of Dualpro, guide catheter, and guidewire using fluoroscopic guidance.
- Do not kink or sharply bend the catheter at any time. This can cause drive cable failure. An insertion angle greater than 45 degrees is considered excessive.

4.3. OTHER RELEVANT ASPECTS OF SAFETY, INCLUDING A SUMMARY OF ANY FIELD SAFETY CORRECTIVE ACTION (FSCA INCLUDING FSN) IF APPLICABLE

No field safety corrective actions (FSCA) or field safety notices (FSN) have been issued.

5. SUMMARY OF CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP (PMCF)

5.1. SUMMARY OF CLINICAL DATA RELATED TO EQUIVALENT DEVICE

The conformity of the Makoto® Intravascular Imaging System (TVC-MC10/TVC-MC10i) and Dualpro® IVUS+NIRS Imaging Catheter (TVC-C195-42) was assessed and endorsed by the NB in part based on equivalence with earlier generations of the device manufactured by Infraredx. These include the TVC-MC8 system with TVC-C195-22 catheter and the TVC-MC9/MC9i system with TVC-C195-32 catheter. Demonstration of equivalence of the different system generations included technical, biological, and clinical equivalence in accordance with MDR 2017/745 Annex XIV, Part A (3).

Product	Basic UDI-DI	Manufacturer
TVC-MC8 & TVC-C195-22	N/A	Infraredx
TVC-MC9/MC9i & TVC-C195-32	N/A	Infraredx

A separate SSCP of the equivalent devices is not available in Eudamed. The summary of clinical data obtained from clinical investigations with the devices is provided in

Section 5.3. Section 5.4 summarizes the long-term safety and performance of the equivalent and current devices.

5.2. SUMMARY OF CLINICAL DATA FROM CONDUCTED INVESTIGATIONS OF THE DEVICE BEFORE THE CE-MARKING

Several human clinical studies were conducted with the subject devices and predecessor models prior to the CE-Marking. The studies reflect results of NIRS technology or combined NIRS and IVUS technology. The clinical study data are used to support the safety and performance of the subject device and are summarized below (as of Dec. 31, 2025).

Coronary Artery Plaque Characterization by NIR Spectroscopy in Patients Undergoing Elective Percutaneous Coronary Intervention (SPECTACL)

System: LipiScan (MC5)

Objective and Design

The SPECTACL study is a multi-center, unblinded, non-randomized, feasibility and pivotal study aimed at examining the feasibility of performing NIR spectroscopy only in 20 patients with stable or progressive angina pectoris and studying the reproducibility of NIR spectroscopy only in 125 additional patients with stable angina pectoris or a stabilized acute coronary syndrome.

Primary Endpoints

- Stage I Feasibility 20 patients: Differences between the spectra obtained within the coronary arteries of patients compared to spectra obtained in blood alone.
- Stage II: Pivotal 125 patients: The similarity between spectra obtained within the coronary arteries of patients and spectra previously obtained from coronary artery autopsy specimens.

Secondary Endpoints

- The number of lipid-rich plaque NIR signals observed in patients with acute coronary syndromes compared to those in patients with stable angina
- Identification of distinct NIR spectral characteristics associated with special coronary artery features identified by angiography and IVUS (culprit lesion, ruptured plaque, thrombus, stent, and sites with intimal thickening only) and patient characteristics (increased cholesterol, elevated CRP).
- Clinical cardiac events during follow-up.

Methods

Intracoronary NIRS was performed in patients undergoing percutaneous coronary intervention using a predecessor to the TVC Imaging System. Acquired spectra were blindly compared with autopsy NIRS signals using multivariate statistics. To meet the

end point of spectral similarity, at least 2/3 of the scans were required to have >80% of spectra similar to the autopsy spectra. A total of 106 patients were enrolled.

Results

Spectroscopic data could not be obtained in 16% of patients due to technical limitations. Most difficulties resulted from inadequate connections between the catheter and the controller and priming artifacts. These issues were most frequently observed with the first generation system and catheter but were virtually eliminated with the adoption of the second generation system. Spectra from 30 patients were unblinded to test the calibration of the lipid core-containing plaque detection algorithm. Eleven of the remaining 59 blinded cases were excluded due to inadequate data.

Of the 48 patients with spectrally adequate scans, 40 (83%) met the criteria for spectral similarity. The median spectral similarity for each pullback was 96%. Inadequate data that led to exclusion of pullbacks or failed spectral similarity metric resulted from either malfunction of the research device, including improper optical connections or impeded rotation of the optical core, or the presence of signals not interpretable by the algorithm (e.g. potential effect of disturbed blood flow or poor wall visibility due to excessive blood depth between the catheter and one side of the vessel wall).

Lipid core-containing plaque was detected in 58% of spectrally similar scans. This relatively high prevalence is likely reflective of the high pretest probability of lipid core plaque in this patient population. Autopsy validation demonstrated that chemograms demonstrating marked lipid core-containing plaque signals were reliably associated with lipid core plaque. The prevalence of lipid core-containing plaque at target lesion sites was calculated in 57 patients in whom the target lesion was imaged. The prevalence of lipid core-containing plaque at identifiable target lesions was 42%. Non-target lipid core-containing plaque was observed in 33% of scanned segments.

There were no serious adverse events attributed to NIRS. One patient experienced chest pain during both IVUS and NIRS imaging. This was attributed to temporary occlusion of the vessel by positioning of the devices across a narrow stenosis. The chest pain promptly resolved each time after removal of the catheter. Six percent of patients experienced a periprocedural myocardial infarction. In five (of six) of these cases, the myocardial infarction was attributed to occlusion of a side branch associated with stenting of the target vessel. In the remaining case, the myocardial infarction was attributed to occlusion of a side branch associated with stenting in a non-target vessel in which the catheter was not introduced. This rate of post-procedure myocardial infarction is within reported rates (5% to 30%) for patients undergoing percutaneous coronary intervention.

Conclusion

This NIRS system safely obtained spectral data similar to those from autopsy specimens. Technical limitations have been reduced with recent design changes. These first-in-human results demonstrate feasibility of invasive detection of coronary lipid core-containing plaque with this novel system.

Chemometric Observations of Lipid Core Containing Plaques of Interest in Native Coronary Arteries Registry (COLOR)

System: LipiScan (MC5) LipiScan IVUS (NIRS-MC7)/TVC Imaging System (TVC-MC7/TVC-MC8)

Objective and Design

The COLOR registry is a prospective, multi-center, non-randomized, open-label, non-controlled, observational, procedural registry of consecutive consented patients. The objectives of the study are to identify associations between lipid core containing plaques of interest or the Lipid Core Burden Index (as measured by the TVC Imaging System) and angiographic native coronary artery disease states and NYHA/CCS classified symptoms upon presentation in a broad catheterization laboratory population. Secondary objectives include: improving physician education on chemogram interpretation and application through presentation and educational seminars, conferences, and peer reviewed publications; generating hypotheses and techniques for future controlled clinical investigation; and identifying associations that lipid core-containing plaque or the Lipid Core Burden Index may have with atherosclerosis appearance, progression, regression, and/or cardiac events during the one year period following the index contact.

Recruitment for this registry began in 2009 and follow-up was completed at the end of 2016. A total of 2066 patients were enrolled in the registry and 24 months of follow up was completed. At this time data is being analyzed for publication.

Coronary Artery Assessment by Near-Infrared of Atherosclerotic Rupture-Prone Yellow Trial (CANARY)

Report: Final data contained in Stone et al, 2015

System: TVC-MC7/TVC-MC8

Objective and Design

The CANARY study is a prospective, open-label, randomized, controlled, multicenter trial examining whether pre-percutaneous coronary intervention plaque characterization using NIRS identifies lipid-rich plaques at risk of peri-procedural myonecrosis and whether these events may be prevented by the use of a distal protection filter.

Primary Endpoints

To test the hypothesis that use of a distal protection device can reduce peri-procedural myocardial infarction in patients undergoing percutaneous coronary intervention at stenotic sites caused by plaques with a large lipid core as assessed by NIR spectroscopy.

Secondary Endpoints

- Identification of chemogram findings most likely to be associated with distal embolization as determined by cardiac biomarker elevations.
- Determine the relationship between the IVUS features of the percutaneous target lesions (plaque volume, relation between LCP and site of maximal stenosis), the NIR detected lipid core-containing plaque, and outcomes.
- Determine the relationship between the change in chemograms (pre and post balloon or pre and post stenting) and outcomes.

Methods

Eighty-five patients undergoing stent implantation or a single native coronary lesion were enrolled. Thirty-one patients with a maximum lipid core burden index over any 4-mm length of greater than 600 were then randomized to percutaneous coronary intervention with distal protection (n=14) or without distal protection (n=17). The remaining 54 patients received percutaneous coronary intervention without distal protection.

Results

Twenty-one patients (24.7%) developed peri-procedural myocardial infarction. Baseline lipid core burden index and maximum lipid core burden index over any 4-mm length were both positively correlated with periprocedural myocardial infarction.

There was no difference in the rate of peri-procedural myocardial infarction in patients treated with a distal protection filter versus those who were not treated with a protection filter.

There were no major in-hospital adverse cardiac events beyond the myocardial infarction discussed above.

Conclusions

Plaque characterization by NIRS identifies lipid-rich lesions with an increased likelihood of peri-procedural myocardial infarction after stent implantation, presumably due to distal embolization. However, in this pilot randomized trial, the use of a distal protection filter did not prevent myonecrosis after percutaneous coronary intervention of lipid-rich plaques.

5.3. SUMMARY OF CLINICAL DATA FROM OTHER SOURCES

HUMAN CLINICAL DATA

Several human clinical studies were completed after the CE-Marking (as of Dec. 31, 2025). The DEBuT-LRP study results were published in EuroIntervention in July 2024. The PREVENT study results were presented at the ACC conference in April 2024 and simultaneously published in The Lancet. Additionally, the results of the FITTER study were presented at ESC 2024 and published in EuroIntervention.

Intravascular Identification and Drug-Eluting Balloon Treatment of Vulnerable Lipid-Rich Plaques (DEBuT-LRP)

System: TVC-MC10

Objective and Design

The DEBuT-LRP study is a conceptual investigator-initiated single center prospective single-arm interventional trial in consecutive ACS patients. The study objective is to determine the change in plaque characteristics of non-culprit lipid-rich plaques, determined with LCBImm4, as measured with IVUS/NIRS, after treatment with a drug-eluting balloon in patients with acute coronary syndrome.

Primary Endpoint

The change in lipid-core burden index in a 4 mm segment (LCBImm4) as measured with IVUS + NIRS from baseline to 9 month follow-up in identified LRPs that are treated with DEB.

Secondary Endpoints

1. To determine changes in plaque volume and characteristics of LRPs treated with DEB measured by CTCA at 9-month follow-up, as compared to baseline;
2. To determine the safety of drug-eluting balloon treatment for LRPs;
3. To determine the risk of LRPs on clinical outcomes, defined as cardiac death, myocardial infarction, ischemia-driven revascularization;
4. To correlate vulnerable plaque characteristics on CTCA with IVUS + NIRS at 9-months follow-up;
5. To develop a non-invasive algorithm that is able to detect LRPs on CTCA.

Results

Between January 2021 and September 2022, 65 patients were screened for inclusion, of whom 45 patients underwent IVUS-NIRS imaging after successful PCI of flow-limiting lesions. Out of 26 patients with >1 LRP, 20 patients were enrolled in the study to undergo PCB treatment of 1 LRP.

Follow-up imaging was performed at 272 days (IQR 256 to 281) in 18 patients (2 patients refused). No complications occurred. A total of 17 patients had analyzable IVUS-NIRS images prior to PCB treatment and after 9 months. The primary endpoint of the median maxLCBI4mm of the PCB-treated LRPs significantly decreased from 397 (IQR 299 to 527) at baseline to 211 (IQR 106 to 349) at follow-up (p decreased from 431 (IQR 362 to 519) at baseline to 331 (IQR 206 to 461) at follow-up (p=0.002), which was an absolute change of −111 (IQR −223 to –54) and a relative change of –24.6%. The maxLCBI4mm within the untreated vessels showed no significant difference between baseline (136 [IQR 98 to 243]) and 9-month follow-up (105 [IQR 61 to 217]; p=0.11).

Over a median follow-up period of 398 days (IQR 394 to 439), a total of 5 patients (25%) had a cardiovascular event. There were no deaths. No index LRP-related events occurred. Other procedural complications occurred, but no IVUS-NIRS-related occurred.

Results of the DEBuT study were presented at TCT in October, 2023, and were later published in EuroIntervention in July 2024.

Preventive PCI or Medical Therapy Alone for Vulnerable Atherosclerotic Coronary Plaque (PREVENT)

System TVC-MC10

Objective and Design

The primary aim of the trial is to determine whether preventive PCI with everolimus-eluting bioabsorbable vascular scaffolds (BVS) (early enrollment period of the trial) or cobalt-chromium everolimus-eluting stents (middle and latter enrollment periods of the trial, after BVS [Absorb] was withdrawn from the market by the manufacturer) plus OMT of functionally insignificant (fractional flow reserve [FFR] >0.80) vulnerable plaques, as determined by intracoronary imaging, would result in a significant reduction of the primary composite outcome of target-vessel failure (TVF, comprised of death from cardiac causes, target-vessel myocardial infarction (MI), target-vessel revascularization (TVR), or hospitalization for unstable or progressive angina at 2 years, compared with OMT alone.

The PREVENT trial was an investigator-initiated, multicentre, open-label, randomised controlled trial.

Results

Between Sept 23, 2015, and Sept 29, 2021, 5627 patients were screened for eligibility, 1606 of whom were enrolled and randomly assigned to percutaneous coronary intervention (n=803) or optimal medical therapy alone (n=803). 1177 (73%) patients were men and 429 (27%) were women. 2-year follow-up for the primary outcome assessment was completed in 1556 (97%) patients (percutaneous coronary intervention group n=780; optimal medical therapy group n=776). At 2 years, the primary outcome occurred in three (0·4%) patients in the percutaneous coronary intervention group and in 27 (3·4%) patients in the medical therapy group (absolute difference –3·0 percentage points [95% CI –4·4 to –1·8]; p=0·0003). The effect of preventive percutaneous coronary intervention was directionally consistent for each component of the primary composite outcome. Serious clinical or adverse events did not differ between the percutaneous coronary intervention group and the medical therapy group: at 2 years, four (0·5%) versus ten (1·3%) patients died (absolute difference –0·8 percentage points [95% CI –1·7 to 0·2]) and nine (1·1%) versus 13 (1·7%) patients had myocardial infarction (absolute difference –0·5 percentage points [–1·7 to 0·6]).

The PREVENT study results were presented at ACC in April, 2024 and simultaneously published in The Lancet.

FITTER

System TVC-MC10

Study Objective To evaluate the effect of maximal LDL-C reduction by Evolocumab on top of optimal background lipid-lowering therapy (ESC guidelines) on FFR of non-IRA lesions, in patients presenting with MVD-ACS. Secondly to correlate baseline lipid core burden with changes in FFR and to investigate the relation between LDL-C reduction and change in pro-inflammatory monocyte phenotypes.

Study Design Multi-center, randomized, placebo controlled clinical trial.

Results

Among 150 patients (mean age 64.2±8.5 years; 27 [18.0%] female) randomised to evolocumab (n=74) or placebo (n=76), 143 underwent follow-up coronary angiography. After 12 weeks of treatment, the adjusted mean change in FFR was 0.00 (95% confidence interval [CI]: −0.02 to 0.02) with evolocumab versus 0.01 (95% CI: −0.01 to 0.03) with placebo (adjusted mean difference: −0.01, 95% CI: −0.03 to 0.01; p=0.6). The adjusted mean change in the maxLCBI4mm was −27.8 (95% CI: −72.2 to 16.6) for evolocumab-treated patients versus −35.6 (95%CI: −82.5 to 11.4) for placebo-treated patients (adjusted mean difference: 7.8, 95% CI: −40.9 to 56.4; p=0.8). No between-group differences in any IVUS-derived parameter were found.

Results of the FITTER study were were presented at ESC 2024 and published in EuroIntervention in 2025.

PACMAN-AMI
System: *TVC-MC8*
Objective and Design

Primary Objective

To determine the effect of LDL-C lowering with alirocumab on top of high-intensity statin therapy on intravascular ultrasound (IVUS)-derived percent atheroma volume (PAV), near-infrared spectroscopy (NIRS)-derived maximum lipid core burden index within 4 mm (maxLCBI 4 mm) and optical coherence tomography (OCT)-derived fibrous cap thickness (FCT) in patients with AMI.

Design

Double-blind, placebo-controlled, randomized, superiority study

Results

From May 9, 2017, through October 7, 2020, a total of 300 patients (52.7% presenting with STEMI and 47.3% with NSTEMI) were randomized to receive treatment with alirocumab (n = 148) or placebo (n = 152). The results presented a primary efficacy endpoint of the change in IVUS-derived percent atheroma volume from baseline to week 52 and two powered secondary endpoints of changes in near-infrared spectroscopy–

derived maximum lipid core burden index within 4mm (higher values indicating greater lipid content) and optical coherence tomography–derived minimal fibrous cap thickness (smaller values indicating thin-capped, vulnerable plaques) from baseline to week 52.

Among 300 randomized patients (mean [SD] age, 58.5 [9.7] years; 56 [18.7%] women; mean [SD] low-density lipoprotein cholesterol level, 152.4 [33.8]mg/dL), 265 (88.3%) underwent serial IVUS imaging in 537 arteries. At 52 weeks, mean change in percent atheroma volume was −2.13%with alirocumab vs −0.92% with placebo (difference, −1.21% [95%CI, −1.78%to −0.65%], P < .001). Mean change in maximum lipid core burden index within 4mm was −79.42 with alirocumab vs −37.60 with placebo (difference, −41.24 [95%CI, −70.71 to −11.77]; P = .006). Mean change in minimal fibrous cap thickness was 62.67 µm with alirocumab vs 33.19 µm with placebo (difference, 29.65 µm [95%CI, 11.75-47.55]; P = .001). Adverse events reported related to the study drug (not subject device) occurred in 70.7%of patients treated with alirocumab vs 72.8%of patients receiving placebo.

The safety of the NIRS-IVUS device was also demonstrated with complications related to the intracoronary imaging procedure reported in 7 patients (2.3%), all of which were transient and without clinical sequelae.

Results of the PACMAN-AMI study were presented at ACC 2022 on April 3rd, 2022 in Washington, DC and simultaneous published online in the Journal of the American Medical Association (JAMA).[11]

Providing Regional Observations to Study Predictors of Events in the Coronary Tree. (PROSPECT II and PROSPECT ABSORB)

System: *TVC-MC8*

Objective and Design

PROSPECT II (Natural History Study): To test the ability of two coronary artery imaging modalities (IVUS and NIRS) to identify angiographically non-obstructive vulnerable plaques that are subsequently responsible for unanticipated coronary events.

PROSPECT ABSORB (Randomized Trial): To determine whether the Absorb® Bioresorbable Vascular Scaffold (BVS) can safely enlarge luminal dimensions as measured 25 months after implantation in high-risk angiographically non-obstructive lesions with IVUS plaque burden ≥65%.

The PROSPECT II and PROSPECT ABSORB Study period is from 2014-2018 with registry follow-up for an additional 15 years (2033). Study enrollment was completed with a total of 902 patients in December, 2017, 182 of which were randomized to the PROSPECT ABSORB treatment arm of the study. Twenty-four month follow-up for the PROSPECT II part of the study and 25-month follow-up for the PROSPECT ABSORB part of the study were completed in January, 2020.

<u>PROSPECT II</u>

The primary outcome was the covariate-adjusted rate of MACE arising from untreated non-culprit lesions (as identified by IVUS) during follow-up. The relationships between

plaques with high lipid content, large plaque burden, and small lumen areas and patient-level and lesion-level events were determined.

High lipid lesions (as identified by NIRS) were an independent predictor of patient-level non-culprit lesion-related MACE with an adjusted odds ratio of 2.27 [1.25-4·13] and non-culprit lesion-specific MACE with an adjusted odds ratio of 7.83 [4·12–14·89]. Large plaque burden (as determined by IVUS) was also an independent predictor of non-culprit lesion-related MACE. Lesions with both large plaque burden by intravascular ultrasound and large lipid-rich cores by NIRS had a 4-year non-culprit lesion-related MACE rate of 7.0% [4.0-10.0].

The results of the study satisfied the primary endpoint, demonstrating that NIRS-IVUS detects angiographically non-obstructive lesions with a high lipid content and large plaque burden that are at increased risk for future adverse cardiac outcomes. The safety of the NIRS-IVUS device was also demonstrated with device-related major complications requiring treatment occurring at <1% (2 of 902 patients).

PROSPECT ABSORB

The primary powered effectiveness endpoint was the IVUS-derived minimum lumen area (MLA) at protocol-driven 25-month follow-up. The primary (nonpowered) safety endpoint was randomized target lesion failure at 24 months. The secondary (nonpowered) clinical effectiveness endpoint was randomized lesion–related major adverse cardiac events at latest follow-up.

The follow-up MLA in BVS-treated lesions was 6.9±2.6 mm^2 compared with 3.0±1.0 mm^2 in guideline-directed medical therapy (GDMT) alone–treated lesions (least square means difference: 3.9 mm^2 [3.3- 4.5; $p < 0.0001$]. Target lesion failure at 24 months occurred in similar rates of BVS-treated and GDMT alone–treated patients (4.3% vs. 4.5%; $p = 0.96$). Randomized lesion–related MACE occurred in 4.3% of BVS-treated patients versus 10.7% of GDMT alone–treated patients (OR = 0.38; [0.11 - 1.28; $p = 0.12$].

The study concluded that percutaneous coronary intervention of angiographically mild lesions with large plaque burden was safe, substantially enlarged the follow-up MLA, and was associated with favorable long-term clinical outcomes.

Results of the main study and sub-study were presented on October 12, 2020 at TCT Connect in a Late Breaking Clinical Trial session. The PROSPECT II study was published in The Lancet in March, 2021 and the PROSPECT ABSORB sub-study was published in JACC Imaging in October, 2020[2,3].

Lipid-Rich Plaque (LRP) Study

System: *TVC-MC8*

Objective and Design

The Lipid-Rich Plaque Study was performed in patients undergoing IVUS-NIRS imaging (the index procedure) in whom a TVC catheter was used for routine clinical indications. The study tested the ability of multi-vessel NIRS scanning for LRP in coronary segments without significant stenoses to predict new coronary events arising from a new culprit

lesion (a non-index culprit lesion). Analyses were performed at both the patient level (vulnerable patients) and the segment level (vulnerable plaques). The LRP study period was from 2014 – 2018.

From February 2014 to March 2016, the LRP Study enrolled 1,563 patients from 44 centers in the US and EU. The primary endpoint analysis population was followed for 24 months to assess the occurrence of MACE. The exposure variable was a quantitative summary metric of lipid core detected by intravascular NIRS imaging reported as the maximum lipid core burden in a 4mm coronary segment (maxLCBI4mm). The pre-specified co-primary endpoints were for vulnerable patient – a proportional hazard model association between maxLCBI4mm in all imaged arteries and future patient-level non-culprit MACE – and vulnerable plaque – a proportional hazard model association between maxLCBI4mm in a segment and incidence of future non-culprit MACE in the same segment.

After adjustment for possible confounding variables, the risk of experiencing a non-culprit MACE event within 24 months was found to be 18% higher with each 100 unit increase in maxLCBI4mm (HR=1.18 [1.05-1.32], p=0.0043). For a threshold of patient maxLCBI4mm > 400, the adjusted hazard ratio for NC-MACE was 1.89 (95% CI [1.26-2.83], p=0.0021). After adjustment for within-patient clustering, the risk of experiencing MACE in a coronary segment within 24 months was found to be 45% higher with each 100 unit increase in maxLCBI4mm (HR=1.45 [1.30-1.60], p<0.0001). For a threshold of segment maxLCBI4mm > 400 the adjusted hazard ratio for NC-MACE was 4.22 (95% CI [2.39-7.45], p<0.0001).

The foregoing results satisfied the primary and key secondary endpoints of the LRP Study, demonstrating an independent and statistically significant association between NIRS-identified coronary lipid cores and the occurrence of patient and plaque level MACE.

Results of the LRP study were presented at TCT 2018 in September, 2018 in San Diego and published in The Lancet in 2019.[1]

5.4. AN OVERALL SUMMARY OF THE CLINICAL PERFORMANCE AND SAFETY

Nine clinical investigations (SPECTACL, COLOR, CANARY, LRP, PROSPECT II/ABSORB, PACMAN-AMI, FITTER, PREVENT, and DEBUT-LRP) have been completed to date. All nine studies confirmed the safety of the subject device and demonstrated the effectiveness of the TVC Imaging System in the identification of lipid accumulation, plaque burden, lipid core burden, calcification, and vulnerable plaque. These studies also demonstrated the ability of the subject device to identify the culprit segments in STEMI patients and for identifying patients at risk of future cardiovascular events.

The adverse events reported in these studies were chest pain, dissection, arrhythmia, air embolism, spasm and periprocedural myocardial infarction. These are known risks associated with intracoronary imaging and coronary intervention and the rates reported were well within reported rates for patients undergoing percutaneous coronary

intervention. The subject device remains clinically relevant and continues to be state of the art.

5.5. ONGOING OR PLANNED POST-MARKET CLINICAL FOLLOW-UP

Several investigator-initiated studies are in progress with the Makoto Imaging System (as of Dec. 31, 2025). The studies reflect combined NIRS and IVUS technology. The clinical study data are used to support the safety and performance of the subject device and are summarized below.

The UCLA Heart Transplant Study and IMPACTavi remain ongoing, with follow-up completion expected in August 2025 and June 2026, respectively. The IDEAL-COR study is actively enrolling, with follow-up completion expected in December 2026 and results in March 2027. The DELETE-LRP study is actively enrolling, with follow-up completion expected in September 2027 and results in January 2028.

IMPACTavi
System: *TVC-MC10*
Objective and Design

Primary Objective

To investigate whether coronary NIRS-IVUS-derived lesion characteristics will allow identification of patients likely to suffer adverse cardiovascular events during clinical follow-up after transfemoral transcatheter aortic valve implantation (TAVI).

Secondary Objectives

Use of NIRS-IVUS in addition to routine coronary angiography is a safe and feasible method to assess relevance of coronary lesions in the context of severe aortic stenosis
Study Design Prospective, non-randomized, observational, single-center cohort study
Design
Prospective, non-randomized, observational, single-center cohort study

UCLA Heart Transplant Study
System: *TVC-MC10*
Objective and Design

Primary Objective

To define the relationship between early lipid accumulation and plaque/coronary allograft vasculopathy (CAV) progression, determine predictors of early lipid accumulation, and evaluate the association of early lipid accumulation with short-term clinical outcomes in a prospective cohort of new heart transplant recipients.

Design

Prospective and retrospective, non-randomized, observational, two-center cohort study.

IDEAL-COR
System: *TVC-MC10*
Objective and Design

Primary Objective

The objective of this study is to investigate, as a proof-of-principle, long-term (52 weeks) effects of tirzepatide once-weekly vs. placebo on changes in coronary plaque composition and progression (assessed by NIRS), plaque burden (assessed by IVUS) and microvascular function (assessed by invasively measured CFR) in overweight and obese individuals with stable coronary artery disease (CAD). In addition, the objective of a baseline cross-sectional sub-study is to explore potential metabolic and cardiovascular (CV) predictors for high arteriosclerotic plaque burden in overweight and obese individuals and to establish a cohort for future research projects.

Design

Double-blinded, randomised (1:1), multi-centre, placebo-controlled, 52 weeks, clinical trial.

DELETE-LRP
System: *TVC-MC10*
Objective and Design

Primary Objective

The objective of this study is to test the hypothesis that paclitaxel-coated balloon treatment of non-obstructive non-culprit vulnerable lipid-rich plaques (LRP) leads to a greater reduction of the lip-core burden index than guideline-directed medical therapy alone.

Design

Prospective two-arm randomized controlled trial.

6. POSSIBLE DIAGNOSTIC OR THERAPEUTIC ALTERNATIVES

6.1. SUBJECT DEVICE

The catheter-based Makoto® Intravascular Imaging System utilizes two imaging modalities, namely, near-infrared spectroscopy (NIRS) and intravascular ultrasound (IVUS).

The NIRS modality delivers near-infrared light to the vessel wall through blood and analyzes the amount of light reflected at different wavelengths to determine the chemical composition of the tissue. NIRS can determine distinct spectroscopic signatures for lipids such as cholesterol and cholesteryl esters. The Makoto® system automatically identifies lipid core plaques (LCP) in coronary arteries based on NIRS and displays the LCPs in a spatial image.[4-10]

The IVUS modality uses reflected ultrasound waves from the vessel wall to create a gray scale spatial image. The image can be segmented to measure the volume of plaque and the diameter and cross-sectional area of the lumen, vessel, or stent. IVUS can also be used to identify coronary calcification and assess stent apposition and expansion. IVUS, however, is limited in its ability to identify LCPs due to confounding or masking by other components such as thrombus, fibrotic plaque, or calcific plaque.[6-10]

6.2. ALTERNATIVE DEVICE

A possible diagnostic alterative for invasive imaging of coronary arteries is optical coherence tomography (OCT) imaging. OCT is a state of the art catheter-based intravascular imaging modality that uses near-infrared light directed at, and reflected from, the vessel wall to generate a spatial image. The high spatial resolution of OCT allows the measurement of the thickness of the cap overlying LCPs. In addition, OCT can provide information about calcification, plaque lipid and macrophages. However, the identification of LCPs is dependent on the absence rather than the presence of signal which can lead to misidentification of LCP. Calcification can also be misinterpreted as LCP. Unlike NIRS or IVUS, OCT requires elimination of blood from the viewing field by injection of contrast media.[5-10]

7. SUGGESTED PROFILE AND TRAINING FOR USERS

The Makoto® Intravascular Imaging System is to be used exclusively by trained physicians and cardiac catheterization laboratory personnel.

Onsite training by Infraredx personnel or certified trainers on the use of the Makoto® Intravascular Imaging System is available at the time of installation and available upon request. Please contact Infraredx Customer Service or your local service provider to schedule onsite training and periodic training competency reviews.

8. REFERENCE TO ANY HARMONISED STANDARDS AND CS APPLIED

The following list includes the Applicable Standards currently applied by Infraredx.

Standard Number	Standard Title
AAMI TIR28:2016 / (R)2024	Product adoption and process equivalence for ethylene oxide sterilization
ASTM D4169-16	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM D4332-14	Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing
ASTM D5276-19 (Reapproved 2023)	Standard Test Method for Drop Test of Loaded Containers by Free Fall
ASTM D6653-13 (Reapproved 2021)	Standard Test Methods for Determining the Effects of High Altitude on Packaging Systems by Vacuum Method
ASTM F88-15	Standard Test Method for Seal Strength of Flexible Barrier Materials

ASTM F756-13	Standard Practices for Assessment of Hemolytic Properties of Materials
ASTM F1980-07 (Reapproved 2011)	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
ASTM F2096-11 (Reapproved in 2019)	Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)
EU – Regulation (EU) 2017/745	REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
IEC 60601-1:2005 + A1:2012	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (Edition 3.1)
IEC 60601-1:2005 + A1:2012 + A2:2020	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (Edition 3.2
IEC 60601-1-2:2014 + A1:2020	Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance – Collateral standard: Electromagnetic compatibility – Requirements and tests (Edition 4.1)
IEC 60601-1-6:2010 + A1:2013	Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability (Edition 3.1)
IEC 60601-1-6:2010 + A1:2013 + A2:2020	Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability (Edition 3.2)
IEC 60601-2-37:2007	Medical electrical equipment – Part 2-37: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment (Edition 2)
IEC 60601-2-37:2024	Medical electrical equipment – Part 2-37: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment (Edition 3.0)
IEC 60825-1:2007	Safety of laser products - Part 1: Equipment classification and requirements (Edition 2.0)
IEC 60825-1:2014	Safety of laser products - Part 1: Equipment classification and requirements (Edition 3.0)
IEC 62304:2006+A1:2015	Medical device software - Software life cycle processes (Edition 1.1)
IEC 62366-1:2015 + A1:2020	Medical devices - Part 1: Application of usability engineering to medical devices (Edition 1.1)
IEC 81001-5-1:2021	Health software and health IT systems safety
IEC TR 60878:2015	Graphical symbols for electrical equipment in medical practice (Edition 3)
ISO 9000:2015 (Clause 3 only)	Quality management systems – Fundamentals and vocabulary

ISO 10993-1:2009	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (Edition 4)
ISO 10993-4:2002/A1:2006	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood (Edition 2, Amendment 1)
ISO 10993-5:2009	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity (Edition 3)
ISO 10993-7:2008	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (Edition 2)
ISO 10993-7:2008 + A1:2019	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (Edition 2, Amendment 1)
ISO 10993-10:2010	Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization (Edition 3)
ISO 10993-11:2006	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (Edition 2)
ISO 10993-12:2012	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (Edition 4)
ISO 10993-23:2021	Biological evaluation of medical devices – Part 23: Tests for irritation (Edition 1)
ISO 11135:2014 + A1:2018	Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices (Edition 2)
ISO 11607-1:2019	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (Edition 2)
ISO 11737-1:2006/ (R) 2011	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on product (Edition 2, Amendment 1)
ISO 11737-1:2018	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on product (Edition 3)
ISO 13485:2016	Medical devices – Quality management systems – Requirements for regulatory purposes
ISO 14161:2009	Sterilization of health care products - Biological indicators - Guidance for the selection, use and interpretation of results (Edition 2)
ISO 14971:2019	Medical devices - Application of risk management to medical devices (Edition 3)
ISO 15223-1:2016	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements (Edition 3)
ISO 20417:2021	Medical devices – Information to be supplied by the manufacturer (Edition 1)

US – Revised 21 CFR 820	Quality Management System Regulation
USP-NF<87> M98833_01_01	Biological Reactivity Test, In Vitro - Direct Contact Test
USP-NF<87> M98833_01_01	Biological Reactivity Test, In Vitro – Elution Test
USP-NF<151> M98900_01_01	Pyrogen Test (USP Rabbit Test)

9. REVISION HISTORY

SSCP revision number	Date issued	Change #	Change description	Initiator	Revision validated by the Notified Body
A	20-Sep-22	DCO-000319	Initial release to production. Added author names and titles, abbreviation definitions, updated 4.1 residual risks, 5.1 clinical data related to equivalent devices, 6 benefit-risk ratio of alternative device, and standard years. English Version of the SSCP has been validated by BSI.	E. Falzone	☒Yes Validation language: English ☐No
B	21-Jul-23	DCO-000350	Annual update for 2022	E. Falzone	☐Yes Validation language: English ☒No
C	07-Mar-24	DCO-000455	Annual update for 2023	E. Falzone	☐Yes Validation language: English ☒No
D	31-Oct-24	DCO-000493	Updated trademarks, name of the report, removed confidential footer, and removed pre-release history.	E. Falzone	☐Yes Validation language: English ☒No
E	08-Sep-25	DCO-000571	Annual update for 2024	E. Falzone	☐Yes Validation language: English ☒No
F	02-Feb-25	DCO-000604	Annual update for 2025	E. Falzone	☐Yes Validation language: English ☒No

10. REFERENCES

1. Waksman R, Di Mario C, Torguson R, et al. Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study. The Lancet. Published online September 2019.
2. Erlinge D, Maehara A, Ben-Yehuda O, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study. The Lancet. 2021;397(10278):985-995.
3. Stone GW, Maehara A, Ali ZA, et al. Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque. Journal of the American College of Cardiology. 2020;76(20):2289-2301.
4. Cha JJ, Hong SJ, Lim S, et al. An Overview of Near-Infrared Spectroscopy-Intravascular Ultrasound and Its Applications in Coronary Artery Disease. J Cardiovasc Interv. 2022;1(1):1.
5. Batty JA, Subba S, Luke P, Gigi LW, Sinclair H, Kunadian V. Intracoronary Imaging in the Detection of Vulnerable Plaques. Curr Cardiol Rep. 2016 Mar;18(3):28.
6. Yonetsu T, Jang IK. Advances in Intravascular Imaging: New Insights into the Vulnerable Plaque from Imaging Studies. Korean Circ J. 2018 Jan;48(1):1-15.
7. Sum S, Madden S, Hendricks M, Chartier S, Muller J. Near-infrared spectroscopy for the detection of lipid core coronary plaques. Current Cardiovascular Imaging Reports. 2009;2(4):307-315.
8. Mintz GS, Matsumura M, Ali Z, Maehara A. Clinical Utility of Intravascular Imaging. JACC: Cardiovascular Imaging. Published online September 2022:S1936878X22003989.
9. Kubo T, Terada K, Ino Y, et al. Combined Use of Multiple Intravascular Imaging Techniques in Acute Coronary Syndrome. Front Cardiovasc Med. 2022;8:824128.
10. Malhotra R, Vengrenyuk Y, Kini A. Fundamentals of Intracoronary Imaging. In: Kini A, Sharma SK, eds. Practical Manual of Interventional Cardiology. Springer International Publishing; 2021:103-117.
11. Räber L, Ueki Y, Otsuka T, et al. Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: The PACMAN-AMI Randomized Clinical Trial. JAMA. Published online April 3, 2022. doi:10.1001/jama.2022.5218
12. Van Veelen A, Küçük IT, Garcia-Garcia HM, et al. Paclitaxel-coated balloons for vulnerable lipid-rich plaques. EuroIntervention. 2024;20(13):e826-e830. doi:10.4244/EIJ-D-23-01073
13. Park SJ. Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial.