

Makoto Integrated Intravascular Imaging System™
User's Guide



makoto™
INTRAVASCULAR IMAGING SYSTEM

User's Guide

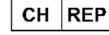
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Makoto Integrated Intravascular Imaging System™

User's Guide



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1 Introduction to the Makoto™ Integrated Imaging System

1.1 Indications for Use

The Makoto Integrated 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.

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.

1.2 Additional Indications for Use – USA Only

The Makoto Intravascular Imaging System™ is intended for ultrasound examination of peripheral intravascular pathology.

- a) Intravascular ultrasound imaging is indicated in patients who are candidates for transluminal peripheral interventional procedures. The System is not indicated for use in the cerebral vessels.



WARNING

The effectiveness of NIRS in the peripheral vasculature has not been established.

1.3 Clinical Benefit

The clinical benefit provided by the Makoto™ Intravascular Imaging System is in the identification of the lipid core plaques (LCPs). By identifying LCP, the Makoto™ Intravascular Imaging System provides information that is not as easily available from other technologies. The potential benefits of NIRS-IVUS-guided management are: 1)

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determination of the length of artery to stent, 2) selection of intensity of medical management, 3) identification and mitigation of the risk of embolic peri-stenting infarction, and 4) identification of patients and plaques at increased risk of future major adverse cardiac events (MACE).

1.4 Training

The Makoto™ Integrated Imaging System is to be used exclusively by trained physicians and catheterization laboratory personnel.

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

1.5 Infraredx Contact Information

Infraredx can be contacted at:

Infraredx, Inc.
28 Crosby Drive, Suite 100
Bedford, MA 01730
USA

www.infraredx.com

Phone (International): +1-800-596-3104

The Instructions for Use can be accessed in electronic form at the above website.

1.6 Patents

The Makoto Integrated Intravascular Imaging System™, catheters, and associated accessories are protected by one or more patents. For a complete listing of issued patents please consult:

<http://www.infraredx.com/infraredx-intellectual-property/>

1.7 Trademarks

Infraredx™, Makoto™, Dualpro™, and TVC™ are trademarks of Infraredx, Inc. The name “Infraredx Dualpro” is a registered trademark in China. The name “Infraredx” is a registered trademark of Infraredx, Inc. in the USA, European Union, Australia, China, South Korea and Japan.

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All other brand names and product names used and referenced in this document are trademarks, registered trademarks, or trade names of their respective holders.

2 How to Interpret this Manual

This manual contains important information for operating the Makoto Integrated Intravascular Imaging System™. Carefully read and review the manual before attempting to operate the product.

2.1 Symbols and Icons

Throughout this manual there may be alerts. These alerts are indicated as Warnings, Cautions, and Notes.



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 Imaging System™ or may result in degradation of system performance.

NOTE: Notes provide helpful reminders and tips for using advanced features.

2.2 Abbreviations

AC	Alternating Current
ANSI	American National Standards Institute
AVI	Audio Video Interleave
CUI	Console User Interface
CPU	Central Processing Unit
DICOM	Digital Imaging and Communications in Medicine standard
DVD	Digital Video Disc
EEM	External Elastic Membrane

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EMC	Electromagnetic conformance
EMI	Electromagnetic Interference
EO	Ethylene Oxide
EtO	Ethylene Oxide
FDA	Food and Drug Administration
FHD	Full High Definition display, 1920x1080pixels
HD	High Definition display
IEC	International Electrotechnical Commission
IP	Internet Protocol
ISO	International Standard Organization
IVUS	Intravascular Ultrasound
JPEG	Joint Photographic Experts Group
LCBI	Lipid Core Burden Index
LCP	Lipid Core Containing Plaque of Interest
NIR	Near-infrared
NIRS	Near-infrared Spectroscopy
PA	Plaque Area
PB	Plaque Burden
PACS	Picture Archiving and Communication System
PTCA	Percutaneous transluminal coronary angioplasty
PTA	Percutaneous transluminal angioplasty
RF	Radio Frequency
RFID	Radio Frequency Identification
UL	Underwriters Laboratories
USB	Universal Serial Bus

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2.3 Actions

The Makoto™ Integrated Intravascular Imaging System is primarily designed for touch screen interaction. In addition to the touch screen monitor, the system is equipped with a mouse. Remembering the following actions and gestures will assist you when interacting with the Makoto™ Integrated Intravascular Imaging System:

Touch	A momentary contact with the touch screen or depress and release of a physical button
Press	Depress and release of a physical button
Right click	A single right button click using the mouse
Left click or Click	A single left button click using the mouse
Double-click	Two left button clicks in rapid succession using the mouse
Scroll Up/Down	A roll of the scroll wheel on the mouse toward the user for down, away from the user for up
Drag	While the finger is in contact with a movable icon, move finger to another location. Lift finger off of the screen to release the icon.

3 Warnings, Safety, and Precautions

3.1 Contraindications

Use of the Makoto Integrated Intravascular Imaging System™ 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 disqualified for PTA
- Patients who are not suitable for IVUS procedures

3.2 Complications

The following complications may occur as a consequence of intravascular examination:

- 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

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3.3 Safety

The Makoto™ Integrated Intravascular Imaging System, or Makoto™, has been designed for the safest possible operation and maintenance. However, any medical instrument can cause injury if it is improperly installed, operated, moved, or serviced and this system is no exception.

The potential hazards are:

- ocular (vision) damage resulting from exposure to direct or reflected laser radiation
- electrical shock from contact with electrical components inside the system
- physical injury incurred while operating or moving the system

Serious incidents involving the Makoto™ Intravascular Imaging System should immediately be reported to Infraredx and the Competent Authority of the Member State in which the user and/or patient is established. Infraredx or your local service provider contact information may be found in Sections 1.5 Infraredx Contact Information or 13.1 About.

NOTE: Information related to the safety and clinical performance (SSCP) of the Makoto™ Intravascular System is available in the European database on medical devices (Eudamed), where it is linked to the UDI-DI located beneath the bar code next to (01) on the product label.

Eudamed Website: <https://ec.europa.eu/tools/eudamed>

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The Makoto™ is equipped with features designed specifically to provide safe operation to users. All catheter laboratory personnel should become familiar with the location and operation of the safety features discussed below. During imaging, moving components are completely contained so that the user is not exposed to mechanical hazards.

Anyone using the Makoto™ for human procedures of any kind should thoroughly understand the implications of such use. The AIUM (American Institute of Ultrasound in Medicine) has published a document titled Medical Ultrasound Safety (AIUM 2009).

ALARA is an acronym for the principle of prudent use of diagnostic ultrasound by obtaining the diagnostic information at a power output that is As Low As Reasonably Achievable. To obtain a copy of this document, please contact the AIUM.











WARNING

Adherence to the precautions discussed in this section must be observed when installing, operating, moving, or servicing the system to avoid potentially hazardous situations.





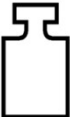






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<i>SYMBOL</i>	<i>EXPLANATION</i>
	Warning
	Caution
	Refer to instruction manual
	Consult instructions for use
	Product meets applicable U.S., European, and Canadian Standards as evaluated by TUV Rheinland.
100-120 V~ 50/60 Hz 5A 220-240 V~ 50/60 Hz 3A	Product operates from a power source that supplies nominally 100VAC, 120VAC, 220VAC, or 240VAC, 50/60 Hertz Maximum current is 5 Amperes at 100-120 VAC, 3 Amperes at 220-240 VAC.
	Manufacturer
	Date of Manufacture
	Catalog number

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	Serial number
	Batch Code
	Medical Device
	Use-by date
	Mass
	Authorized representative in the European Community
	Authorized representative in Switzerland
	Importer
	Protective earth (ground)
	Defibrillation-proof direct cardiac application (type CF applied part)
	Quantity contained in package.

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	Compatible guide catheter inner diameter
	Compatible guidewire outer diameter
	Laser aperture
	Keep away from sunlight
	Non-pyrogenic
	Keep dry
	Temperature limit
	Humidity Limitation
R_x Only	This device for sale by or for use on the order of a physician

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	Do not use if package is damaged
	Do not re-use
	Do not resterilize
	Sterilized using ethylene oxide.
	Not evaluated for safety when used with MRI
	CE Mark, indicates product complies with European Union law; number denotes specific notified body performing conformity assessment.

There are no user serviceable parts in the Makoto™ Integrated Imaging System Stationary Console, Integration Interface Module, Local Junction Box or Controller. All adjustments are made at the factory before shipment to customers or on site by trained service personnel.



Tampering with or any attempt to modify the Makoto™ Integrated Imaging System will void the product warranty and may also result in improper operation of the system.

Device degradation or product failure may result.

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3.4 Optical Precautions



WARNING

Failure to follow the information in this section may result in bodily injury and/or equipment damage.



WARNING

Product contains a Class 1M laser product that emits invisible laser radiation. Do not view directly with optical instruments.



WARNING

Never look directly into the laser beam coming from the system or reflected from a surface.



WARNING

Do not look into the laser beam through lenses, binoculars, magnifiers, camera-finders, telescopes, or any optical element that may focus the light into the eye.



WARNING

Never permit reflective objects such as jewelry, watches, metal instruments, or mirrors to intercept and reflect the laser beam.

The Makoto Integrated Intravascular Imaging System™ contains a laser system and is classified as a "Class-1M Laser Product" under a U.S. Department of Health and Human Services (DHHS) Radiation Performance standard according to the Radiation Control for Health and Safety Act of 1968 and per IEC 60825-1, Safety of Laser products.

Light energy emitted by this system lies in the invisible, near-infrared region of the electromagnetic spectrum at wavelengths between 1 and 2 microns. This fact should be remembered when taking precautions to avoid inadvertent exposure.

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NOTE: Laser safety eyewear is NOT required during use of the Makoto Integrated Intravascular Imaging System™.

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3.5 Electrical Precautions



WARNING

Failure to follow the information in this section may cause equipment damage, bodily injury, even death.



WARNING

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.



CAUTION

Medical electrical equipment needs special precautions regarding EMC and needs to be installed according to the EMC information provided in Appendix H: Electromagnetic Compliance.



CAUTION

DO NOT position the Makoto Integrated Intravascular Imaging System™ close to other equipment as electrical interference may result.



CAUTION

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 Integrated Intravascular Imaging System™ uses AC line voltage inside the console. Disconnecting the Makoto™ power cord plug from the outlet will interrupt power to the system causing an abrupt stop to all operations.

No part of the exterior housing should be displaced except by a trained and authorized technician.

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To reduce the risk of electric shock, do not connect the system's input power connection to equipment that is not protectively earth grounded. Do not connect the system to Class II equipment.

Radio frequency (RF) communications equipment can affect the performance of the Makoto Integrated Intravascular Imaging System™. This type of equipment should be located as far from the Makoto™ as possible. Either radiated or conducted RF emissions may cause image distortion or other artifacts in the IVUS display.



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.

Infraredx recommends the use of an uninterruptible power supply in any facility in which voltage dips or interrupts may occur.

The Makoto™ system is intended to be connected via network cable to a protected and secure hospital information system. When a network cable is connected to the Makoto Integrated Intravascular Imaging System™ to transfer data to a hospital information system, then the cable should be a shielded Cat5e or Cat6 ethernet cable (see Section 3.9). Use of a nonconforming cable may result in increased RF emissions or decreased RF immunity.

3.6 Mechanical Precautions



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.

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WARNING

Ensure that cables originating from or connecting to the Makoto Integrated Intravascular Imaging System™ lay flat on the floor.

During normal use of the Makoto Integrated Intravascular Imaging System™ mobile console various cables may be connected to or originating from the system components. Ensure that the cables lay flat on the floor to minimize tripping hazards. Wherever it is possible, avoid laying cables across high foot traffic areas in the room.

The Makoto™ Controller should be placed on a flat surface during the course of the procedure, especially during data acquisition. The Makoto™ Controller should be positioned in the storage cradle of the console when the console is being moved or the controller is not in use.

3.7 Chemical and Fire Precautions



WARNING

This equipment is not intended for use with flammable anesthetics or liquids, or oxygen rich (>25%) environments.

There are no known chemical or fire hazards associated with the Makoto™ Integrated Imaging System.

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3.8 Catheter & Accessory Precautions



WARNING

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.



WARNING

Catheters and 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.



WARNING

DO NOT use the catheter if the inner package is open or damaged.



WARNING

When connected to the Makoto™ Controller, DO NOT stare at the distal tip of the catheter or view directly with optical instruments.



WARNING

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.

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WARNING

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.



WARNING

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.



WARNING

If resistance is met upon withdrawal of the catheter, verify resistance using fluoroscopy, and then remove the entire system simultaneously if appropriate.

The Makoto Integrated Imaging System™ emits near infrared laser radiation from the laser located in the Makoto™ Stationary Console through the Makoto™ Controller and to the connected catheter. Near infrared light is invisible to the human eye. Staring at or focusing near-infrared light through the cornea and onto the retina may cause vision damage.

The Infraredx Makoto Integrated Intravascular Imaging System™ designed for use with the Dualpro™ IVUS+NIRS coronary imaging catheter (REF: TVC-C195-42) and the Infraredx Clarispro™ HD-IVUS peripheral imaging catheter (REF: TVC-E195-42) with Extended Bandwidth™, single use, disposable catheters.

NOTE: The Infraredx Clarispro™ HD-IVUS Catheter is approved only in select markets.

Prior to use, carefully examine all equipment to be used during the procedure to ensure proper performance. The catheter has been inspected and sterilized using Ethylene Oxide (EtO) gas prior to shipment. Prior to use, inspect the catheter and its packaging for damage or breach of the sterile packaging seal(s).

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Store packaged catheters in a cool, dry place.



DO NOT kink or sharply bend (>45 degrees) the catheter at any time. This can result in drive cable failure.

3.9 Compliance with Safety Standards



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™ was designed to conform to all applicable standards (IEC, ANSI, ISO, UL, etc.) for the safe use of lasers, ultrasound and electrical equipment in healthcare facilities.

The following accessories have been tested to be compatible with the Makoto Integrated Imaging System™: DVI-D cable (PN2665), shielded Cat5e cable (PN2690), Cat6 Cable (PN6485), Optical Extension Fiber (PN0370), Detachable DVI Module (PN6497), and Medical Grade Power Supply (PN0407). Contact your sales representative to order.

Specific standards include, but are not limited to, the following:

Standard	Description
IEC 60601-1 ANSI/AAMI ES60601-1 Canada: CAN/CSA 22.2 No. 60601-1 KS C IEC 60601-1	Medical electrical equipment -- Part 1: General requirements for safety and essential performance

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Standard	Description
IEC 60601-1-2	Medical electrical equipment -- Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests
IEC 60601-1-6 CAN/CSA 22.2 No. 60601-1-6	Medical electrical equipment – Part 1-6: General requirements for basic safety and essential performance –Collateral standard: Usability
IEC 60601-2-37 CAN/CSA 22.2 No. 60601-2-37 KS C IEC 60601-2-37	Medical electrical equipment -- Part 2-37: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment
IEC 60825-1 CFR Title 21 part 1040.10 and 1040.11	Safety of laser products – Part 1: Equipment classification and requirements
IEC 62304 CAN/CSA-CEI/IEC 62304	Medical device software – Software life cycle processes
ISO 10555-1	Intravascular catheters - Sterile and single-use catheters - Part 1: General requirements
ISO 10993	Biological evaluation of medical devices
ISO 11135	Sterilization of health care products – Ethylene Oxide
IEC 62366 CAN/CSA-IEC 62366	Medical devices – Application of usability engineering to medical devices
ISO 15223-1	Medical device – Symbols to be used with medical device labels, labeling and information to be supplied-Part 1: General Requirements.

4 System Description



WARNING

The Makoto Integrated Intravascular Imaging System™ is designed to be used exclusively by trained physicians and catheterization laboratory personnel.

The Makoto Integrated Intravascular Imaging System™ provides catheter based intravascular imaging using both IVUS and NIRS technologies. The system uses both sound and light to characterize intravascular features.

The system consists of six major components:

- *Makoto™ Stationary Console*
- *Makoto™ Workstation*
 - *Integration Interface Module, Mouse, and Cables*
 - *Touch Screen Workstation Monitor*
 - *Keyboard (optional)*
- *Makoto™ Controller*
- *Makoto™ Local Junction Box and Cable*
- *Makoto™ Storage Solution*
- *Catheter*
 - *Dualpro™ IVUS+NIRS Imaging Catheter with Extended Bandwidth™*
(See Catheter Instructions for Use)
 - *Infraredx Clarispro™ HD-IVUS Catheter*
(See Catheter Instructions for Use)

The system has three minor components:

- *Wireless Mouse (optional)*
- *Makoto™ Controller Sterile Barrier* (packaged with catheter)
- *Priming Accessories*
 - *Catheter Priming Accessories* (includes priming syringes, packaged with catheter)

4.1 Makoto™ Stationary Console

The Makoto™ Stationary Console contains many of the major components of the Makoto Integrated Imaging System™.

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The Stationary Console contains a power module that distributes power to the various parts of the system. The console supplies power to the central processing unit (CPU), laser, Makoto™ Controller, and the Integration Interface Module. The Workstation Monitor receives power from a dedicated medical grade power supply.

The Stationary Console contains the CPU for the system. The CPU manages, stores, and renders data recorded with the Makoto™ Controller. It also controls the function of the graphical user interfaces provided to the user. The system contains a data drive that is capable of storing at least 1,000 scans. Data may be exported from the system onto optical discs (DVD or Blu-Ray), USB drive, or to a network location via Ethernet cable.

The system may be configured to send data to PACS networks.



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.

The laser light source for the performance of NIRS is contained within the Stationary Console. This laser is controlled by the CPU and user interface. The light is delivered by fiber optic cable to the Makoto™ Local Junction Box and to the Controller where the catheter is connected during use. It is this light pathway that permits the system to generate a Chemogram, or probability map of lipid core containing plaques of interest.

The Stationary Console distributes video for display to the users on the workstation display as well as to the compatible x-ray system. There is also an auxiliary video output on the rear of the Stationary Console that will export a color video signal of up to 1920x1080 resolution (16:9 aspect ratio) by way of a shielded DVI-D video cable.

If the Makoto Integrated Imaging System™ is configured for PACS or Modality Worklist, then the network connectors can be found on the rear of the Stationary Console.

The Stationary Console may be positioned up to 30 meters from location of the Workstation and up to 30 meters from the location of the Makoto™ Local Junction Box (LJB). This permits the Stationary Console to be installed in the Control Room, Procedure Room, or some other convenient location, such as a technical room.

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4.2 Makoto™ Workstation

The Workstation consists of an Integration Interface Module, a touch screen display, a mouse input device, and an optional keyboard.

The touch screen display serves as a primary screen and interface device for the non-sterile operator. If necessary, this screen can also serve as a primary display for the sterile operator. The technician display is a 15.6 inch 1920x1080p touch enabled monitor.

The mouse is provided as a secondary precision input device for the system.

Both the touch screen display and the mouse connect directly to the Integration Interface Module. The Integration Interface Module contains the power button for the entire system. The Integration Interface Module also contains a read/write optical disc drive (DVD-R, Blu-Ray) as well as user accessible USB ports. The user may output data or import data via these devices.

The Makoto™ Workstation can be located up to 30 meters away from the Stationary Console. This allows the Workstation to be positioned in the Control Room or the Procedure Room for convenient operation and interaction.



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.

4.3 Makoto™ Local Junction Box

The Makoto™ Local Junction Box (LJB) provides a connection point for the Controller near its point of installation. In most circumstances the Controller will be installed near the point of use of the catheter. The LJB may be installed up to 30 meters from the Stationary Console.

The Stationary Console provides power, light, and data to the Controller via the LJB. The Controller returns data to the Stationary Console by way of the connection at the LJB.

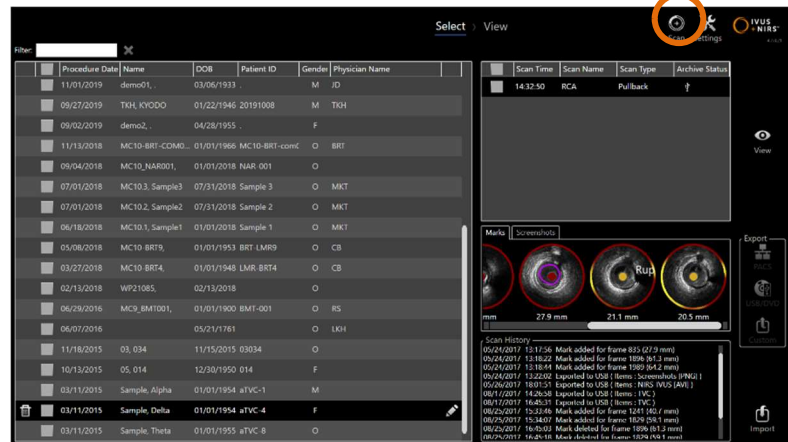
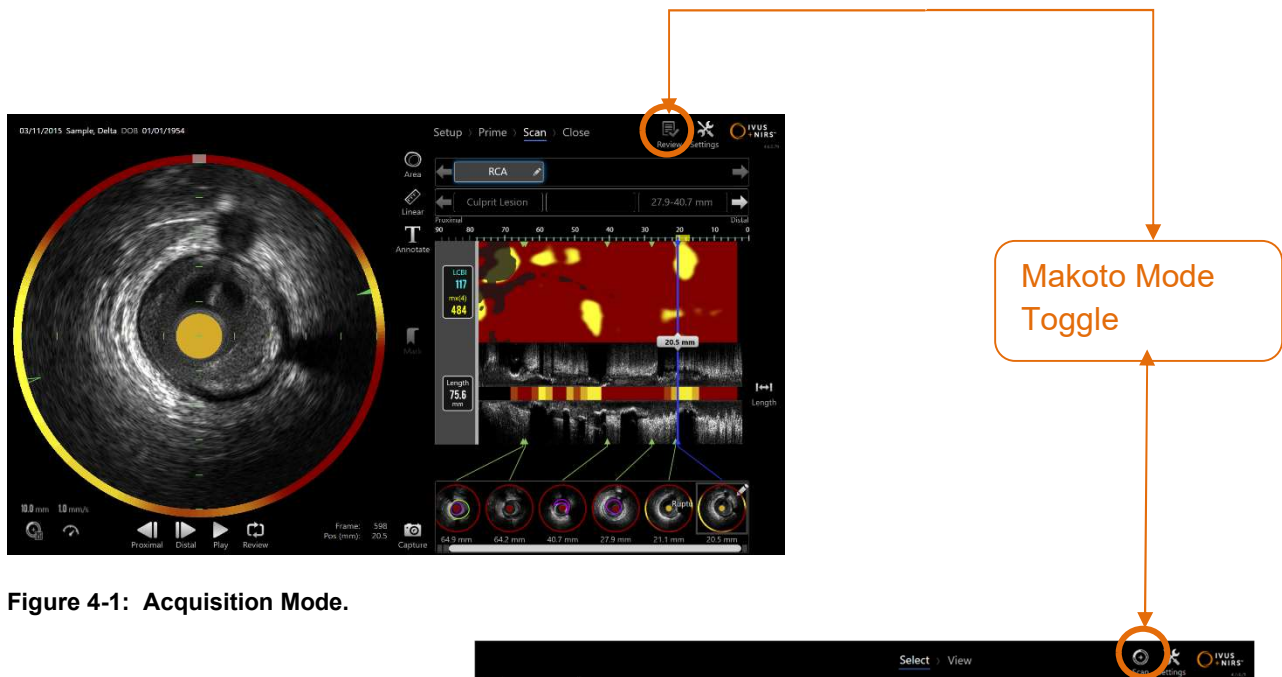
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4.4 Makoto™ Storage Solution

The Makoto Integrated Imaging System™ includes a storage location or cradle and a cable management system for the Makoto™ Controller.

4.5 Makoto Integrated Intravascular Imaging System™ Graphical User Interface

The Makoto Integrated Intravascular Imaging System™ functions are controlled by way of the software graphical user interfaces: Acquisition Mode and Review Mode.



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4.5.1 Acquisition Mode

The Acquisition Mode is the operational mode in which new data may be recorded by the Makoto Integrated Intravascular Imaging System™. It is comprised of four different phases: “Setup”, “Prime”, “Scan” and “Close”. By utilizing the Progress Strip the operator may move easily and quickly between the phases to match the pace of the procedure.

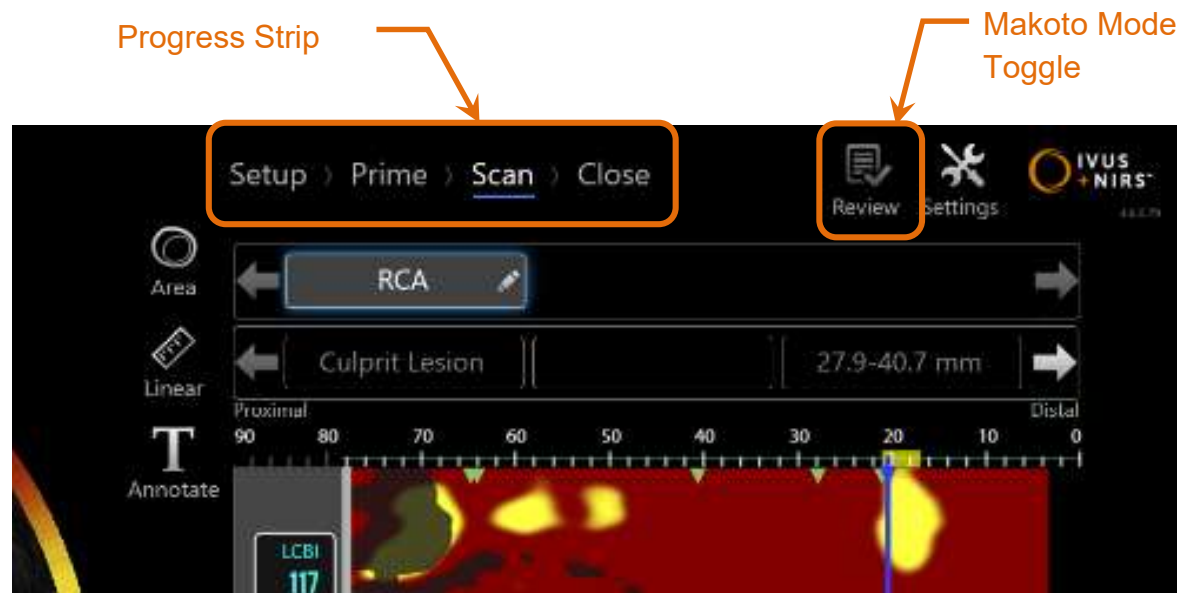


Figure 4-3: Acquisition Mode displayed with focus on the Procedure Progress Strip control to change Phases and the Makoto Mode Toggle control to change modes of operation. The Scan Phase of Acquisition Mode is active and the Makoto Mode toggle to access Review Mode is disabled in the image.

The Progress Strip describes the different stages or phases of data acquisition and also provides a control to change phases. Touch the different phase names to move to the desired phase.

NOTE: Phases in the Acquisition Mode are not order dependent. Any step may be skipped and then returned to if necessary or convenient.



Touch the Makoto™ Mode Toggle control, Review icon, to enter the Review Mode of operation. This can only be done when there is no active procedure in progress. Any active procedures must be closed before transitioning modes.

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4.5.1.1 Setup Phase

Setup Phase allows the operator to enter information about the patient and the procedure to facilitate archiving and later retrieval for review.



Care should be taken when entering patient information to ensure accuracy.

Name	Date of Birth	Gender	Patient ID
Doe, Jane X	10/01/1951	F	8675309
Jones, Casey	11/04/1973	M	0987654321
Smith, Joe J	11/03/1961	M	1234567890

Figure 4-4: Setup Phase of the Acquisition Mode.

NOTE: Scan data may be recorded before the Setup Phase is completed.

Procedure and patient information may be configured manually or by selecting from data already on the system or from the modality workload. Using the semi-automatic completion features can reduce transcription errors and improve accuracy of information entry.

NOTE: Using the semi-automatic completion features can reduce transcription errors and improve accuracy of information entry.

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NOTE: The Setup Phase is not accessible during active scanning.

See Section 7 for more detailed information for procedure setup.
See Section 13.3 for more detailed information on configuration of Modality Worklist connections.

4.5.1.2 Prime Phase



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™.

The Prime Phase provides guidance to the operator on the process of priming a catheter and the connection of the catheter to the Makoto™ Controller.

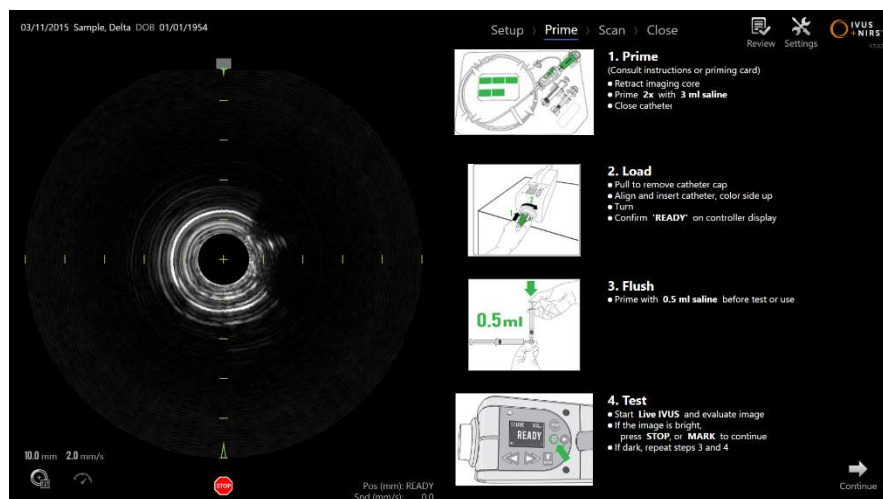



Figure 4-5. Prime Phase of the Acquisition Mode.

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NOTE: Press the **Mark** button on the Makoto™ Controller, , to progress to the next phase.

NOTE: The Prime Phase is not accessible during active scanning.

See Section 8 for more information on catheter connection and the instructions for use packaged with the catheter for more detail on priming.

4.5.1.3 Scan Phase

The Scan Phase of the procedure allows the operator to record IVUS and NIRS scan data during the current procedure. The operator is also able to replay, review, delete, measure, annotate, and change the next pullback rate during the current procedure when active imaging is not underway.

This phase includes many of the displays of complex imaging data including the Chemogram, Block Level Chemogram, Chemogram Halo, Transverse and Longitudinal IVUS images.

The two sets of information, NIRS and IVUS, recorded by the Makoto Integrated Intravascular Imaging System™ are co-registered and can be reviewed using synchronized playback.

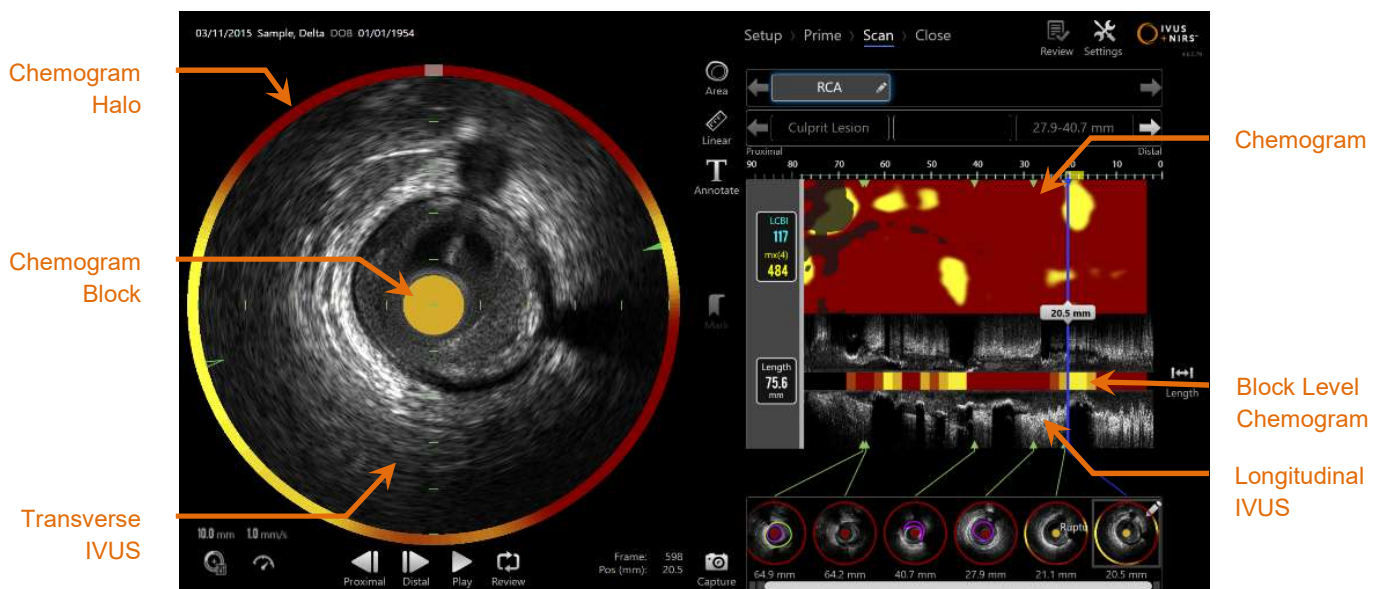


Figure 4-6: Scan Phase of Acquisition Mode with the main displays of image information indicated.

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The Scan Phase also provides access to Annotation and Measurement features that are accessible during an active procedure. Scans may be renamed, annotated, and have individual frames marked for easy retrieval for review. Frame measurements may also be performed.

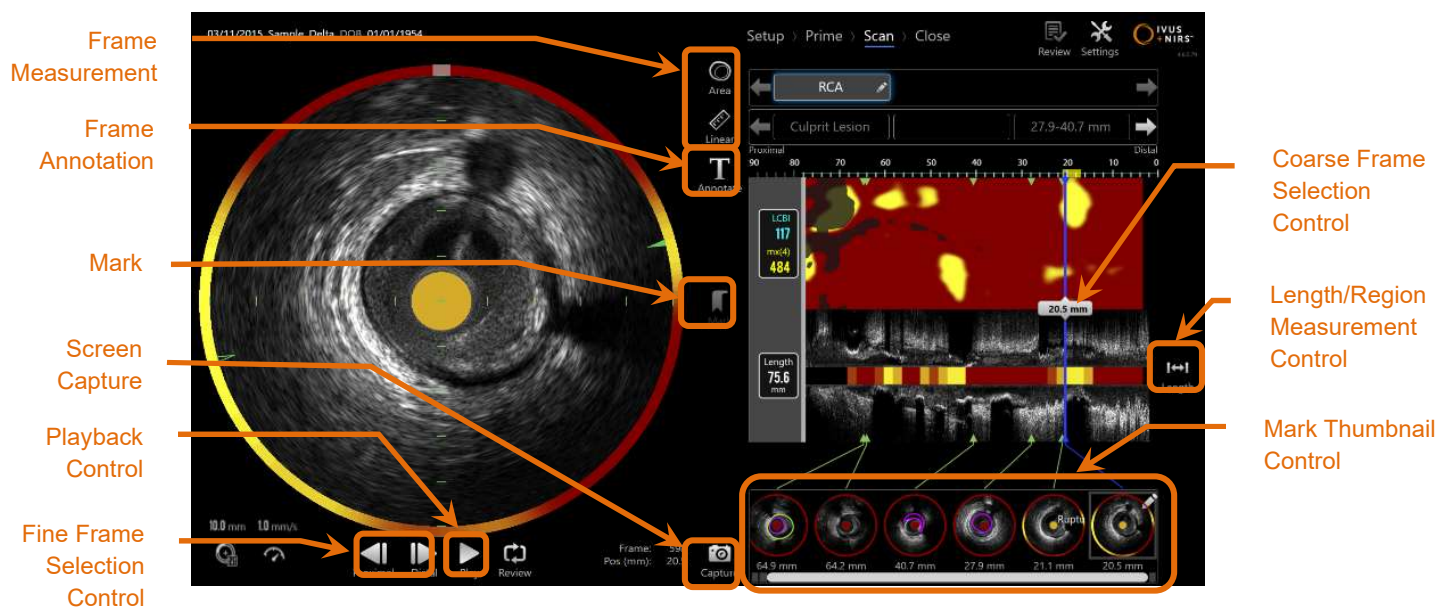


Figure 4-7: Scan Phase of the Acquisition Mode with basic controls indicated.

See Section 9 and 10 for more detailed information on scan acquisition, navigation, and measurement.

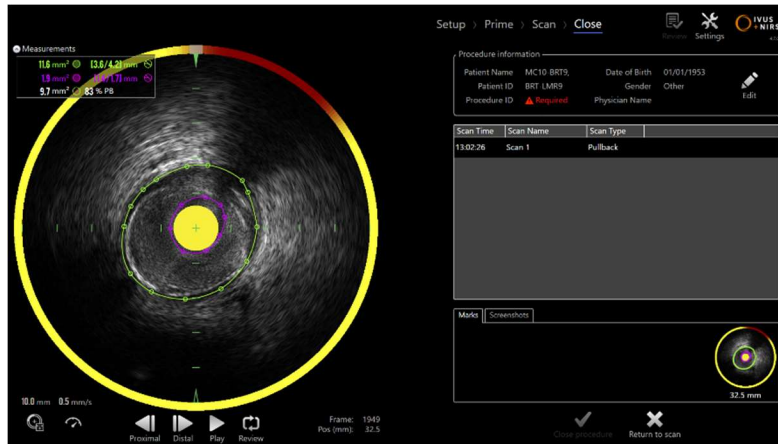
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4.5.1.4 Close Phase

The Close Phase of the procedure allows the operator to review a summary of the data obtained during a procedure prior to archiving on the system.

It is important to complete the Close Phase for every procedure prior to powering off the system.



4-8: Close Phase of the Acquisition Mode.

NOTE: Beginning a new acquisition from the Makoto™ Controller will return the Acquisition Mode back to the Scan Phase automatically.

NOTE: You must enter the minimum required patient and procedure information on the Setup Phase screen to complete the Close Phase.

NOTE: Procedures that were not closed prior to system shut down or power off are accessible by the Review Mode. The procedure may be resumed and can then be Closed and Archived.

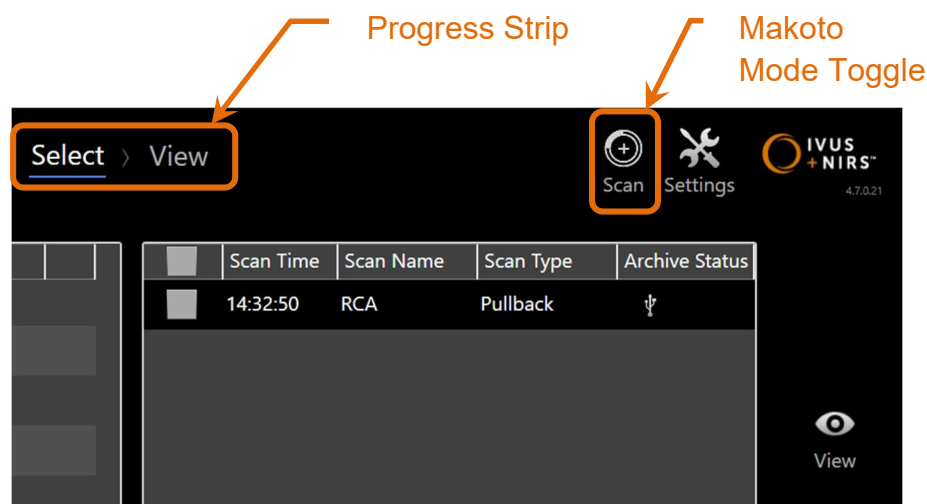
See Section 11 for more detailed information on procedure closure.

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4.5.2 Review Mode

The Review Mode is comprised of two phases. They are the Select and View phases. These phases will allow the user to select a procedure and then to either view or export for later viewing.



4-9: Review Mode with the Progress Strip and Makoto™ Mode Toggle controls highlighted.

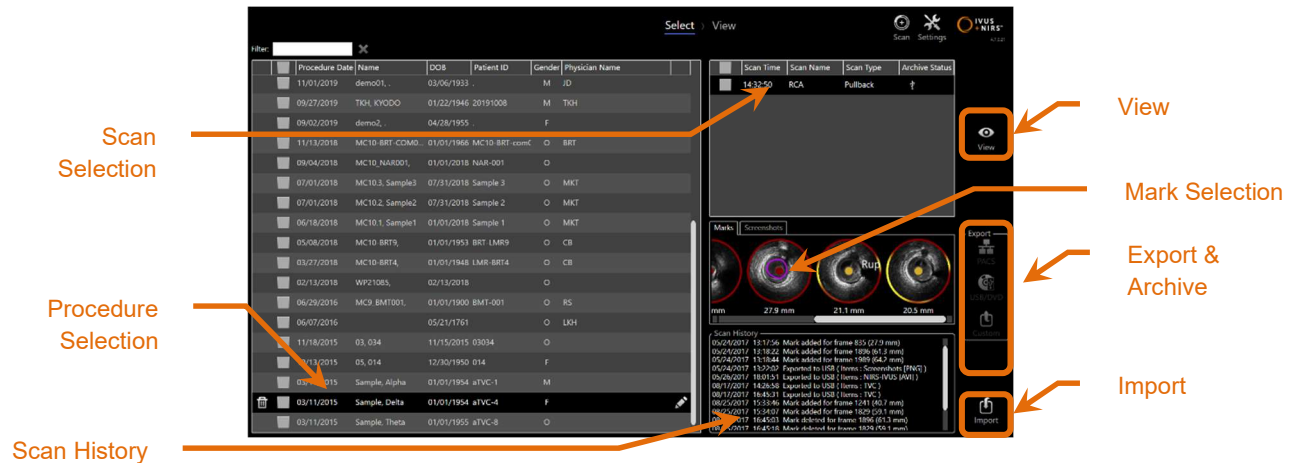


Touch the Makoto™ Mode Toggle control, Scan icon , to enter the Acquisition Mode of operation. This can be done at any time when in the Select Phase of Review Mode.

4.5.2.1 Select Phase

The Select Phase allows the operator to search for and choose previously saved procedures for viewing, editing, deleting, printing, or archiving to other media.

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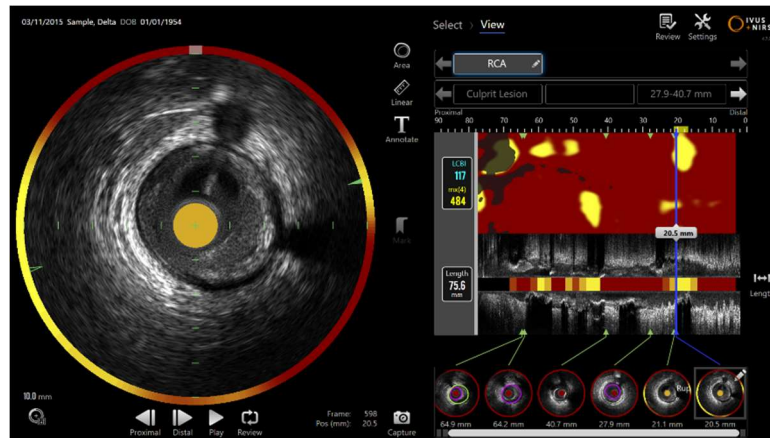
4-10: Select Phase of Review Mode.

During this phase, properly formatted data may be selected from other media to be imported to the Makoto Integrated Intravascular Imaging System™.

See Section 12 for more detailed information on selection, export and import functions.

4.5.2.2 View Phase

The View Phase provides many of the same controls found during the Scan Phase of the Acquisition mode. Data here may be reviewed, analyzed, annotated and deleted using familiar controls as described in Section 10.



4-11: View Phase of Review Mode.

NOTE: Data from one procedure may be viewed at a time.

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Touch the Makoto™ Mode Toggle control, Review icon, to return to the Select Phase of Review Mode.

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4.6 Makoto™ Controller

The Makoto™ Controller (see below) is the interface between the catheter and the Makoto™ Console. The catheter handle is inserted into a socket on the front face of the controller and then turned to complete the physical, optical and electrical connections. These connections allow for the unit to simultaneously actuate the inner imaging core and stabilize the catheter's outer sheath. The pullback mode of the Makoto™ Controller permits automated rotation at approximately 1800 RPM and distal-to-proximal longitudinal motion at a rate of 0.5, 1.0, and 2.0 mm/s. The catheter imaging core can perform a continuous automated pullback in the distal to proximal direction over a total length of 150 mm.

The Makoto™ system is equipped with an RFID receiver that is designed to work with RFID emitters within the compatible catheter handle for identification of catheter model, adjustment of display, and facilitate other user workflows.

4.6.1 Indicators

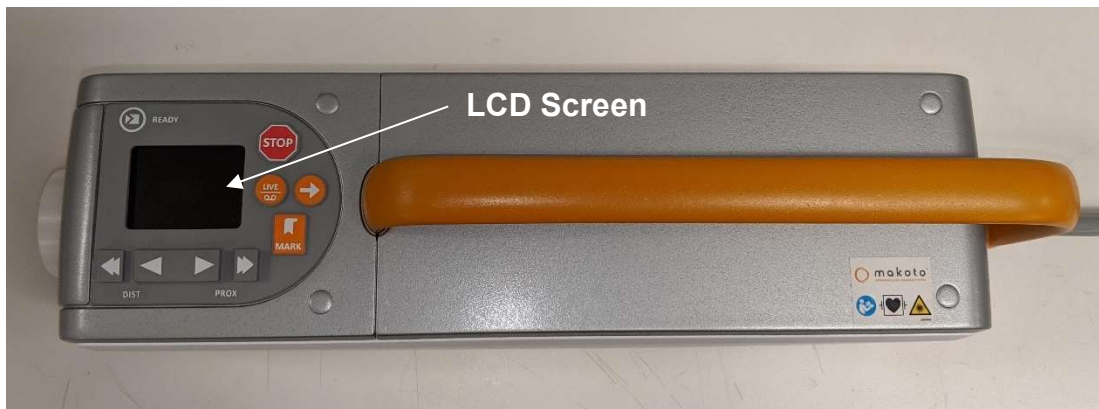


Figure 4-12 Makoto™ Controller.

The Makoto™ Controller is equipped with a LCD screen which will provide status messages and graphics to the user.

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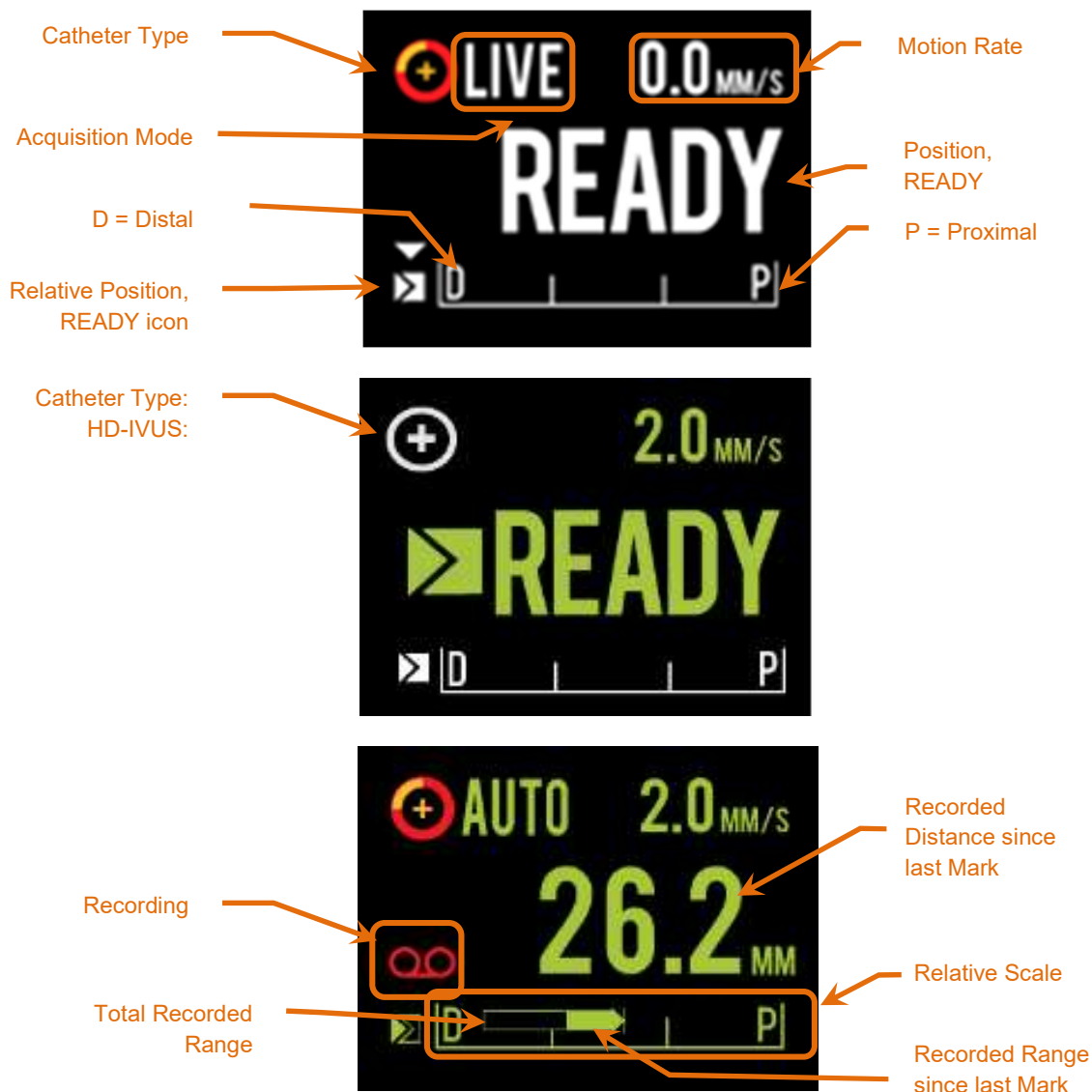


Figure 4-13. Makoto™ Controller LCD screen indicators in Live IVUS acquisition in the READY position with a Dualpro™ IVUS+NIRS catheter(top), idle with a Infradex Clarispro™ HD-IVUS catheter connected at READY position (middle), and during automated pullback acquisition with a Dualpro™ IVUS+NIRS catheter (bottom).

The controller identifies for the user two important positions for operation: READY and 0.0mm position.

READY

This position is the most distal position that the Makoto™ Controller catheter socket can reach. This position indicates the location where the controller is ready for the user to properly LOAD (connect) or unload (disconnect) a catheter, or begin imaging. This is also the position where the transmission window of the connected catheter is most resistant to push-related kinking and is ready to be tracked on a guidewire

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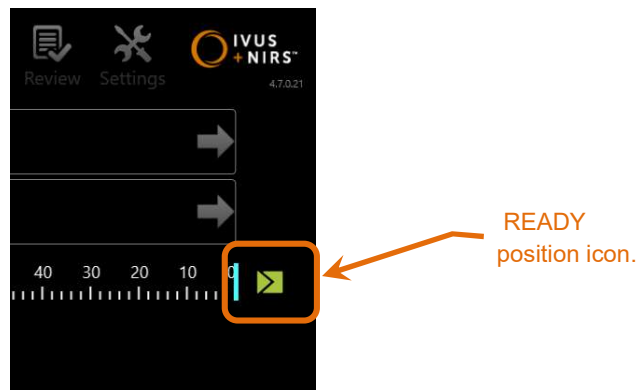




Figure 4-14. When the Makoto™ Controller is in the READY position, the READY icon will appear on the right side of the Makoto™ Console display.

“0.0mm” This position is the start location of continuous uninterrupted imaging during a pullback or translated Live IVUS scan. The “0.0mm” position is approximately 5mm proximal to the READY position. Transverse IVUS images are not available for viewing or recording in the locations between READY and 0.0mm.

As illustrated in Figure 4-13, the LCD screen of the Makoto™ Controller is used to communicate important status information from sensors, modes of operation, and status:

Catheter Type	This symbol,  , will appear to indicate that an IVUS+NIRS catheter has been connected to the controller. This symbol,  , will appear to indicate that an HD-IVUS catheter has been connected to the controller.
Acquisition Mode	This indicator will appear as the text “LIVE”, “AUTO” or blank/none to indicate the current image acquisition mode of the system.
Motion Rate	This indicator will communicate the current speed of translation when image acquisition is occurring. When there is no image acquisition in process the motion rate will communicate the setting of the Next Pullback Rate control (see section 9.2.1)

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- READY** When the display reads “READY” this will indicate that the system is in the READY position or most distal position that can be achieved by the user when operating the Makoto™ Controller.
- Relative Scale** The range of continuous image acquisition, 0.0 - 150.0 mm, is indicated on the controller with demarcation at 50.0 mm and 100.0mm.
- Relative Position** When the Makoto™ Controller is moved proximally from the READY position, the current location of the imaging tip is represented by a vertical line within the Relative Scale.

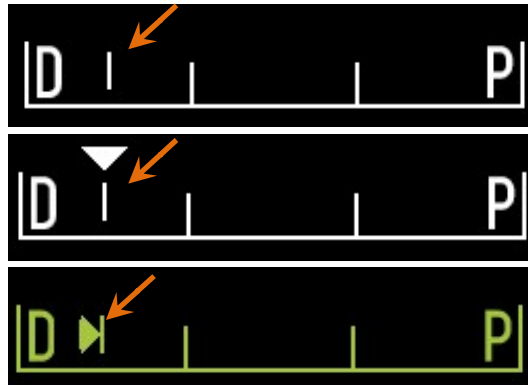


Figure 4-15 Relative Position indicator during no imaging (top), Live IVUS (middle), and Pullback (bottom).

- Position/Distance** In Live IVUS or Pullback imaging the distance displayed is from the start of imaging or most recent Mark location in millimeters. When not imaging, the current position of the imaging tip is displayed.
- Recording** The Recording indicator will appear when the system is recording the images displayed to the operator.
- Recorded Range** The range of recording of the current Live IVUS or Automated Pullback acquisition is represented by a solid rectangle. Translated Live IVUS acquisitions will appear white and Automated Pullback acquisitions will appear green. The solid portion indicates the recorded range since last Mark.

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Figure 4-16. Recorded Range during the current acquisition: Live IVUS with current position the same as the start position (top), Recorded Live IVUS with current position proximal to the last Mark press (middle-top), Automated Pullback with no Marks (middle-bottom), Automated Pullback with solid bar indicating recorded range since last Mark (bottom).

LOAD

This message indicates that the Makoto™ Controller is in the READY position and a catheter may be loaded into the socket.



Figure 4-17 The Makoto™ Controller LCD screen indicating LOAD status.

TURN

This message indicates that the Makoto™ Controller has detected an incomplete catheter handle connection.

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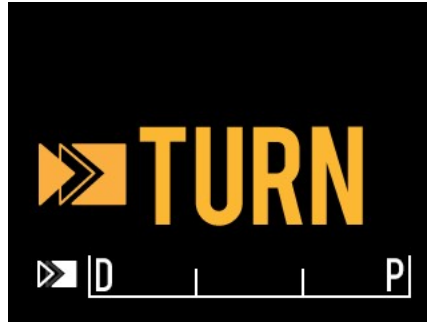


Figure 4-18 The Makoto™ Controller LCD screen indicating a instruction to turn the catheter handle.

WAIT

The Makoto™ Controller is waiting for the Makoto™ Console and software user interface to initialize.



Figure 4-19 The Makoto™ Controller LCD screen indicating a status to wait for the system to complete start up.



WARNING

Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.

SEE DISPLAY

An error or fault condition has been detected by the Makoto™ Controller. This message instructs the operator to consult the Makoto Integrated Intravascular Imaging System™ displays for more detailed instructions.

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Figure 4-20 The Makoto(tm) Controller error message (left) and internal fault (right) messages. In both cases the user should consult the system monitor for instruction on the error or fault and next actions.

NOTE: If the “See Display” message appears repeatedly after following the onscreen cues, then contact your local service provider or Infraredx Customer Service for assistance.

If the Makoto™ Imaging System monitors system interactions for periods of inactivity. If the inactivity time limit and conditions are met then the controller will enter a power save mode. The system will not enter power save mode if a procedure is in progress or if there is a catheter connected to the system. User log in will cause the system to exit power save mode.

NOTE: Users with Administrator permissions may adjust the inactivity time, see section 13.8 System settings.

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4.6.2 Acquisition Controls



WARNING

Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.




WARNING

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.



WARNING

If at any time the **STOP** button, , on the Makoto™ Controller does not halt catheter motion, immediately unplug the Makoto Integrated Intravascular Imaging System™.

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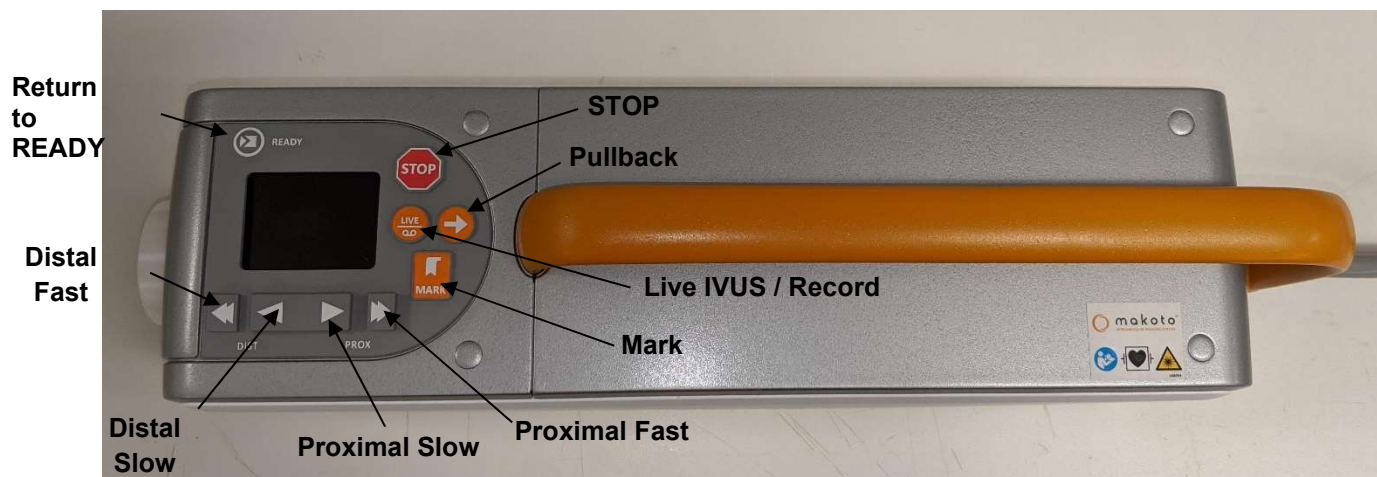
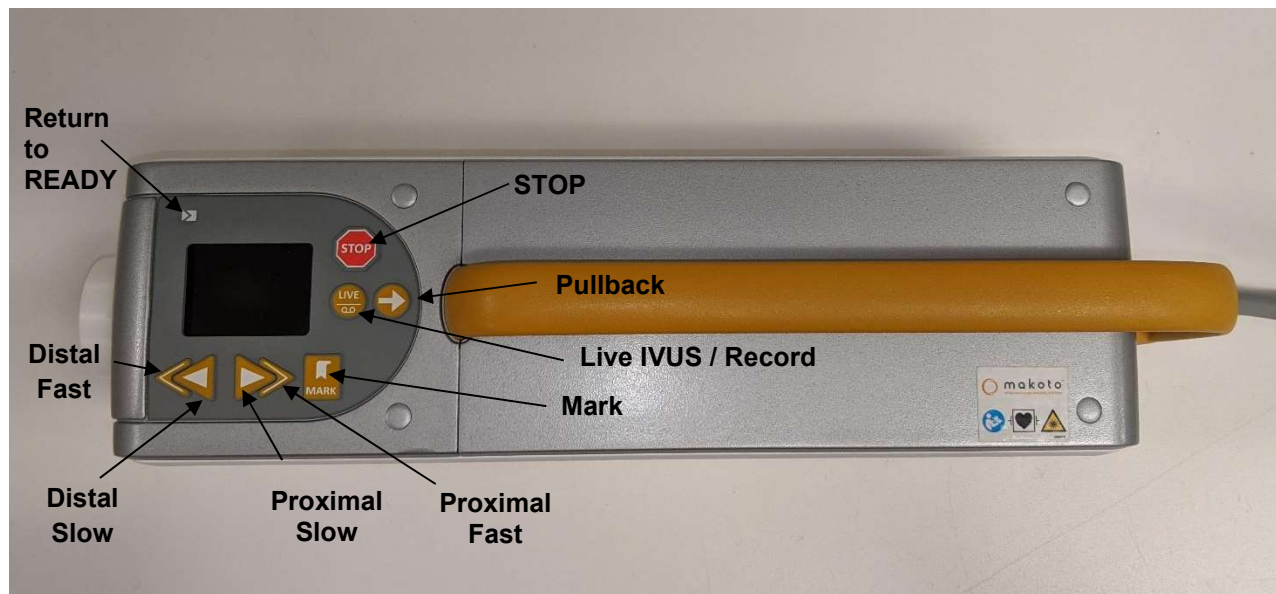


Figure 4-21. Makoto™ Controller with function buttons, two models available (top, bottom).

The Makoto™ Controller is equipped with simple buttons to allow the user to control the motion of the system and data acquisition.

Return to READY

This button will automatically move the catheter imaging core from its current location to the most distal or READY position. This core position is required prior to catheter movement within the patient or catheter connection/disconnection.

STOP

This button will halt the motion of the Makoto™ Controller and stop any data collection in progress.

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Pullback

This button will initiate automated rotation and automated pullback of a connected catheter. The rotation speed is fixed at approximately 1800 rpm, however the pullback speed will correspond to the rate selected on the Makoto™ Console (either 0.5, 1.0, or 2.0 mm/sec).

From READY: A press and release of the Pullback button will move imaging core to the “0.0 mm” position and start Live IVUS to permit a preview of the scan starting imaging location. Press pullback again to start the scan. Pressing and holding the Pullback button in the READY position will skip the preview and begin automated motion and recording. The button can be released when the display indicates that “AUTO” imaging has started.

From position ≥ 0.0 mm: A press and release of the Pullback button will start immediate motion and recording the scan.




The **Pullback** button, , may be pressed while the Makoto™ Controller is stationary or while rotating during a Live IVUS acquisition.

Live IVUS / Record

The first press of this button will initiate automated rotation of the catheter imaging core (without pullback). A live transverse IVUS image will appear on the display of the Makoto™ Console.



Additional presses of the **Live IVUS** button, , will toggle on and off a recording of the Live IVUS acquisition in progress. This will not stop the rotation of the catheter imaging core.

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Mark

This button will bookmark a frame or position within a scan for later reference or review.

During image acquisition, this button will zero the controller display. The distance displayed by the controller will be measured from the location of the most recent Mark press.

During unrecorded Live IVUS, this button will record a single IVUS frame.

During the Prime Phase of acquisition, this button will advance the system to the Scan Phase.

Distal Fast

Pressing and holding this button will move the catheter imaging core distal at a rate of 10 mm/s.

Press and release of this button will move the catheter imaging core in the distal direction a fixed increment of 0.5 mm.

Distal Slow

Pressing and holding this button will move the catheter imaging core distal at a rate of 2 mm/s.

Press and release of this button will move the catheter imaging core in the distal direction a fixed increment of 0.1 mm.

Proximal Slow

Pressing and holding this button will move the catheter imaging core proximal at a rate of 2 mm/s.

Press and release of this button will move the catheter imaging core in the proximal direction a fixed increment of 0.1 mm.

Proximal Fast

Pressing and holding this button will move the catheter imaging core proximal at a rate of 10 mm/s.

Press and release of this button will move the catheter imaging core in the proximal direction a fixed increment of 0.5 mm.

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4.7 Compatible Imaging Catheters

Compatible imaging catheters are packaged separately and are sterilized for single use. Please consult the Instructions for Use packaged with the catheter for more information on the catheter as well as its proper preparation and use.

4.8 Near Infrared Spectroscopy (NIRS)

The Makoto Integrated Intravascular Imaging System™ when combined with the Dualpro™ IVUS+NIRS Imaging Catheter is designed to identify lipid core containing plaques of interest, through blood, in the coronary arteries of a beating heart via a scanning coronary catheter. The system uses near-infrared spectroscopy (NIRS) to identify the chemical composition of the artery wall as an aid to the interventional cardiologist in assessing coronary plaques. The fundamental basis of this imaging capability is the principle of diffuse reflectance spectroscopy, which is well established and used in many scientific disciplines.

In summary, incident NIR light is scattered and absorbed by tissue and the collected light contains information about tissue composition based on its scattering and absorption properties. These absorption and scattering properties are governed by the chemical composition and morphology of the tissue.

4.8.1 Chemogram

After a pullback of the Dualpro™ IVUS+NIRS catheter imaging core through the artery, the system software displays a graphical representation, in the form of a map, indicating the likelihood that a lipid core containing plaque of interest (LCP) is present. This map is called a Chemogram. It provides an image of the artery that indicates the probability of finding a lipid core plaque of interest at a particular location in the scan. High probability is displayed as yellow, and decreasing probability smoothly transitions to red.

4.8.2 Reading the Chemogram Display

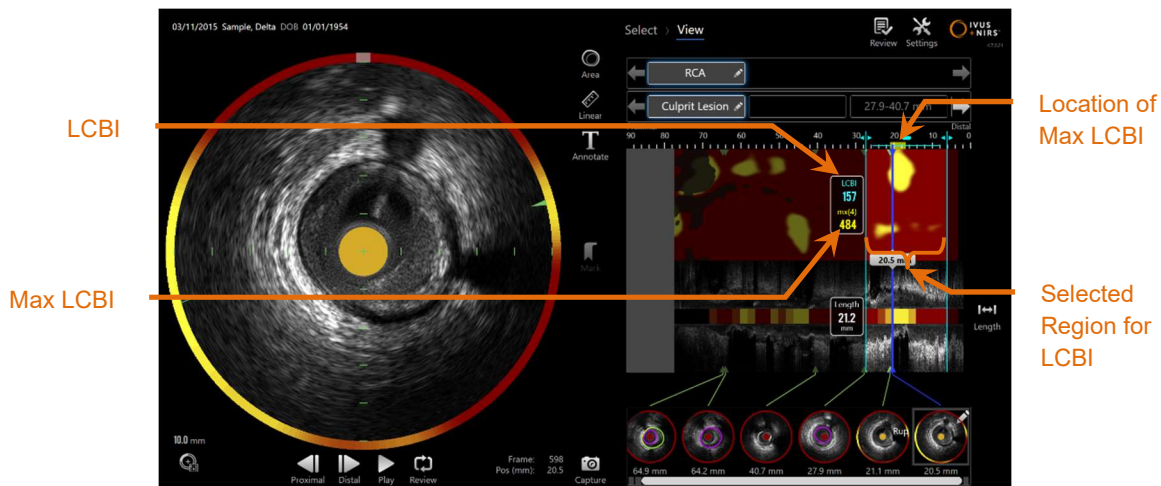
During real-time data acquisition, the Guidewire Detection Map identifies the location of the artifact that an imaged guidewire produces and assists the physician in identifying image artifacts within the spectroscopy data. At the completion of a pullback scan, the Makoto Integrated Intravascular Imaging System™ monitor displays two pseudo-color maps of the artery wall. These maps are the Chemogram and Block Level Chemogram. The Chemogram and Block Level Chemogram indicate areas in the coronary artery that are likely to contain lipid core containing plaques of interest.

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The longitudinal views of the display represent the scan from right to left (distal to proximal). The x-axis indicates the pullback distance in millimeters from the distal end of the catheter transmission window. The y-axis in the Chemogram and the Guidewire Detection Map correspond to the relative angular position of the features of the vessel wall in degrees (the starting angular position in relation to the wall is arbitrary). The portion of the scan inside the guiding catheter may be indicated in solid gray on the proximal ends of the Chemogram and Block Level Chemogram, if the system detects that the scan entered the guiding catheter.

The Chemogram is colored in a scale from red to yellow, low to high probability of lipid. The yellow color is apparent to the user when the probability of lipid exceeds 0.6 at any point in the display. A black semi-transparent masking will appear over the Chemogram in areas where the LCP detection algorithm has determined that there is low signal or other interference.

The system monitor displays the Lipid Core Burden Index (LCBI) results to the left of the Chemogram. The LCBI is a ratio of positive lipid probability scores (>0.6) to total valid lipid probability scores in the selected range of the Chemogram, on a scale of 0 to 1000 (low to high lipid core burden), within a defined segment. In studies (see Section 17.2 Appendix B) with histologically-determined autopsy specimens, the LCBI was shown to correlate with the presence and volume of fibroatheroma in the artery.



4-22: Regional and Maximum LCBI for the selected region are displayed to the left of the Chemogram.

The software will display the maximum LCBI of a fixed length window (4 mm default) within a segment and display the location within the region.

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LCBI	Lipid Core Burden Index computed for each pullback performed with a capable catheter and within a user defined regions of interest.
Max LCBI	Lipid Core Burden Index computed on a specified width within a whole pullback or scan region specified by the user. The maximum value found will be presented to the user.

The Block Level Chemogram, which supplements the Chemogram, is displayed in the center of the longitudinal IVUS view and is dimensionless in the y-direction. The Chemogram Block associated with the currently displayed frame will appear in the center of the transverse IVUS view. The Block Level Chemogram is divided into 2mm wide blocks and summarizes all the valid prediction scores within the corresponding segment of the Chemogram. The Block Level Chemogram is represented in 4 colors from highest to lowest probability: yellow, tan, orange, and red. If the number of pixels within the block on the Chemogram that is impacted by interference or low signal exceeds 25%, then the block color is black.

NOTE: If the percentage of spectra that are too weak to contribute to chemogram generation exceed 12%, then no chemogram will be generated.

4.9 Intravascular Ultrasound

The Makoto Integrated Intravascular Imaging System™ is designed to identify the lumen and vessel wall, through blood, in the vessels of the body, excluding cerebral vessels, via a scanning imaging catheter. The system uses ultrasound to assess luminal and vessel wall boundaries and aids the physician in assessing atherosclerotic plaques. Ultrasound is capable of identifying other characteristics of the artery such as implanted stents and of atherosclerotic plaques such as calcification.

This information is assessed by sending pulses of sound to the vessel wall from the imaging tip of the catheter and receiving the echo. The morphological features of the artery absorb and reflect the sound differently. These signals are then presented on the screen for interpretation.

Utilizing angiography images, assessments of lesion progression can be made by comparing two diameters within the area of interest. Typically these diameters are selected from a reference location and the location with the minimum lumen diameter

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within the target area. The reduction of this diameter is referred to as a diameter stenosis. Use of the angiogram to assess diameters in a single projection can create challenges when assessing lesions or target locations with eccentric lumens. IVUS permits a better assessment of the lumen, including eccentric lumens.

Comparing lumen area can also provide an additional way of assessing the progression of a lesion. The Makoto Integrated Intravascular Imaging System™ will compare two areas at different locations to provide a lumen Area Stenosis (AS).

$$\text{AS\%} = (\text{Area}_{\text{max}} - \text{Area}_{\text{min}}) / \text{Area}_{\text{max}}$$

5 Storing, Moving, and Positioning the Makoto Integrated Imaging System™

5.1 Moving the Makoto Integrated Imaging System™

The Makoto Integrated Imaging System™ is not intended to be moved after installation.



DO NOT reposition the Makoto Integrated Imaging System™ components after installation by a certified technician.

5.2 Positioning the Makoto Integrated Imaging System™ for Use

The Makoto Integrated Imaging System™ is designed for flexible installation of components. The Makoto™ Stationary Console may be installed in the control, procedure, or technical rooms of the catheterization lab. The Makoto™ Workstation may be installed in either the control or procedure rooms. The Makoto™ Local Junction Box must be positioned near the controller point of use, which is typically the catheterization laboratory procedure table.

5.3 Storing the Makoto™ Controller Between Uses



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.

The Makoto™ controller should be stored in its designated location with the umbilical neatly coiled.

6 Starting the Makoto Integrated Intravascular Imaging System

6.1 Powering On

1. Power on the system by pressing and releasing the power button located on front of the Makoto™ Integration Interface Module.

After the system powers on, the log in screen will be presented.




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.

NOTE:

If the Makoto Integrated Intravascular Imaging System™ is powered on and it is not in the READY position, when prompted by the System please use the distal motion controls to advance the imaging core distally until the READY position is achieved.

6.2 Powering Off



If at any time the **STOP** button, , on the Makoto™ Controller does not halt catheter motion, immediately unplug the Makoto Integrated Intravascular Imaging System™.

Press and release the power button located on the front of the Makoto™ Integration Interface Module to power off the 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.

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6.3 User Log In

The Makoto™ Imaging System is configurable to support different user profiles to control accessibility of certain features, settings or patient data.

Review section 13.10 **User Management** for more information about user profiles, permissions, and restrictions.



Figure 6-1. Makoto(tm) Imaging System user log in screen

6.3.1 Standard Log In

When the system is powered on, a valid username and password combination will be requested to record access to the system and set the proper permissions and visibility of data saved on the system.

6.3.2 Skip or Anonymous Log-in

In some cases of an emergent procedure or if users have forgotten their Makoto™ user credentials, it is still possible to operate and obtain data. When a user has logged into the Makoto Integrated Imaging System™ without using a valid username or password features and functions of the system are limited to those that are essential to conduct a procedure.

6.4 User Log Out

The Makoto™ Imaging System supports the ability for users to log out of the active session without powering off the system.

The user may Log Out of the system by touching or clicking the “Options” icon and then selecting “Log Out Username”.

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If the system remains inactive beyond the configured time limit with no catheter then the system will automatically log out if there is no active procedure or catheter connected.

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7 Setup of Patient and Procedure Information

In the Acquisition Mode during the Setup Phase, the user may enter information about both the patient and the procedure to permit archiving and to facilitate retrieval for later review. This information may be entered at the beginning of the procedure or at any time prior to ending the procedure.

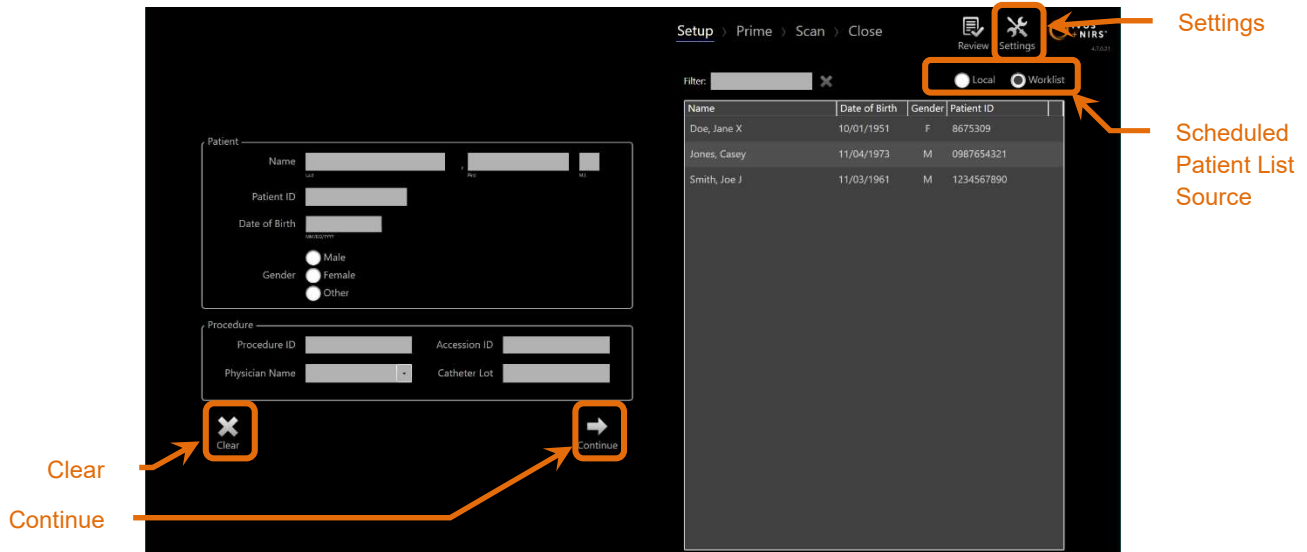


Figure 7-1: Setup Phase of Acquisition Mode with main controls highlighted.

There are four pieces of patient identification elements that can be entered for each procedure. These elements include the Patient Name, ID number, Gender, and Date of Birth (DoB). Data fields that are configured as “required” must be completed to close the procedure for later review and archive.

Patient Name	The name of the patient may be entered in the format of last or family name, first or given name, and middle name initial.
Patient ID	The medical record number or file number for the imaged patient.
Gender	The Makoto Integrated Intravascular Imaging System™ provides three different gender options to help describe the patient.

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Date of Birth The month, day and year of the patient may be specified.

NOTE: Use the “Other” gender option for anonymous patient entry.

There are four additional fields that may be used to further identify the procedure:

Procedure ID	The number or code used to identify this imaging procedure.
Accession ID	This is a procedure identification value often assigned at time of patient registration for the procedure and may be used by PACS to verify transferred data. This value is typically entered automatically when Modality Worklist features are used.
Physician	The name of the attending physician for this imaging procedure.
Catheter Lot	The catheter build lot number used during this imaging procedure.



Ensure correct entry of patient information to avoid mislabeled data or misplacement of procedure data.

NOTE: Required Fields for patient and procedure identification may be configured in Settings, see section 13.

NOTE: Enter the catheter lot number prior to acquiring data to automatically enter the catheter lot number into each scan file when it is recorded.

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7.1 Manual Entry of Patient and Procedure Information

Manual entry of patient and procedural information can be performed using the on-screen software keyboard.



Touch **Clear** to remove the patient and procedure data from the Setup fields and begin again.

NOTE: Information fields may be completed at any time prior to closing the procedure when the system is not actively acquiring image data.

7.2 Semi-Automated Entry of Patient and Procedure Information

Patient data may be directly entered into the fields provided as described above, or to improve consistency of entry for returning or scheduled patients, it is possible to select information from the Local Directory or Scheduled Patient listing (Worklist).

NOTE: Touch the column titles in the Scheduled Patient listing to sort the list in different ways.

NOTE: Type text in the Filter to reduce the list to Names and Patient IDs that match your entry. Either delete the text or press clear to return to the complete list.

NOTE: The local patient list appears by default. Worklist option appears when the system is configured for Modality Worklist connection.

NOTE: Selecting from the list will overwrite corresponding fields in the Patient and Procedure information fields.

7.2.1 Local Patient Listing

The system will automatically load patient information from previously recorded procedures remaining on the system into the Scheduled Patient listing.

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Touch the desired name in the list to complete setup of the Patient Name, Patient ID, Gender, and DoB.

The remaining procedure fields will require manual entry.

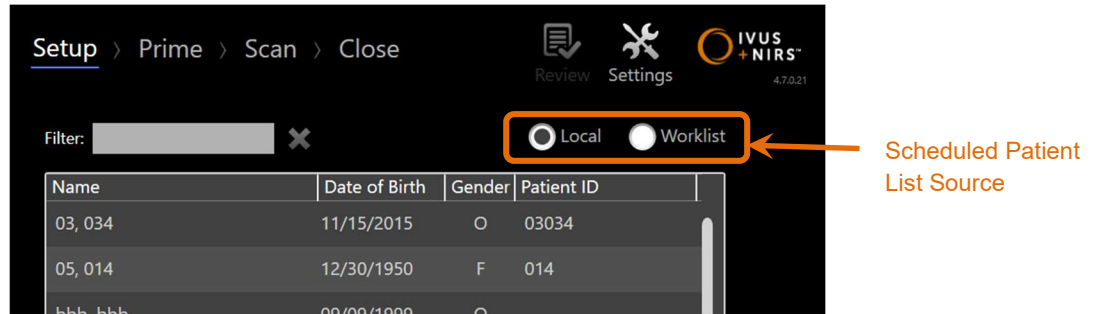


Figure 7-2: Setup Phase with selection control for the source of the scheduled patient listing highlighted.

7.2.2 Modality Worklist

If the system has been configured to load modality worklist information from the hospital information system (HIS), then the Scheduled Patient listing content can be switched from a local patient listing to the modality worklist retrieved from HIS.

See Section 13 to configure the Modality Worklist connection features.

The system will automatically retrieve all patient and procedure details for X-ray angiography, "XA", modality type for the current date and make it available for selection on the system.

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Touch the desired name in the list to complete setup of the Patient Name, Patient ID, Gender, DoB, and procedural information made available by the HIS, such as the Accession ID.

The remaining procedure fields will require manual entry.

NOTE: To refresh the displayed modality worklist entries, switch between the “Local”, , and “Worklist”, , options.


7.3 Clearing Patient and Procedure Information

To clear all patient and procedure information and start again, touch **Clear** .


This action will not delete any recorded scan data in the active procedure.

7.4 Proceeding to the Next Phase

Once the patient and procedure data have been entered, to move to the Prime Phase of


the Acquisition Mode, touch **Continue** .

NOTE: Use the Progress Strip control to change phases; press the desired Phase to skip phases of the procedure.

NOTE: With a catheter connected, pressing **Live IVUS** button, , on the Makoto™ Controller will immediately progress to the Prime Phase.

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NOTE:

With a catheter connected, pressing **Pullback** button, , on the Makoto™ Controller will immediately progress to the Scan Phase.

8 Priming the Catheter & Preparing the Makoto™ Controller for Use

The next phase of the procedure begins with priming the imaging catheter. In parallel, the Makoto™ Controller may be placed into the sterile field for use. The preparation for imaging concludes with connecting the imaging catheter to the controller and evaluating the catheter preparation.

8.1 Priming the Catheter



The sterile catheter must be primed and prepared in accordance with the instructions for use document that is included inside the catheter package.

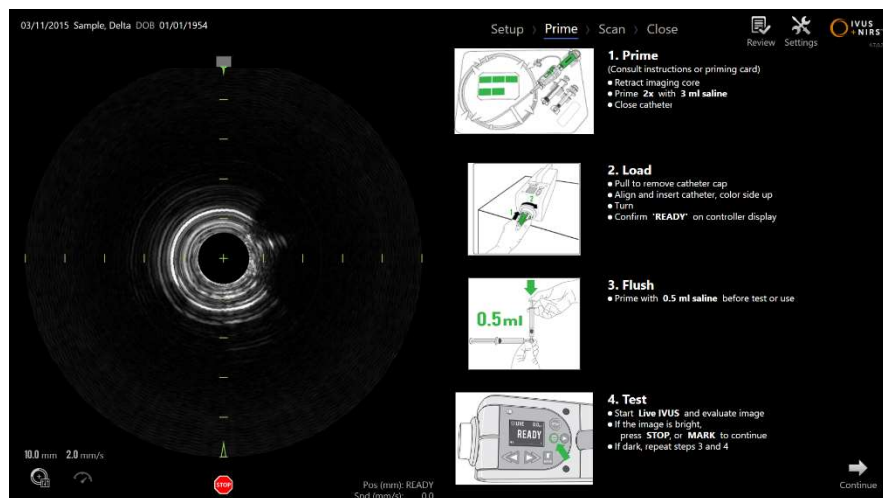


Figure 8-1. Onscreen priming guidance provided in the Prime Phase of Acquisition Mode.

The Makoto Integrated Intravascular Imaging System™ will provide onscreen guidance on the main steps for priming a catheter that is attached to the Makoto™ Controller.

These steps are intended to illustrate and augment the instructions included with the catheter and does not replace the need for the user to be trained, and to read and understand the Instructions for Use packaged with the catheter.

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Using the on screen illustrations, graphical guidance provided with the catheter, and the written catheter Instructions for Use, the sterile operator must prime the catheter.

8.2 Preparing the Makoto™ Controller

The Makoto™ Controller must be placed into a Makoto™ Controller Sterile Barrier before it is placed on the procedure table.

Please note that the following instructions require the participation of a sterile operator and a non-sterile operator to apply the sterile barrier and place the Makoto™ Controller into the operating field:



WARNING

If the Makoto™ Controller Sterile Barrier is damaged at any time, immediately replace with a new sterile barrier.



WARNING

Keep the sterile operator's hand outside of the blue cover on the sterile barrier.



WARNING

Position the Makoto™ Controller in a stable location on the procedure table. DO NOT place the controller near the edges of the table.



WARNING

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.



WARNING

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.

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WARNING

DO NOT allow sterile items to contact Makoto™ Controller through the catheter socket opening of the Makoto™ Controller Sterile Barrier.



WARNING

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.

To position the Makoto™ Controller within the sterile field, perform the following steps:

1. The non-sterile operator removes the sterile barrier from the catheter box.
2. The non-sterile operator opens the package containing the Makoto™ Controller Sterile Barrier.
3. The sterile operator removes the Makoto™ Controller Sterile Barrier from the packaging, and unfolds the two short folds on the barrier revealing the white gasket with the blue plastic cover.
4. The non-sterile operator removes the Makoto™ Controller from the storage cradle, which is outside the sterile field.
5. The non-sterile operator holds the Makoto™ Controller parallel to the floor in the air near the sterile field while holding the handle at the rear of the controller.
6. The sterile operator inserts their right hand into the Makoto™ Controller Sterile Barrier fold indicated with a hand and an arrow. The barrier should be oriented so that the blue cover for the socket is aligned with the top of the Makoto™ Controller.

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7. The left hand is inserted into the fold on the other side of the Makoto™ Controller Sterile Barrier also indicated by a hand and an arrow.
8. The sterile operator holds the Makoto™ Controller Sterile Barrier open.
9. The non-sterile operator transfers the Makoto™ Controller to the sterile operator by placing the controller into the open Makoto™ Controller Sterile Barrier.
10. The sterile operator grasps the Makoto™ Controller through the Makoto™ Controller Sterile Barrier by the handle on the top of the controller, supporting the full weight.
11. The non-sterile operator then releases the controller and then grips the edges of the Makoto™ Controller Sterile Barrier opening indicated by arrows and pulls the barrier to cover the umbilical cable of the Makoto™ Controller.
12. The sterile operator places the enclosed Makoto™ Controller on the procedure table.
13. The sterile operator aligns the white gasket of the Makoto™ Controller Sterile Barrier with the socket of the Makoto™ Controller and secures the barrier gasket to the socket.
14. The non-sterile operator should secure the position of the umbilical to prevent the bagged portion from leaving the sterile procedure area during use.

The Makoto™ Controller is now ready for catheter connection.

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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.

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8.3 Connecting the Catheter



WARNING

The sterile catheter must be handled and prepared in accordance with the instructions for use document that is included in the catheter package.



WARNING

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 catheter instructions included in this manual are for general guidance only. Always follow the Instructions for Use documentation packaged with each Infraredx catheter.

The catheter must be connected to the Makoto™ Controller by a sterile operator.



CAUTION

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.



CAUTION

Do not contaminate the fiber faces of the catheter or Makoto™ Controller socket during the connection process.

1. Confirm that the white gasket of the sterile Makoto™ Controller barrier is secured to the Makoto™ Controller socket.
2. Remove the blue covering from the sterile Makoto™ Controller barrier along the perforated lines and discard out of the sterile field.
3. Confirm that the Makoto™ Controller is in the READY position as indicated by the "LOAD" message on the LCD screen located on the top of the controller.

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4. Align the catheter handle with the colored side facing up.
5. Insert the catheter handle into the Makoto™ Controller catheter socket.
6. Turn the catheter handle clockwise until the controller LCD screen indicates that the catheter is fully connected by observing the “READY” message.

NOTE: If the Makoto™ Controller identifies a partial catheter connection, then instruction will be indicated on the LCD screen or “See Display” will be indicated on the controller LCD screen and additional detailed instruction will be provided on the Makoto™ System display.

8.4 Testing the Catheter

After priming the catheter as directed by the instructions packaged with the catheter and connecting it to the Makoto™ Controller, the catheter performance can be verified by using the “Live IVUS” function on the system.

Prime the attached catheter with an additional 0.5mL of saline and press “**Live IVUS**”,




, on the Makoto™ Controller to begin imaging. If an IVUS image appears as concentric circles and the image brightness is acceptable then either touch “**STOP**”,




, on the screen or press “**STOP**”,  , on the Makoto™ Controller.


NOTE: If the image is not acceptable or is dark, continue to flush the catheter using the priming syringe.

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Proceed to the Scan Phase by touching “Scan”, , in the Progress Strip control at the top of the screen.

NOTE: Assessment of the quality of the catheter prime can be performed on either the “Prime” or “Scan” Phase screens.

NOTE: While the catheter is rotating and image is updating, press **Mark** button, , on the Makoto™ Controller to advance to the Scan Phase.

NOTE: Press Pullback button, , on the Makoto™ Controller to advance the system to the Scan Phase and begin an automated pullback acquisition.

9 Acquiring Makoto™ Intravascular Scan Images



WARNING

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.

After assessing the quality of the catheter prime, the catheter should be positioned onto the guidewire and advanced as directed by the catheter Instructions for Use.

There are two types of data acquisition that may be performed using the Makoto Integrated Intravascular Imaging System™: Live IVUS and Automated Pullback acquisitions.

A Live IVUS acquisition will generate IVUS images without a Chemogram. An Automated Pullback will generate IVUS images with a Chemogram.

9.1 Live IVUS Acquisition

During a Live IVUS data acquisition the system will start rotation of the catheter imaging core without starting automated pullback (proximal translation) of the imaging core. A transverse IVUS image will appear on screen and will be updated while Live IVUS is enabled.

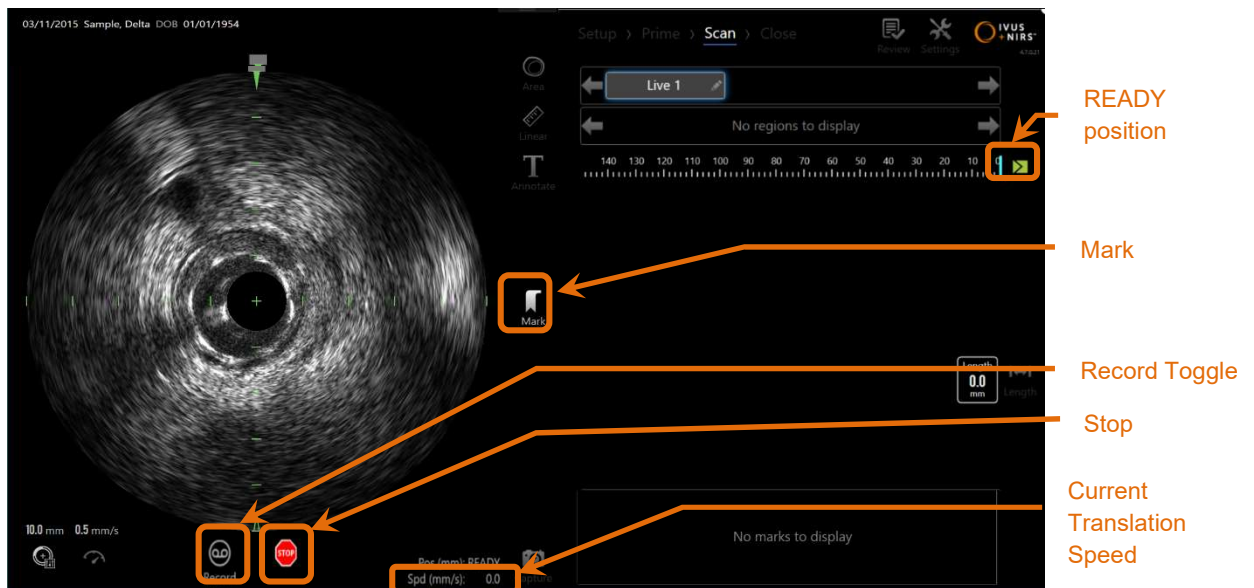


Figure 9-1: Makoto™ Acquisition Mode during an unrecorded Live IVUS scan.

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NOTE: A Live IVUS scan will not be saved to system memory unless the user chooses to record the scan.

NOTE: Live IVUS will produce an IVUS image only; no NIRS data will be displayed or Chemogram generated.

NOTE: Live IVUS will produce a live transverse IVUS image. The IVUS image will also be displayed in the Longitudinal IVUS display area during a recorded Live IVUS scan.

9.1.1 Starting Live IVUS


Press the **Live IVUS** button, , on the Makoto™ Controller to enable real time IVUS imaging. The imaging mode status on the LCD screen will update to show “LIVE” and the position information is printed using white text.



Figure 9-2. Makoto™ Controller with Dualpro IVUS+NIRS catheter connected showing Live IVUS acquisition that is not recorded at the READY position (left) and 0.0 mm position (right).

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9.1.2 Translating Live IVUS



WARNING

Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.




WARNING

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.

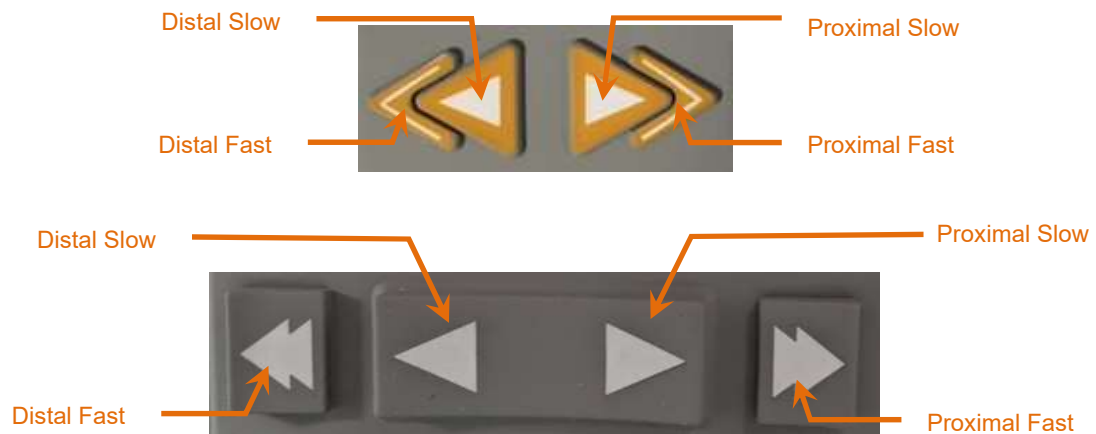


Figure 9-3: Imaging Core Translation Controls, different configurations (top, bottom) may be available.

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While performing a Live IVUS scan, use the distal and proximal motion controls on the Makoto™ Controller to adjust the position of the current image within the vessel.

Pressing and holding the slow motion controls will translate in the desired direction at a rate of 2.0 mm/s. Pressing and releasing will translate in the desired direction a fixed distance of 0.1 mm.

Pressing and holding the fast motion controls will translate in the desired direction at a rate of 10.0 mm/s. Pressing and releasing will translate in the desired direction a fixed distance of 0.5 mm.

NOTE: While actively imaging in the READY position, translation in the proximal direction will result in the image core position moving into the continuous imaging range of 0 mm to 150 mm.

Returning to the READY position can only occur when the system is not acquiring images.


NOTE: While actively imaging, proximal AND distal translation will occur only within the range of 0mm to 150 mm. Translation will stop automatically when these extreme positions are achieved and imaging will continue.

NOTE: While at the 0 mm position and not imaging, pressing either of the distal position controls,  or , will return the controller and catheter imaging core to the READY position.

9.1.3 Recording a Live IVUS Frame

While performing an unrecorded Live IVUS scan, a single frame may be saved to document the procedure. This frame may be saved, reviewed, measured, or discarded.

During a Live IVUS scan, press the **Mark** button on the Makoto™ Controller, ,

or touch the **Mark** control, , on the Makoto™ System display to bookmark the frame. This frame will be recorded as a single frame scan.



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

9.1.4 Recording a Live IVUS Scan

A series of Live IVUS frames may be recorded in a single scan file.



Figure 9-4: Makoto™ Acquisition Mode during a recorded Live IVUS scan.

Press the **Live IVUS** button on the Makoto™ Controller, , or touch **Record**, , on the Makoto™ System display near the transverse IVUS image to enable recording.

Press the **Live IVUS** button on the Makoto™ Controller, , or touch **Record**, , again on the Makoto™ System display to stop the recording of data only. The catheter will continue to rotate and the transverse IVUS image will continue to update.

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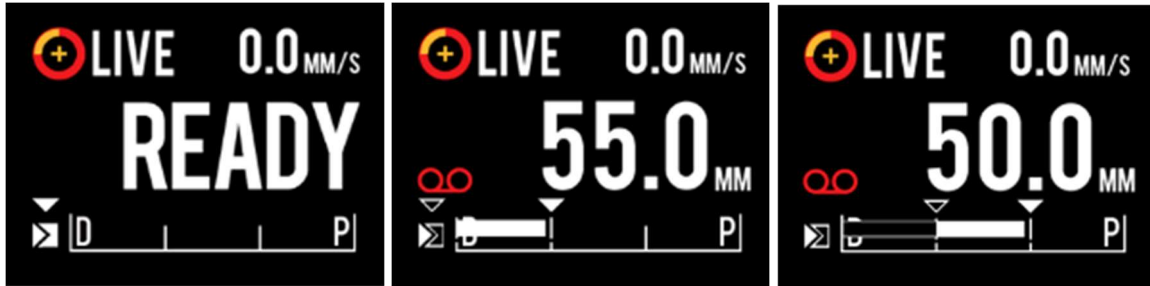



Figure 9-5. Makoto™ Controller LCD screen with a Dualpro IVUS+NIRS Imaging Catheter connected during the process of transitioning from the start of unrecorded Live IVUS at READY (left) to recording then translation proximal and stationary Live IVUS (middle) to zeroing and translating proximal while recording (right). Note the appearance of the recording icon during recorded Live IVUS. When translation is performed during recorded Live IVUS a solid bar appears where the recording in this acquisition was already performed since the last Mark (middle and right) and recording prior to the most recent mark is an empty bar (right).

During translation of Live IVUS, the relative position, actual position, and translation speed indicators will update.


NOTE:

Press either the **STOP** button on the Makoto™ Controller,



or touch **STOP**  on the Makoto™ System display to halt catheter rotation and motion AND terminate the recording.

NOTE:

Press the **Pullback** button on the Makoto™ Controller, , to terminate the current Live IVUS recording and begin a new Automated Pullback scan at the current pullback rate setting. Automated Pullback scans are always recorded.

NOTE:

Marks may be made in the scan file and transverse IVUS measurements may be made on the frames of a recorded Live IVUS scan to further document the procedure.

9.1.5 Marking and “Zeroing” during Live IVUS

During recorded Live IVUS acquisition, Marks can be placed and reviewed later by pressing the Mark button on the controller or touching the Mark icon on the screen.

During unrecorded Live IVUS acquisition, Marks can be placed and reviewed later as single frame recordings by pressing the Mark button on the controller or touching the Mark icon on the screen.

Adding a Mark during any Live IVUS acquisition will reset the display of distance traveled back to 0.0mm.

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9.1.6 Stopping Live IVUS

A Live IVUS scan may be discontinued in two ways:

- a. Press the **STOP** button, , on the Makoto™ Controller or touch **STOP**, , on the user interface to halt Makoto™ Controller motion, cease updates of the transverse IVUS image, and end the recording any Live IVUS scan in progress.

Or,

- b. Press **Pullback**, , to complete the Live IVUS scan and immediately begin an automated pullback acquisition.

NOTE: After stopping the Live IVUS, the Makoto™ Controller panel will display the distance traveled since the last press of the Mark button. This will remain on the panel until Live IVUS, Pullback, Return to READY, or a translate button is pressed.

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9.2 Automated Pullback Acquisition

An automated pullback acquisition will start rotation and pullback of the Makoto™ Controller and catheter imaging core. This action will also start the collection and recording of both IVUS and NIRS data when used with a Dualpro™ IVUS+NIRS catheter or just IVUS data when used with a Infraredx Clarispro™ HD-IVUS catheter at the pullback rate set by the user.

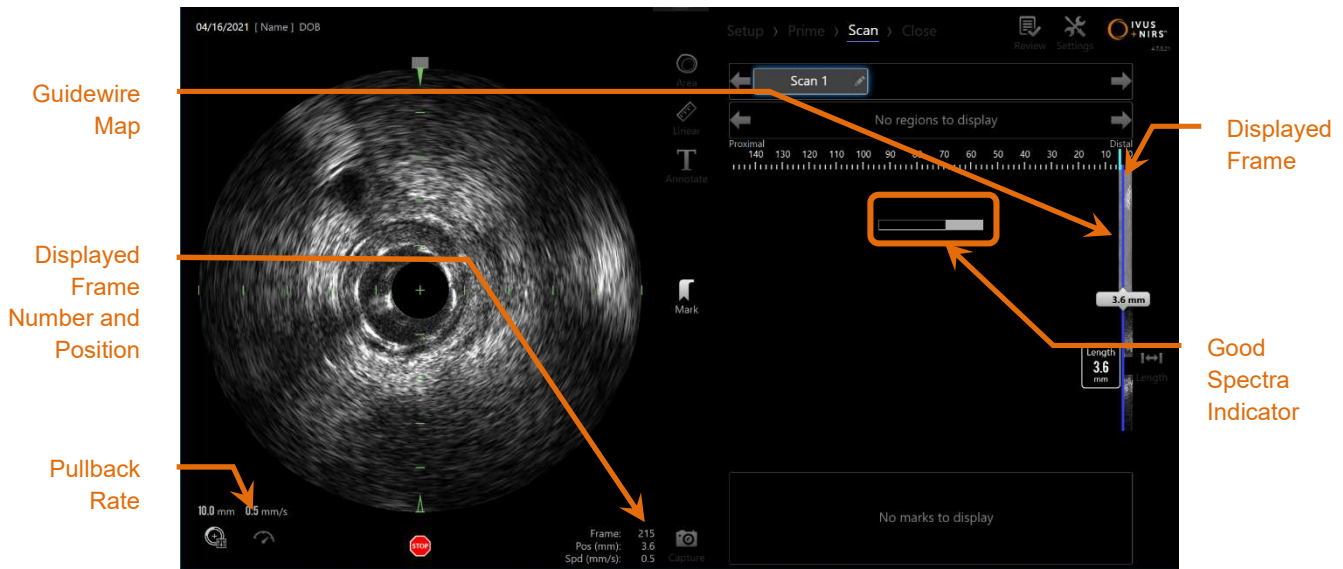


Figure 9-6: Acquisition Mode with automated pullback acquisition in progress.

9.2.1 Setting the Next Automated Pullback Rate

The rate of translation for an automated pullback must be configured by the user prior to starting any imaging.

Set the desired pullback translation rate by touching the Pullback Rate control,



and selecting the desired speed from the options available:

0.5 mm/s


1.0 mm/s

2.0 mm/s

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9.2.2 Starting Automated Pullback

Press the **Pullback** button, , on the Makoto™ Controller to begin an automated pullback acquisition. During a pullback, Transverse IVUS, Longitudinal IVUS, Guide Wire Detection Map, and Good Spectra Indicator are updated real-time.

9.2.2.1 Automated Pullback Acquisition with Preview

When starting an Automated Pullback Acquisition from the READY position using the

Pullback button, , the system will first move to the “0.0mm” position and begin Live IVUS acquisition. This permits an intravascular preview of the pullback starting

location. After previewing, press the **Pullback** button, , again to proceed with the acquisition.

9.2.2.2 Good Spectra Indicator

At the start of an Automated Pullback scan, the Makoto Integrated Intravascular Imaging System™ will monitor the quality of the light spectrum recorded. The system requires a minimum number of spectra to generate a Chemogram. As good spectra are recorded the Good Spectra Indicator will fill. When the minimum number has been reached, it will disappear.

NOTE: When the Makoto™ System collects enough data necessary for the system to create a Chemogram, the Good Spectra Indicator will disappear from the screen.

NOTE: Approximately 12 mm of pullback scan data, minimum, must be recorded to have enough data to generate a Chemogram.

NOTE: Even if the Good Spectra indicator fills due to the initial collection of good quality spectra, if the percentage of spectra that are too weak to contribute to chemogram generation exceed 12%, then no chemogram will be generated.

NOTE: Good Spectra indicator will be presented only when automated pullbacks with NIRS capable catheters are performed.

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9.2.3 Stopping Automatic Pullback



WARNING

Imaging within the guiding catheter should be minimized for optimum chemogram results.

Once the desired pullback distance has been reached or the desired amount of data has been recorded, the Makoto Integrated Intravascular Imaging System™ may be halted in two ways:

- a. Press the **STOP** button, , on the Makoto™ Controller;


Or

- b. Touch **STOP**, , on the Makoto™ Console user interface.

Either of these actions will halt both the Makoto™ Controller motion and stop data acquisition.



CAUTION

In case of emergency use the **STOP** button, , on the Makoto™ Controller.

NOTE: The Makoto™ Controller automatically stops the pullback if the most proximal point is reached (position 150.0 mm).

NOTE: After stopping the pullback, the Makoto™ Controller panel will display the distance traveled since the last press of the Mark button. This will remain on the panel until Live IVUS, Pullback, Return to READY, or a translate button is pressed.

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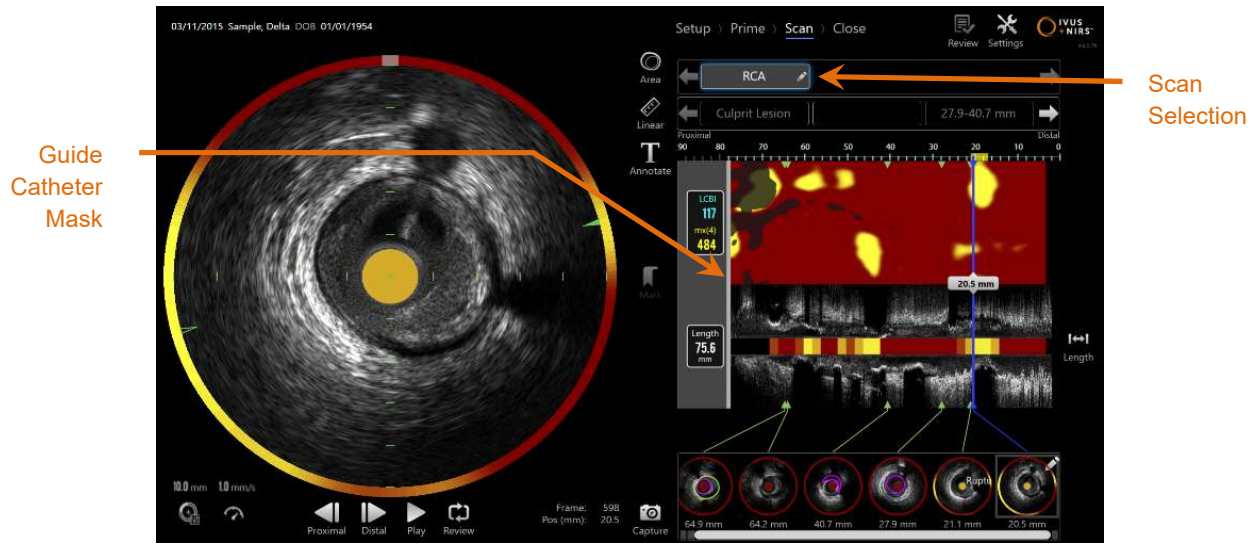


Figure 9-7: Acquisition Mode after the completion of an automated pullback scan with detected guide catheter.

Upon completion of the automatic pullback acquisition with a capable catheter, the Chemogram, Block Level Chemogram, and Lipid Core Burden Index will update. The Guidewire Detection Map will be hidden from view. See Section 10.2.8 for more information.

If the guiding catheter is detected by the Makoto Integrated Intravascular Imaging System™, then a gray guide catheter mask will be applied to the Chemogram, Longitudinal IVUS and block level Chemogram. See Section 10.2.7 for more information on how to remove the guide catheter mask from view.

NOTE: If the Guide Catheter Mask is enabled, the portion of the Chemogram within the Guide Catheter Mask will be excluded from LCBI calculation.

9.2.4 Marking or “Zero-ing” during Automatic Pullback

During Automatic Pullback acquisition Marks can be placed and reviewed later by pressing the Mark button on the controller, image, or touching the Mark icon on the screen.

Adding a Mark during pullback acquisition will reset the display of distance traveled back to 0.0mm distance.

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9.3 Performing Additional Scans with the Makoto Integrated Intravascular Imaging System™



WARNING

See catheter Instructions For Use document for guidance on preparing the catheter for additional scans.



WARNING

Hazardous situations, including injury to the patient or operator, may occur if display warnings are ignored.




WARNING

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.

Multiple scans can be performed within each procedure. The catheter may require an additional flush of heparinized saline prior to subsequent imaging.

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Press the **Live IVUS** button, , or the **Pullback** button, , on the Makoto™ Controller to acquire additional data. The previous scan will be saved and a new active scan will appear.

Each new scan will create a new button to activate the scan for review located above the location for the Chemogram on the screen.

NOTE: If more than three scans are recorded, use the left and right arrows to bring the desired scan button into view.

NOTE: A total of 20 recordings may be saved per procedure. If the limit is reached, delete unwanted scans or close the procedure and start a new procedure.

NOTE: Annotation of a scan name will change the text on the associated button.

10 Reviewing, Measuring, and Annotating Scans

10.1 Scan Selection

After multiple scans have been recorded it is possible to switch between scans using the Scan Selection controls.

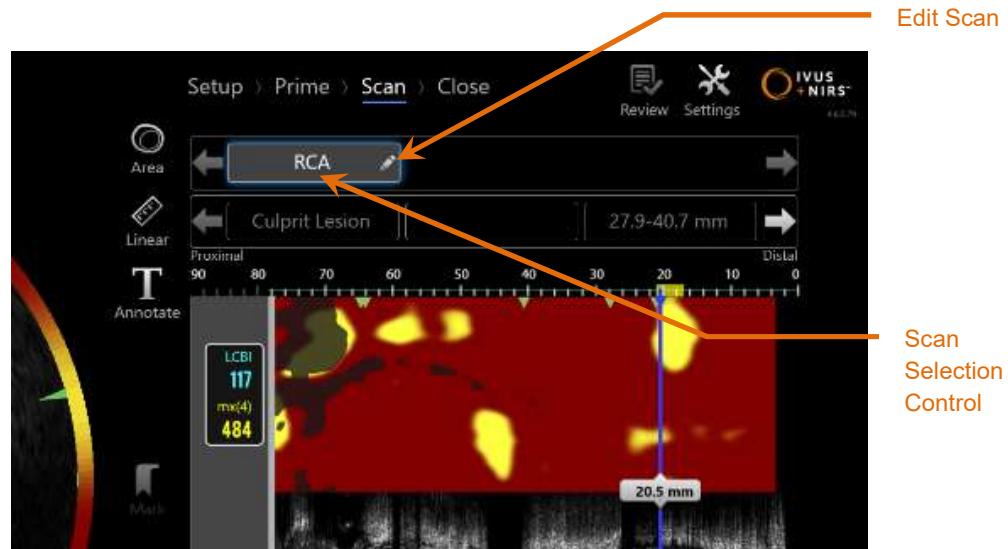


Figure 10-1: Scan Phase of Acquisition Mode with “RCA” scan selected for review.

Touch the desired scan name to select and load the data for display on the screen.

Up to three scans are visible at any time within the Scan Selection Control. Touch the arrow controls on either side of the Scan Selection Control to move other scans into view.

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10.2 Editing Scans

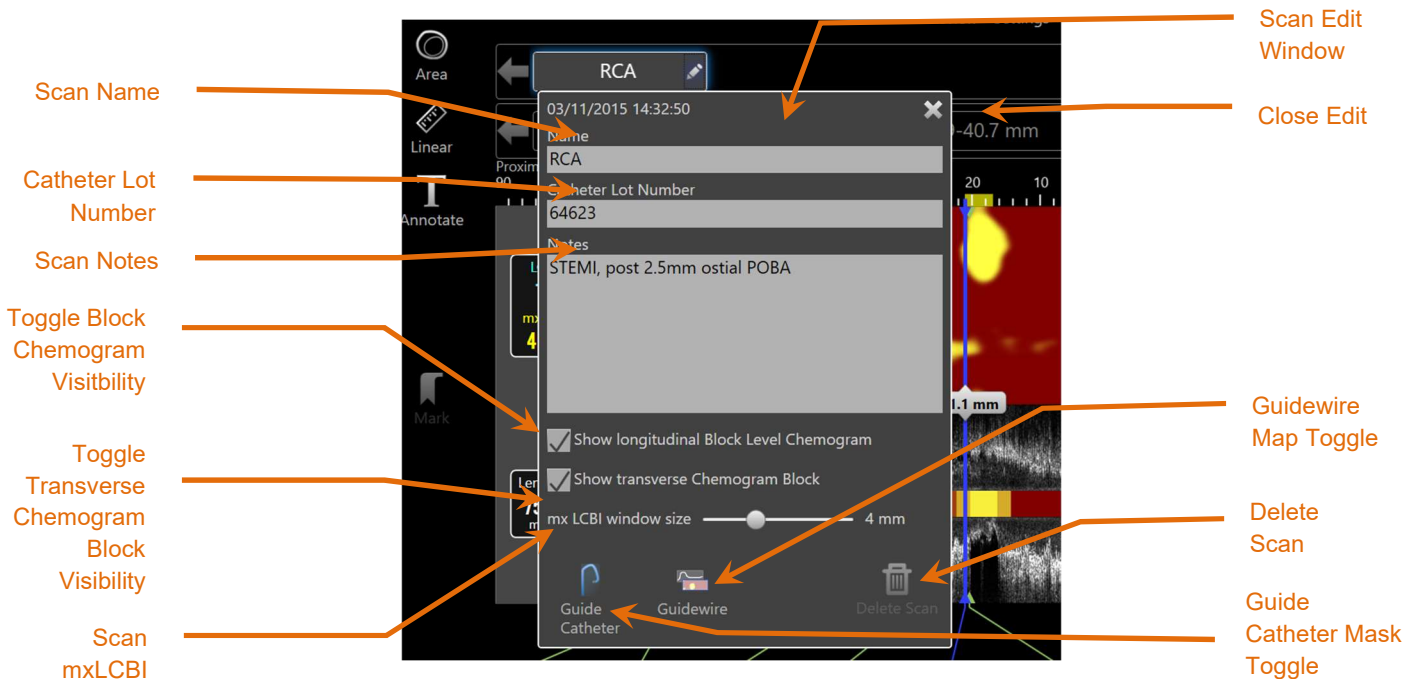


Figure 10-2: Edit Scan Window open for “RCA”.

Scan information can be edited to provide additional detail and facilitate later selection.

Touch the **Edit** button, , on the selected scan to bring up the Scan Edit window.

Touch the “X”, , or outside the Scan Edit Window to close and save all changes.

10.2.1 Scan Name

The Scan Name may be customized to reflect information about the scan. It can include artery names, locations, or timing (i.e. “pre” or “post”). The name can be set by entering information in the Name field.

This Scan Name will appear in the directory of completed procedures and scans, as well as DICOM files and reports.

NOTE: Use the Filter on the Select Phase of Review Mode to search for Scan Names. See Section 12.1 for more information.

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10.2.2 Catheter Lot Number

Each scan is collected with a catheter that has an associated production lot number. This information can be recorded independently for each scan by entering the value from the catheter package in the Catheter Lot Number field within the Scan Edit window.

NOTE: Enter the Catheter Lot Number during the Setup Phase to automatically populate this field for scans as they are recorded.

NOTE: If available the system will read the catheter lot number from the catheter and enter it automatically into the field.

NOTE: Use the Filter on the Select Phase of Review Mode to search for Catheter Lot Numbers. See Section 12.1 for more information.

10.2.3 Scan Note

Notes about the collected scan may be recorded in the Notes field of the Scan Edit window.

NOTE: Use the Filter on the Review Mode, Select Phase screen to search for important scan details recorded in the Scan Notes. See Section 12.1 for more information.

10.2.4 Scan Longitudinal Block Level Chemogram Visibility

The visibility of the Block Level Chemogram within the Longitudinal IVUS display may be toggled on or off using this check box. This selection will only affect the current scan.

NOTE: The default visibility setting of the Block Level Chemogram for all new scans can be set in the Settings of the system. See Section 13.6 **Scan Display**.

NOTE: This setting can be adjusted quickly by using the mouse to Right Click on the Block Level Chemogram and change the appropriate setting.

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10.2.5 Scan Transverse Chemogram Block Visibility

The visibility of the individual Chemogram Block within the Transverse IVUS display may be toggled on or off using this check box. This selection will only affect the current scan.

NOTE: The default visibility setting of the Chemogram Block for all new scans can be set in the Settings of the system. See Section 13.6 **Scan Display**.

NOTE: This setting can be adjusted quickly by using the mouse to Right Click on the Chemogram Block and change the appropriate setting.

10.2.6 Scan mxLCBI

The maximum LCBI window size can be adjusted per scan from the default value. Use the slider to adjust the window used to calculate the mxLCBI from 1mm to 10mm.

NOTE: The default value for all new scans can be set in the Settings of the system. See Section 13.6.5 **mx LCBI Window Size**.

10.2.7 Guide Catheter Toggle



WARNING

Imaging within the guiding catheter should be minimized for optimum chemogram results.

Within the Scan Edit window, use the Guide Catheter mask toggle control to alternate visibility of the Guide Catheter mask on the Chemogram, Guidewire Map, Longitudinal IVUS, and Block Level Chemogram.

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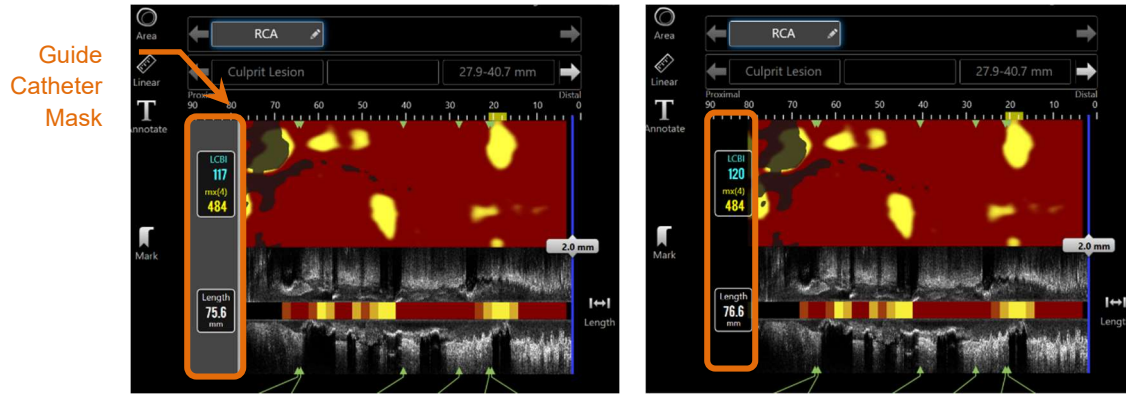


Figure 10-3: Scan Edit with Guide Catheter mask enabled (left). Scan Edit with Guide Catheter mask disabled (right).

10.2.8 Guidewire Map Toggle

Within the Scan Edit window, use the Guidewire Map toggle control to alternate visibility of the Guidewire Map and the Chemogram. When the Guidewire Map is visible the control will appear blue.

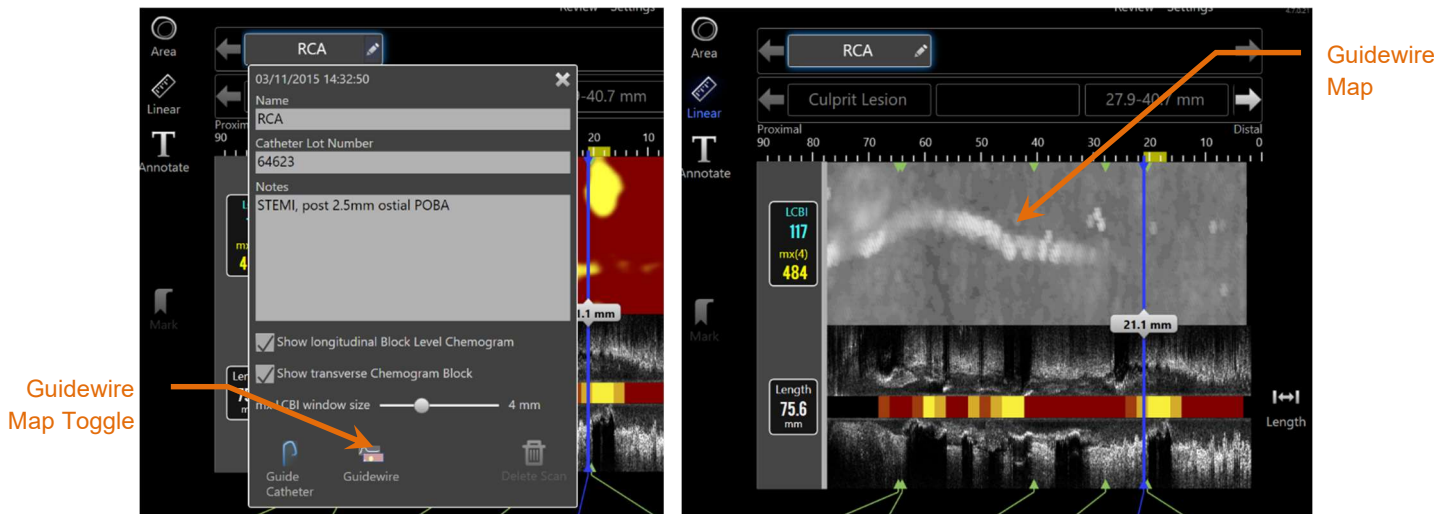


Figure 10-4: Scan Edit window with Guide Wire Map toggle enabled (left); Chemogram is hidden and Guidewire Map is visible (right).

NOTE: Guidewire Map toggle does not change the display if there is not optical data available.

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10.2.9 Delete Scan

Individual scans may be deleted via the Scan Edit window. A confirmation prompt will be provided to the user.

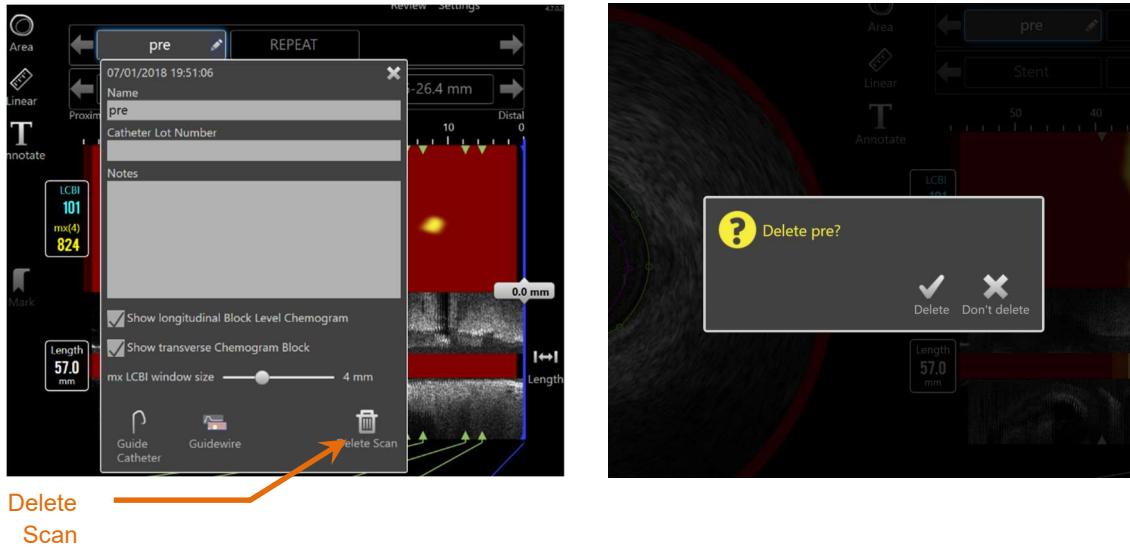


Figure 10-5: The Delete Scan control within the Edit Scan window (left) and the confirmation prompt (right).



Once confirmed by user, the deletion of a scan cannot be undone.

10.3 Scan Navigation

The selected scan may be reviewed using several controls.

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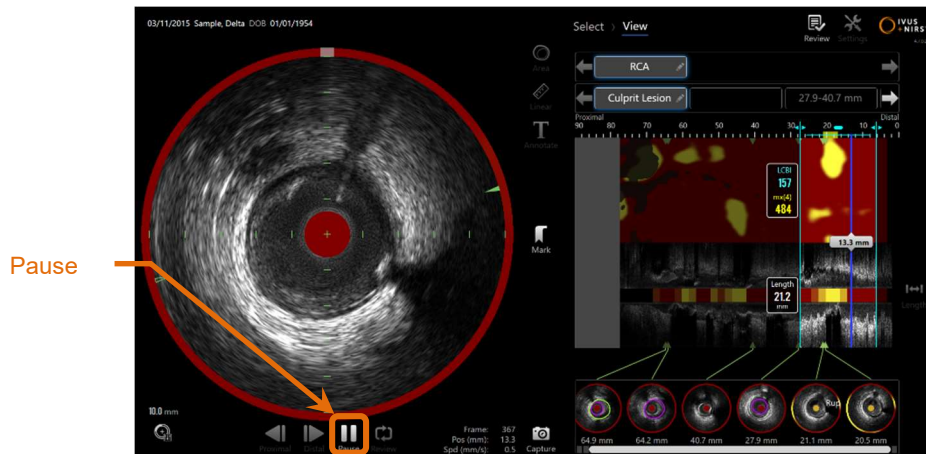
Figure 10-6: Scan Phase of Acquisition Mode with Scan Selection and Playback controls highlighted.

10.3.1 Automatic Playback



Touch the **Play/Pause** control, **Play** / **Pause**, located beneath the Transverse IVUS image to automatically cycle the recorded frames in the order they were recorded.

The playback will occur at approximately 16 frames per second for Live IVUS recordings or 30 frames per second for Automated Pullback recordings.



10-7: Scan Phase of Acquisition Mode during automatic playback with the Pause control highlighted.

Pausing will halt playback on the displayed frame. Resuming playback will begin cycling the frames from the last displayed frame.

NOTE: When the last recorded frame is reached, the playback loop will resume with the first frame in the series.

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
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NOTE: When a region is selected, automatic playback will loop the frames in the selected region.

10.3.2 Lumen Review

As an aid to making measurements and reviewing individual frames, Lumen Review will play a very short loop of frames to accentuate the differences in IVUS appearance of stationary vessel and plaque from the motion related to flowing blood.




Toggle Lumen Review by touching the Lumen Review control, , to the right of the automatic playback button.

NOTE: Adjust the duration or range of the Lumen Review within the system settings. See Section 13.6.2 **Lumen Review Range of Frames**.

10.3.3 Manual Playback


The selected scan may also be played back manually. Touch and hold either Fine



Frame Selection Control, , to play the scan slowly in the desired direction. In this manner playback will stop when the last frame is reached for the selected scan or region; it will not loop the selected frames.

NOTE:



Press and hold the Distal Fine Frame Selection Control, , to play back the selected frames in reverse order of collection.

10.3.4 Frame Selection

10.3.4.1 Coarse Frame Selection


Drag the Coarse Frame Selection control between the Chemogram or Guidewire Map and the Longitudinal IVUS or anywhere on the blue line to quickly update the displayed frame.

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NOTE: Dragging the Coarse Frame Selection control is a variable rate playback.

10.3.4.2 *Fine Frame Selection*

Touch the Proximal Fine Frame or Distal Fine Frame Selection controls, , to change the displayed frame in increments of one frame.

NOTE: With the cursor over the Chemogram, Guidewire Map, Transverse IVUS, or Longitudinal IVUS, roll the mouse wheel to change the displayed frame in increments of one frame.

10.4 Marks

During and after the scan is completed, Marks may be made. During acquisition of the scan, press or touch the **Mark** controls,  or . During review, navigate to the desired frame and touch 'Mark' on the screen.

NOTE: Only one Mark can be made on each frame.

NOTE: Up to 30 Marks may be created within a single scan.

NOTE: Up to five Marks may be in full view on the screen at any time.

NOTE: Completing a Transverse IVUS measurement or on frame annotation will automatically create a Mark for the frame.

NOTE: Use the Mark button while in the Setup or Prime phases to advance to the next phase of Acquisition Mode.

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NOTE: During image acquisition, use the Mark button to reset the displays of distance traveled back to 0mm distance.

A Mark's relative position within the scan is indicated by small green triangles on the Chemogram and Longitudinal IVUS. When the Mark is selected the Current Displayed Frame indicator will connect the triangles.

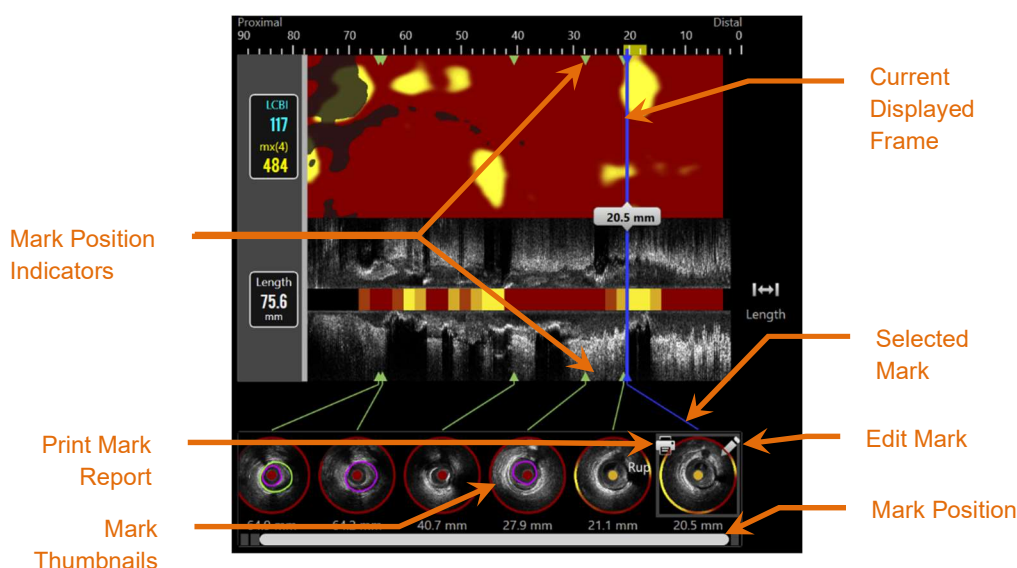



Figure 10-8: Mark positions are displayed by green triangle indicators on the Chemogram and Longitudinal IVUS and with a visual thumbnail showing content of the frame.


10.4.1 Mark Selection

A Mark Thumbnail image will be created for each placed Mark. The thumbnail image is the control to select the marked position for later review. It also provides a visual representation of the content at the frame location.

Touch the desired Mark image to update the display and show the frame in the Transverse IVUS display.

10.4.2 Mark Edits

Marks may be deleted or annotated. Touch the **Edit** button, , on the selected Mark to open the Mark Edit window.

Touch the “X”, , or outside the Mark Edit window to close the window, saving the changes.

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10.4.2.1 Mark Notes

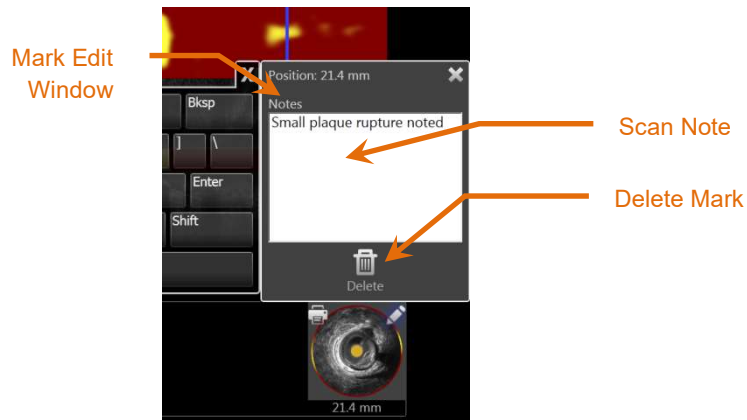



Figure 10-9: Mark Note entered in the Mark Edit Window.

Notes about the content of a frame may be recorded in the Notes field of the Mark Edit window.

10.4.2.2 Deletion


Marks may be discarded using the **Delete** control, , within the Mark Edit Window.

NOTE: Deleting a Mark cannot be undone.

NOTE: Deleting a Mark with measurements or frame annotations will require a confirmation.

10.4.3 Print

Mark Reports are condensed one page summaries of the procedure focused on the findings within the selected frame.

On the selected Mark, touch the **Print** button, , to send a 1 page report to the configured default printer for the system.

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10.5 Measurements

The Makoto Integrated Imaging System™ provides controls with the Scan Phase to perform measurements on the Transverse Display and the Longitudinal Displays (Chemogram and Longitudinal IVUS).

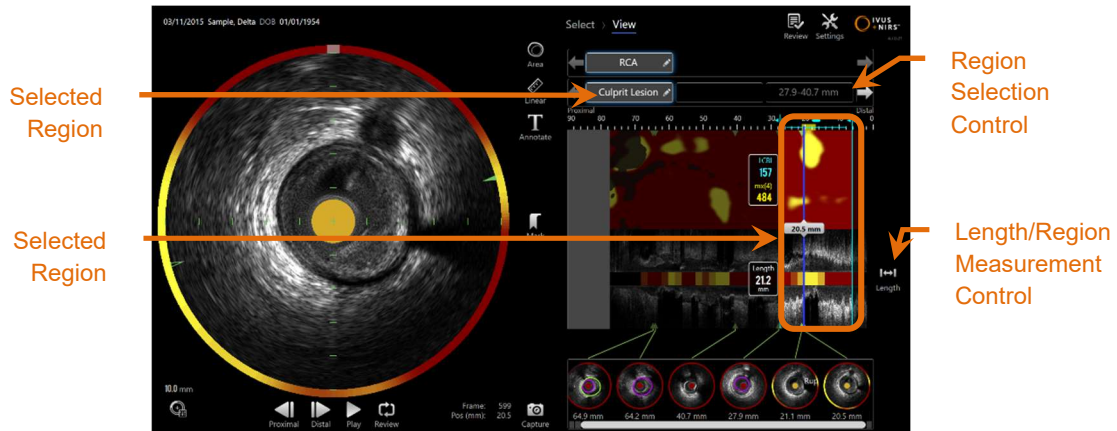


Figure 10-10: View Phase with a Region Selected within the “RCA” scan.

10.5.1 Length, Lumen Area Stenosis and LCBI Measurement

Length, Lumen Area Stenosis and LCBI measurements are made on the longitudinal IVUS view and Chemogram through the creation of Regions.

10.5.1.1 Region Creation

Regions are sub-segments of a scan that have some relevance for the operator or physician. These segments may encompass lesions, normal segments, stents, etc.

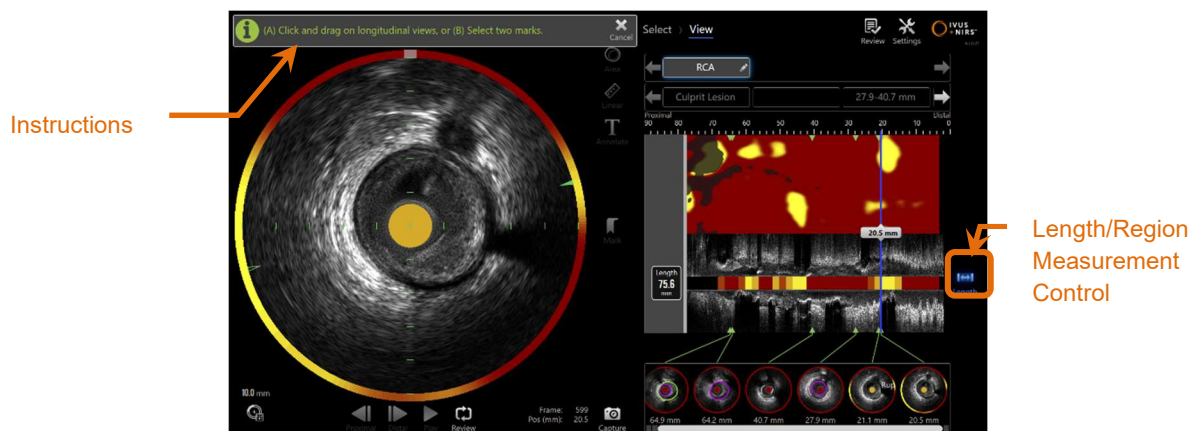


Figure 10-11: View Phase with a Region creation in process. Note the on-screen instruction on completing the region.

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Regions are created by touching the Length control, and then indicating a start and end location of the Region on the Longitudinal IVUS or Chemogram. The Region may be defined by:

(14) touch and hold the desired start position then dragging to the desired end position

or

(B) touch the start and end Mark positions from the Mark Thumbnails.

NOTE: Use Marks to set the start or end of a desired region with increased precision.

When the Region is created, areas of the longitudinal displays outside the region are dimmed and a Region Selection control will appear below the Scan Selection controls.

NOTE:



Use the Playback control, to loop the selected region.

The LCBI and results are presented to the left of the Chemogram region and the Length presented to the left of the Longitudinal IVUS.

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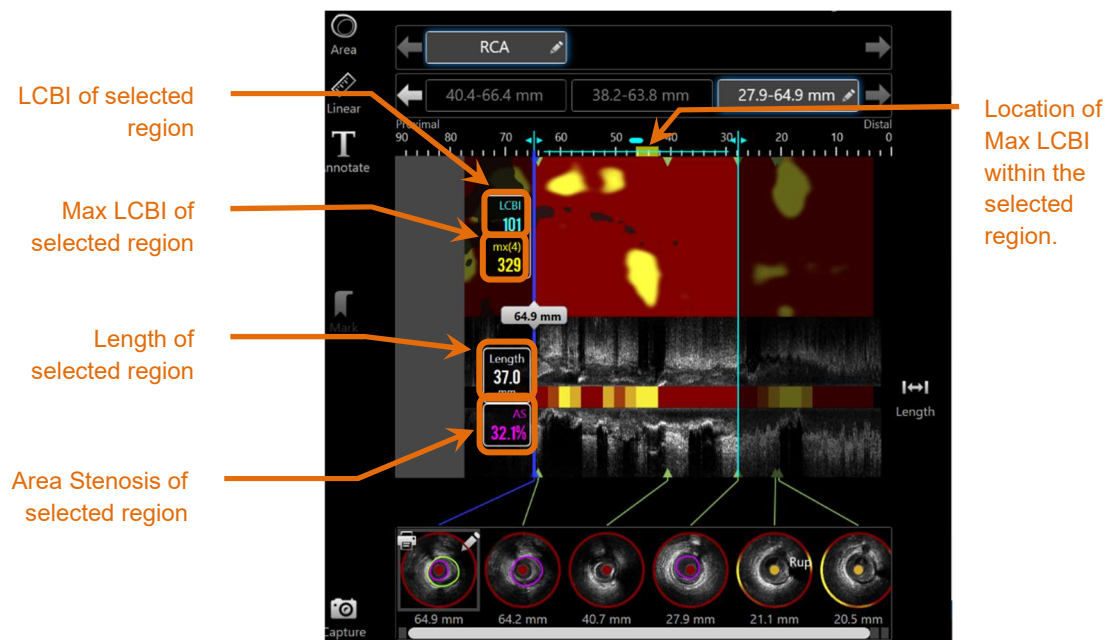


Figure 10-12: View Phase with Region selected.

10.5.1.2 Region Editing

Regions that have been created within the chemogram can be adjusted for position within the scan or their start and end locations adjusted.

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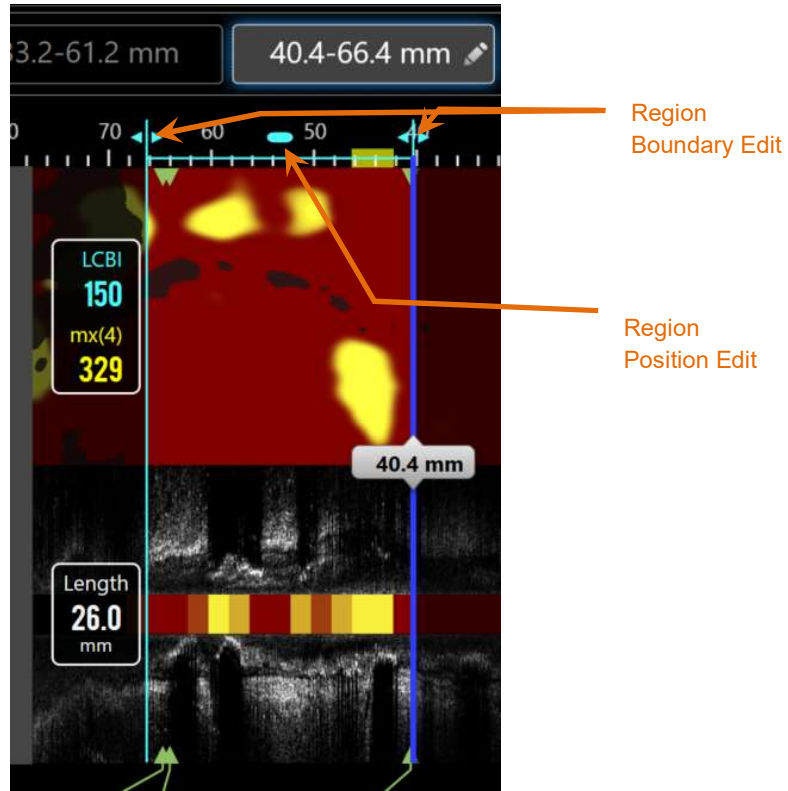


Figure 10-13. Region Editing Controls.

Drag the Region Position to move the defined region without changing the length of the region.

Drag the proximal or distal boundaries of the region to make a coarse adjustment to the selected end of the region. The length of the region will update automatically. The LCBI will update upon completion of the edit.

NOTE: Position the mouse pointer over the edit start or end location controls and use the mouse wheel to make fine adjustments to the location of the region boundary.

NOTE: Lock the region to avoid accidental adjustment. See Section 10.5.1.7 **Region Locking**.

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10.5.1.3 *Length, LCBI, & max LCBI*

Upon completion of Region creation, three measurement results related to the Region are presented.

Length:	This is the distance in millimeters (mm) between the start and end position of the region.
LCBI:	This is the Lipid Core Burden Index of the region. The LCBI is a ratio of lipid positive signals to total valid pixels in the selected region on a scale from 0 to 1000.
Mx(4):	This is the maximum Lipid Core Burden Index of a fixed window size within the boundaries of the region. The default window size is 4mm.

NOTE: LCBI and Mx(4) values are only provided if NIRS data is recorded by the system.

10.5.1.4 *Lumen Area Stenosis (AS%)*

Lumen Area Stenosis (AS) can be computed when a Region is created using two Marks that each contain an area measurement that the system has identified as the lumen.

NOTE: Add lumen measures to the start and end frame of an existing region to obtain Lumen Area Stenosis for the region.

10.5.1.5 *Selecting & Deselecting*

Select Regions by touching the corresponding button within the Region Selection control. The longitudinal display, Length, LCBI, and max LCBI results will update accordingly.

Deselect Regions by pressing the corresponding region button again or select the current scan or other scan.

NOTE: Attempting to create a new region will deselect the current region.

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10.5.1.6 *Region Annotation*

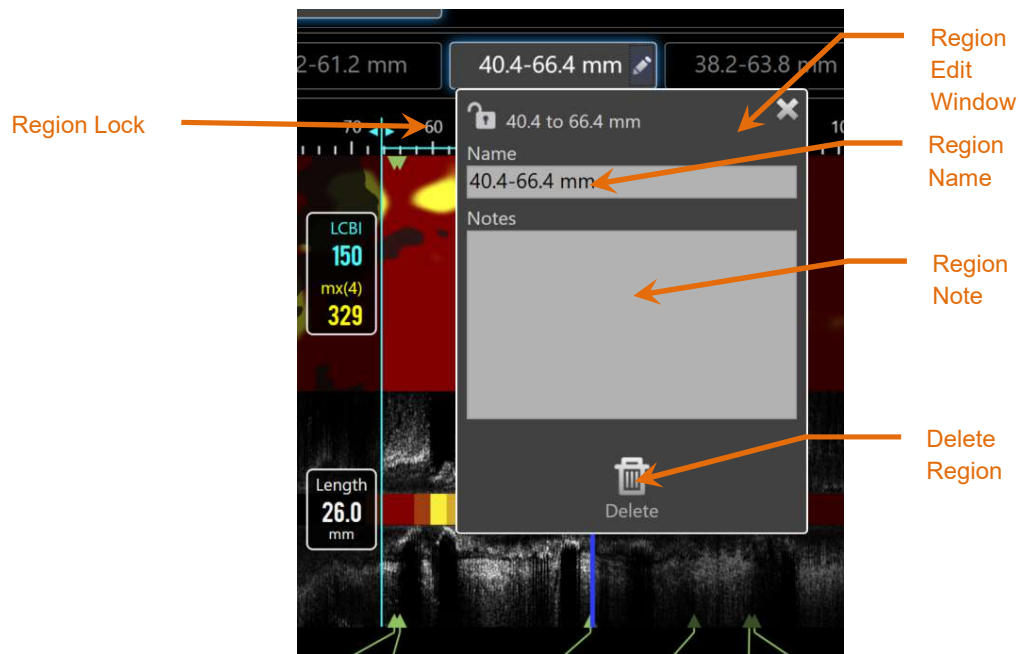




Figure 10-14: Region Name entered in the Region Edit Window.

Touch the **Edit** button, , on the Selected Region button to open the Region Edit window. Touch the desired field to update its contents.

Touch the “X”, , or outside the Region Edit window to close and save your entry.


10.5.1.7 *Region Locking*


Touch the Edit button, , on the Selected Region button to open the Region Edit window. Touch the Region Lock icon, , to toggle the ability to adjust region position or the start and end position of the region.

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10.5.1.8 *Region Deletion*

Touch the Edit button, , on the Selected Region button to open the Region Edit

window. Touch the Delete control, , to discard the region.

NOTE: Deleting a region cannot be undone.

10.5.2 On Frame Measurement


Measurements can be made on any transverse IVUS frame to clarify or quantify the content of the frame.

NOTE: Completing an On Frame Measurement will automatically create a Mark for the frame.

NOTE: Completing a measurement on a frame will update the Mark Thumbnail image.

NOTE: When active, touch the tool to abandon the measurement or on-frame annotation in progress.

10.5.2.1 *Area Measurement*

The Area Measurement tool, , can be used to quantify area and minimum and maximum diameters of features in the image.

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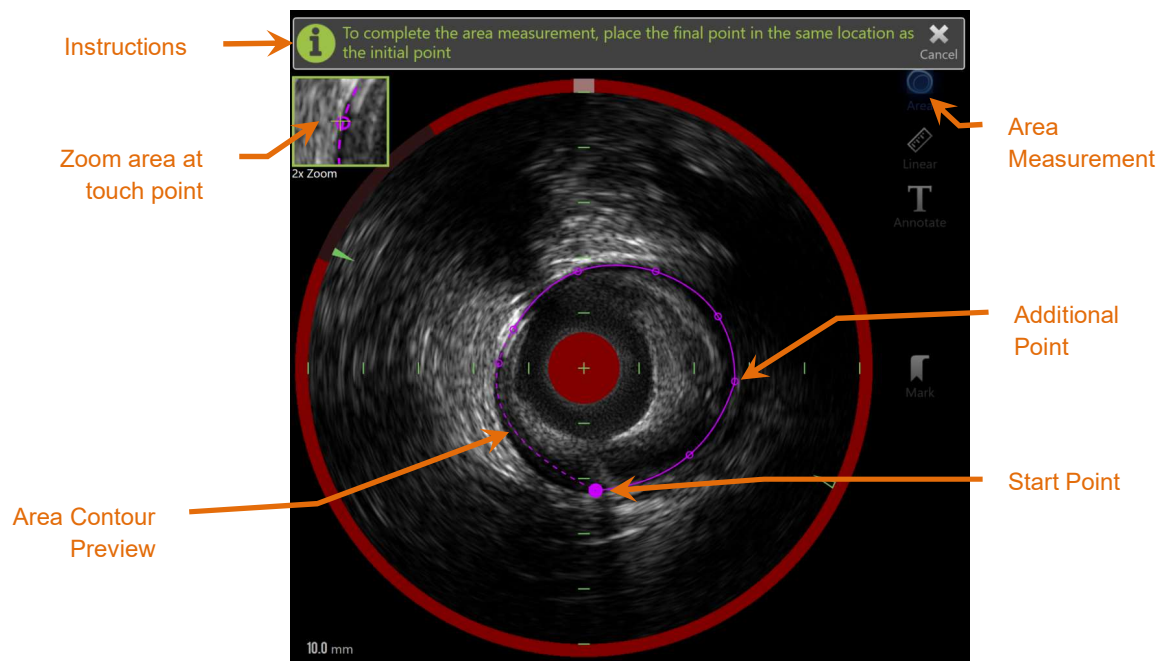



Figure 10-15: Scan Phase with Area Measurement enabled and in progress. Note that the first point placed is denoted as a larger solid circle.




Touch the Area Measurement tool, , to start the measurement. The icon will turn blue when active. Instructions will appear above the Transverse IVUS image as a guide to complete the measurement.

Touch the Transverse IVUS image to place points along the feature of interest to begin to define the area. Continue to add points until the area is defined.

NOTE: After the third point is added to define the area, a preview of the area will appear with a dotted line. This will illustrate how the completed area appears if the starting point is touched or clicked to complete the area.

NOTE:



Touch **Cancel**, , in the on-screen instructions to abandon the measurement in progress.

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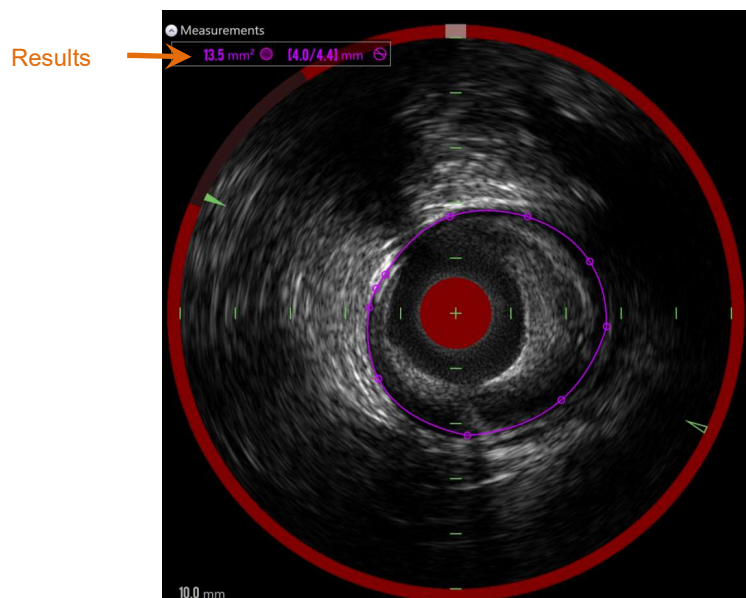


Figure 10-16: Area Measurement completed and results presented.

Touch the first point to complete the measurement and present the results. For each area completed, the cross sectional area with minimum and maximum diameters will be presented in the top left corner of the Transverse IVUS image.

NOTE: Touch the measurement result to display the minimum and maximum diameters in the image.

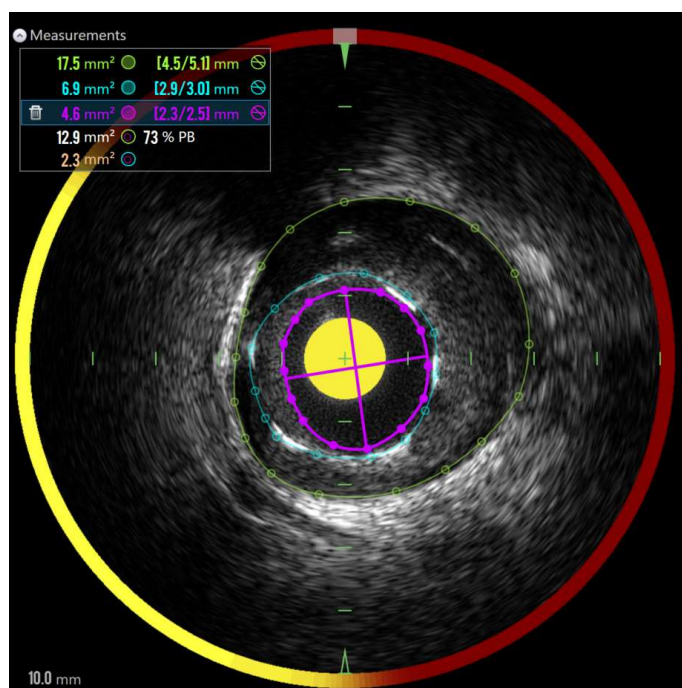


Figure 10-17: Color coded contours and results are presented when areas are drawn completely within another area. The lumen contour is selected and the minimum and maximum diameter locations are shown.

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If more than one area contour is drawn, then the results will be color coded.

NOTE: Up to three areas may be drawn on each frame.

NOTE: Each Area measurement result is color matched to its contour. Each computed area icon, for example plaque area, is color coded to the contours used to define the computed area result.

NOTE: If one area is completely contained within a second area on the same frame, then the Makoto™ System will automatically assign one to represent the “Lumen” and one to the “EEM” and a plaque area, and a Plaque Burden , “PB%”, will be computed.

NOTE: If three nested areas are drawn on the same frame, Area 1 drawn completely within Area 2 and Area 2 is drawn completely within Area 3, then the Makoto™ System will automatically assign the outer most area to represent the “EEM”, the inner most to represent the “Lumen”, and the middle one to represent the “Stent”. A Plaque Area and a Plaque Burden , “PB%”, will be computed between the “EEM” and “Lumen”. An additional area will be computed between the “Stent” and the “Lumen”.

Resize or reshape the area by touching the existing points and dragging them to desired location. To refine the shape of the completed area make additional points to the completed area by touching and dragging or clicking and dragging the area contour between existing points. The presented results will update upon completion of the edit.

NOTE: Drag measurement points to open the Local Zoom and enhance visualization of the image near the cursor or underneath the operator's finger.

10.5.2.2 *Linear Measurement*

Linear measurements can be made on the Transverse IVUS image to measure features in the image, such as diameters or thicknesses.

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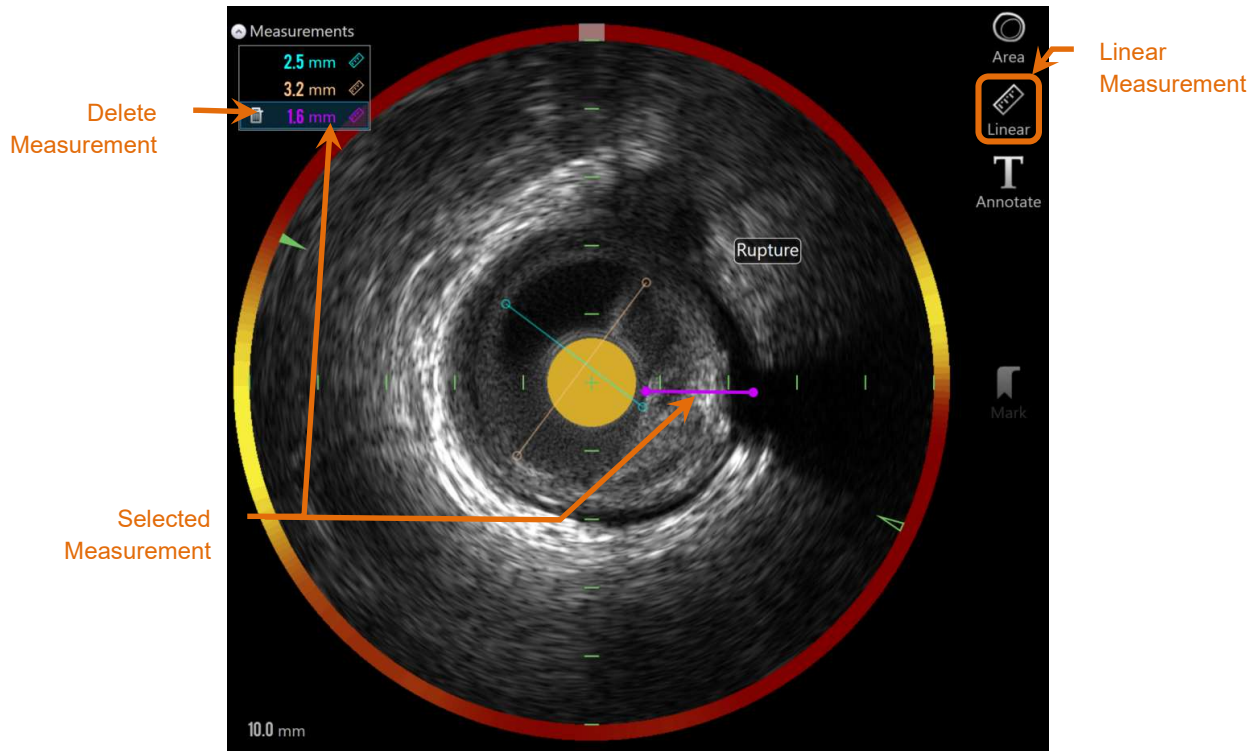



Figure 10-18: Linear Measurement completed. Three Linear Measurements have been made on this section.



Touch the **Linear** Measurement tool, , to start the measurement. The icon will turn blue when active. Instructions will appear above the Transverse IVUS image as a guide to complete the measurement.

Touch the start point of the feature to be measured in the Transverse IVUS image. Touch the end position of the feature to complete the measurement. The linear measurement will be displayed on the transverse IVUS image with the distance between the two points in millimeters.

NOTE: When using the mouse or dragging the end point a preview of the line and distance will appear prior to placing the end point.

NOTE: Up to six linear measurements may be drawn on each frame.

Drag either the start or end points to adjust the measurement.

10.5.2.3 *Deleting On Frame Measurements*

To delete individual on-frame measurements, select the measurement result to begin.

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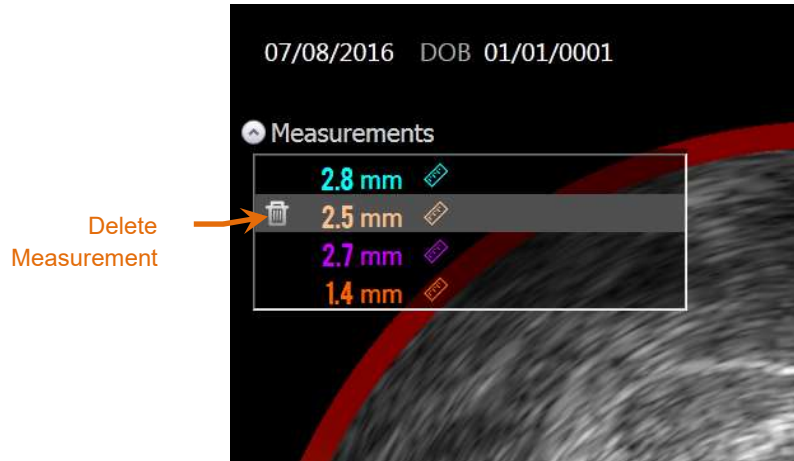




Figure 10-19: Mark with a linear measurement selected. Note the option to delete the measurement and result.

When selecting measurement results, a Delete control, , will appear to the left of the selected result. Touching the Delete control, , will clear the measurement and the result from the scan.

NOTE: Deleting measurements cannot be undone.


NOTE: Deleting individual measurements does not require confirmation.

NOTE: Delete the Mark to clear ALL measurements from a frame in a single step.

10.6 On Frame Annotation

In addition to measurements, comments can be made directly onto the transverse IVUS image.



Touch the On-Frame Annotation control, , to begin making on-frame comments. Determine the location where the note should appear, this will set the left edge of the note. Touch <Enter> on the virtual keyboard to complete the annotation.


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NOTE: Completing an On Frame Annotation will automatically create a Mark for the frame.

NOTE: Completed On Frame Annotations can be dragged to new positions on the current frame.

NOTE: Completing an On Frame Annotation will update the Mark Thumbnail image.

To delete an On Frame Annotation, touch the annotation to select it then touch the Delete control, .

10.7 Screen Capture

Images of the entire screen can be recorded during the Scan and View phases. This image will capture all the content on screen as well as buttons and controls.

While reviewing a scan, navigate to the desired frame using the coarse or fine frame adjustment controls.

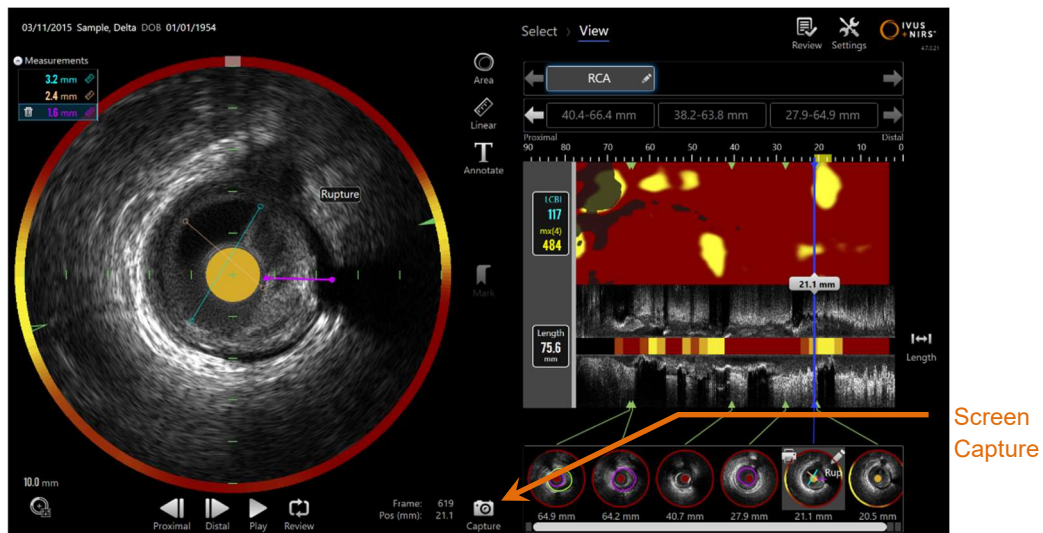



Figure 10-20: Scan phase of Acquisition Mode with the Screen Capture control indicated.

Touch the Capture control, , to record an image of the entire screen for later use.

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NOTE: A limit of 30 screen captures may be recorded for each scan.

NOTE: Screen Captures may be printed or deleted from the Close Phase of Acquisition Mode or the Select Phase of Review Mode.

10.8 Display Setting

The Makoto Integrated Intravascular Imaging System™ provides several controls to optimize the display layout and the image quality of the rendered IVUS images.

10.8.1 Longitudinal IVUS rotation

The Longitudinal IVUS image is created from the image data along the marked axis in the Transverse IVUS Image. The marked axis in the Transverse IVUS image is denoted by the solid and open triangles on the axis. The solid triangle on the axis identifies the portion of the image that will be drawn in the top half of the Longitudinal IVUS.

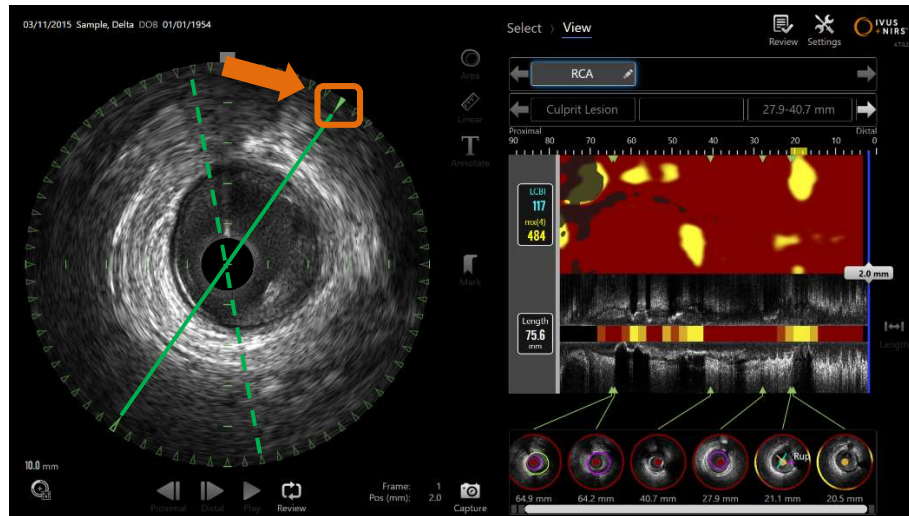


Figure 10-21: Longitudinal IVUS rotation. The dashed green line illustrates where the axis of the longitudinal IVUS started and the solid line illustrates where the axis is currently. The lines are enhanced here for illustrative purpose.

To adjust the data displayed in the Longitudinal IVUS drag the solid triangle on the marked axis to a new location on the circumference of the Transverse IVUS Image.

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NOTE: Adjustment of this view of the Longitudinal IVUS will not affect adjustments made to the chemogram rotation.

10.8.2 Chemogram rotation

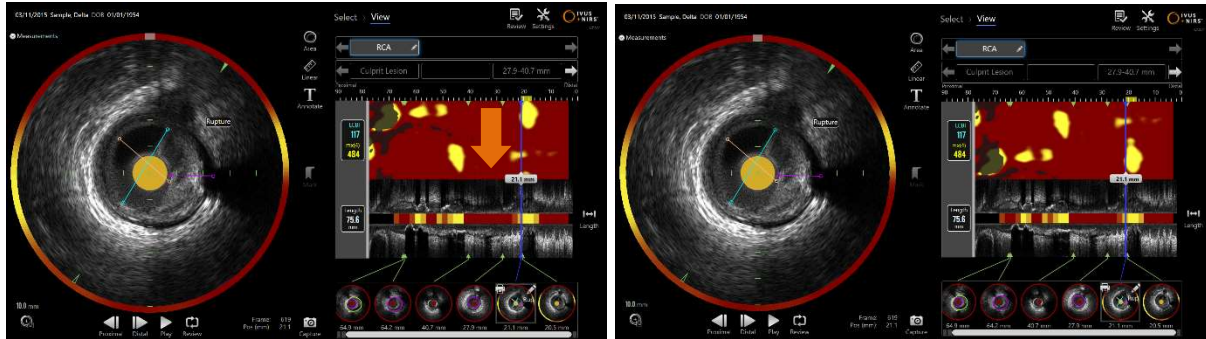


Figure 10-22 Chemograms can be rotated to move the lipid pools away from the edge of the chemogram for easier viewing and interpretation.

The chemogram vertical axis is a continuous 360 degree dimension. This means the top edge of the chemogram is connected to the bottom edge. The cut location is arbitrary in order to represent it in a two dimensional map. This may result in some features being separated to the top and bottom edges.

Touch or Click in the chemogram and Drag in the vertical direction to adjust the cut location of the chemogram.

NOTE: The system will remember this chemogram cut line adjustment and apply it to future scan viewing or report generation. Screen captures will not be adjusted.

NOTE: Adjustment of this view of the chemogram will not affect adjustments made to the Longitudinal IVUS.

10.8.3 Transverse IVUS rotation

The Transverse Image may be rotated to facilitate comparison with other scans or to help the user better visualize the anatomy.

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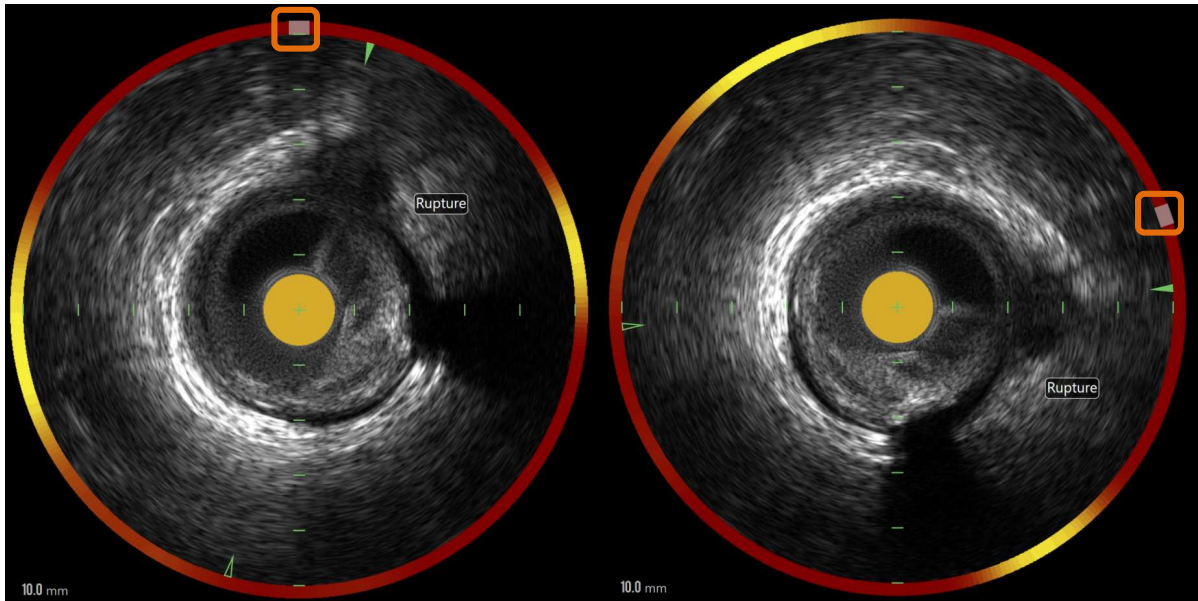


Figure 10-23. Transverse IVUS rotation. Left image shows the default orientation and the Right image shows image after rotation by dragging the control on the chemogram halo to a new location.

To adjust the rotation of the Transverse Image, drag the gray arc control that appears in the Chemogram Halo to a new location.

NOTE: The Transverse IVUS image and the Chemogram Halo are rotationally linked. Rotating the Transverse Image will also rotate the Chemogram Halo.

NOTE: The rotation of the Transverse Image is applied to all frames in the scan.

NOTE: The Longitudinal IVUS image rotation is relative to the Transverse IVUS rotation, so adjusting the Transverse IVUS rotation will not disrupt the selected Longitudinal IVUS view.

NOTE: The Transverse IVUS rotation will appear in reports, avi, and DICOM images created in Review Mode.

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10.8.4 Transverse Image Settings

The transverse IVUS image may be adjusted using the Image Settings control. These controls contain both a basic and advanced control set.

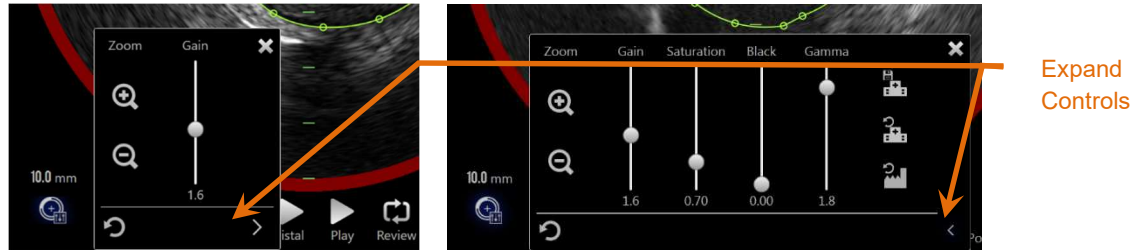




Figure 10-24: Transverse Image Settings. Basic controls, left. Advanced controls, right.

Touch the Image Settings Control to gain access and then use the **Expand** control, , to reach advanced settings and functions.

Touch the “X”, , or outside the window to use the current settings and close the window.

10.8.4.1 Zoom

The transverse IVUS field depth may be adjusted using Zoom controls near the transverse IVUS image. The transverse IVUS image depth can be adjusted from 6 mm to 16 mm in 2 mm increments.

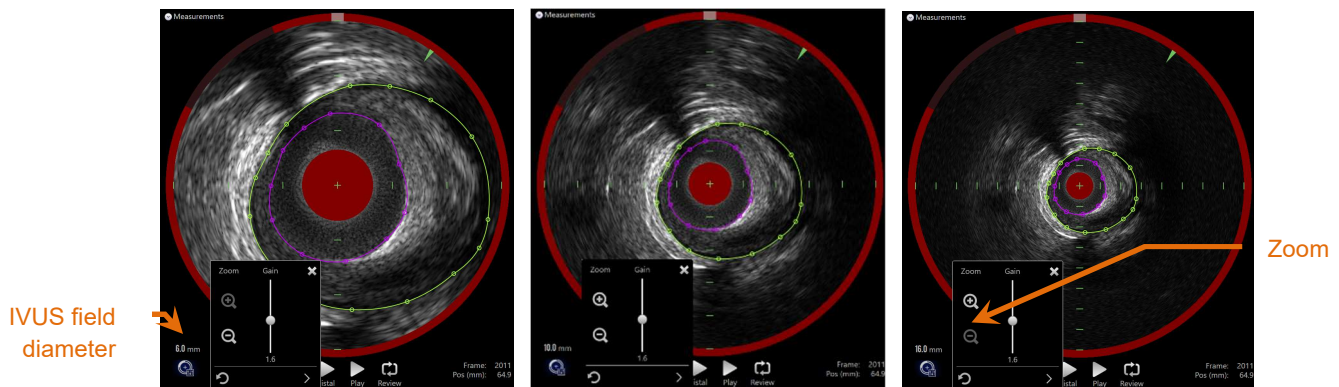




Figure 10-25: Transverse IVUS diameter is adjusted using the Zoom control. 6mm diameter, left. 10mm diameter, center. 16mm diameter, right.

Touch the Zoom controls to increase, , or decrease, , the transverse IVUS magnification. A corresponding update will be made to the longitudinal IVUS display.

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10.8.4.2 *Gain*

Drag the slider to adjust the value of the Gain Setting. The range is from 0.5 to 3.0.

Low values will produce a dark image, while high values will produce a brighter image.

10.8.4.3 *Saturation*

Drag the slider to adjust the value of the Saturation Setting. The range is from 0.50 to 1.50.

Low values will produce a dark image, while high values will produce a brighter image. Use in combination with the Black setting to control dynamic range.

10.8.4.4 *Black*

Drag the slider to adjust the value of the Black Setting. The range is from 0.00 to 0.50.

Low values will produce a bright image, while high values will produce a darker image. Use in combination with the Saturation setting to control dynamic range.


10.8.4.5 *Gamma*

Drag the slider to adjust the value of the Gamma Setting. The range is from 0.5 to 2.6.

Low values will produce a whiter image, while high values will produce a darker image.

10.8.4.6 *Return to Previous Setting*



Touching the Return to Previous control, , will return the settings to the values when the settings window was opened. This will not affect Zoom.

10.8.4.7 *Save to Local Default Settings*




Touching the Save to Local control, , will save the current settings as the default. All new procedures will start with these image settings, including Zoom.

These values will be used when the Return to Local Settings control is touched.

10.8.4.8 *Return to Local Settings*




Touching the Return to Local Settings control, , will load the default local settings.

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10.8.4.9 *Return to Factory Settings*



Touching the Return to Factory Settings control, , will load the default settings established by the manufacturer.

11 Closing Procedures

At the Close Phase of the procedure, details of the procedure may be reviewed prior to committing the scans and analysis to local system memory.

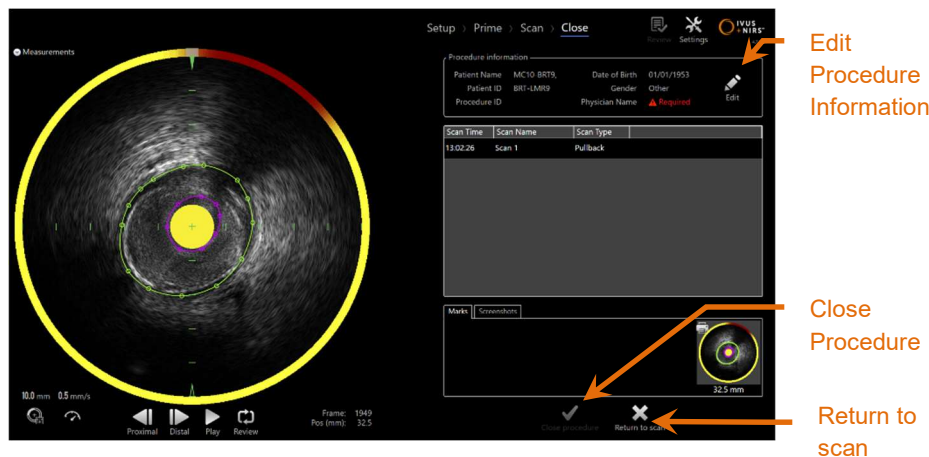


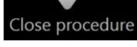
Figure 11-1: Close Phase of Acquisition Mode with the Close Procedure control enabled.

Details of the procedure setup, collected scans, marks, and screen captures are presented for confirmation. This is an opportunity to review the Setup Phase data or delete unwanted scans prior to closing the procedure.

NOTE: If critical information necessary to minimally identify a procedure is missing, then the operator will be alerted to return to the Setup Phase.

NOTE: If a scan is initiated from the Makoto™ Controller, the Acquisition Mode will automatically return to the Scan Phase.

If changes are required then touch the **“Return to scan”** or **Edit** controls, , or touch the appropriate phase from the Progress Strip control to edit the procedure.

Touch the **“Close Procedure”**, , confirmation to commit all scans to local memory and reset the Acquisition Mode for a new procedure.

12 Reviewing and Archiving Procedures

Previously recorded procedures may be reviewed, archived, edited and deleted in Review Mode.

To enter Review Mode from the Acquisition Mode, touch the Makoto™ Mode Toggle when there is no active procedure underway.

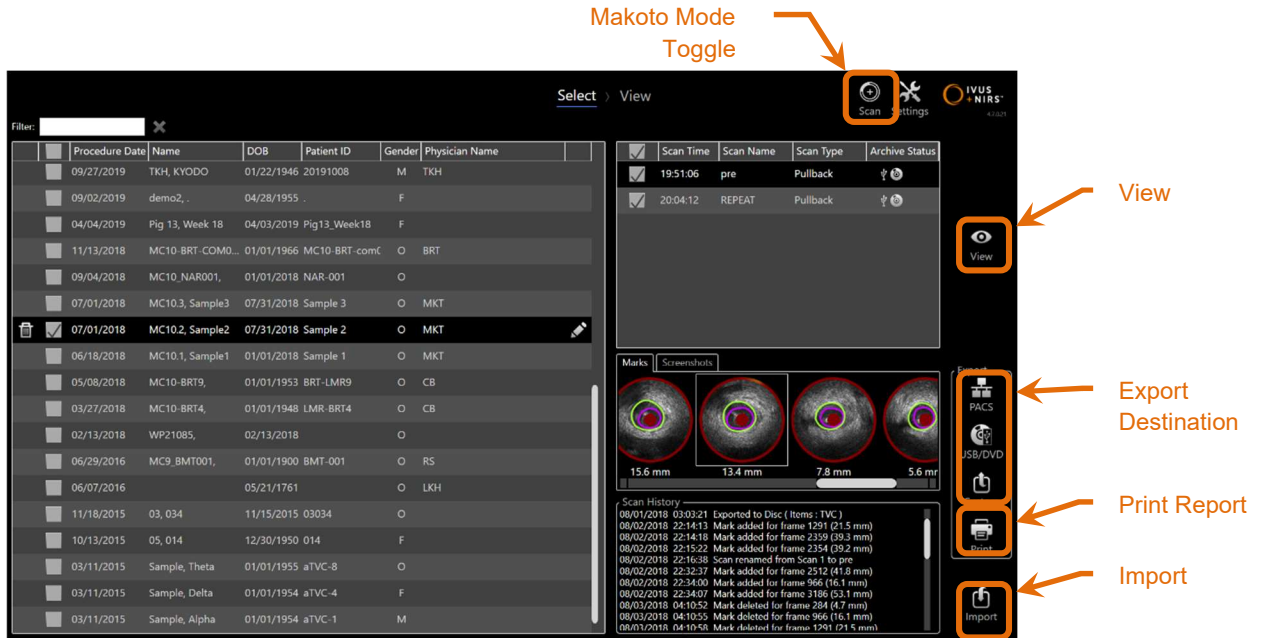


Figure 12-1: Review Mode showing the Select Phase.

Upon entering Review Mode the operator is presented with the Select Phase of the review workflow. During this phase the operator will make a selection of procedures and scans upon which to perform additional actions. The operator may choose to edit, view, delete or print reports with the selected procedure or scans.

Scans may also be selected for import into local memory.

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12.1 Selecting Procedures and Scans

Procedures and individual scans may be selected for further action within the Select Phase of the Review Mode.

Data contained on the system is arranged into three tables based on information type. There is a table for procedures, scans within the selected procedure, and the Marks and screen captures within the current scan selection.

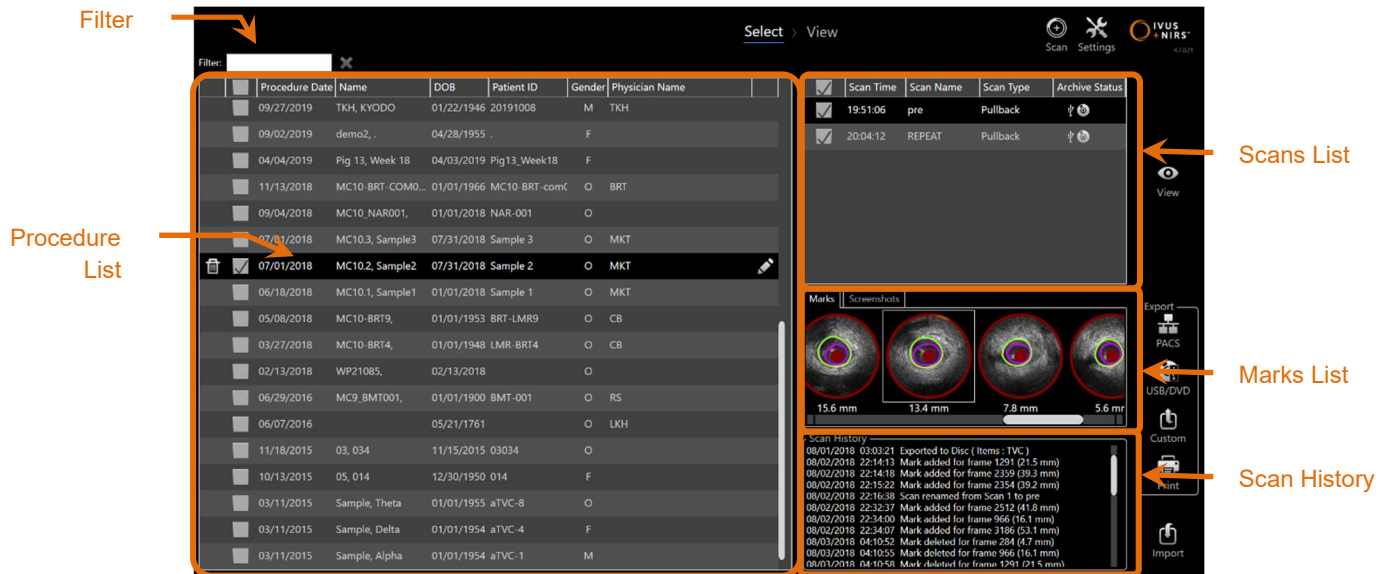


Figure 12-2: Select Phase of Review Mode with information lists highlighted.

Selected procedures may be viewed or have screen capture or Mark Reports printed. Checked procedures may be exported and viewed. They may also have their screen captures printed or Mark Reports printed if the checked procedure is also the current selection.

To make a single procedure selection, touch any point within a single row of procedure information within the Procedure List. The selected procedure will become the current selection. The scans within that procedure will appear in the Scan List.

Touch the check boxes to select multiple procedures for exporting data as a batch from the system.

NOTE: Procedures will be ordered with the most recent procedure date at the top of the list by default.

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NOTE: Scans will be ordered in chronological order by default with the earliest scan at the top of the list.

NOTE: Touch the column headers in the Procedure and Scan Lists to re-order the information.

NOTE: For a checked procedure, all scans contained will be checked by default.

To make multiple procedure selections, touch the check box next to the information about the desired procedure. Remove procedures from the multiple selection by touching the check box again.

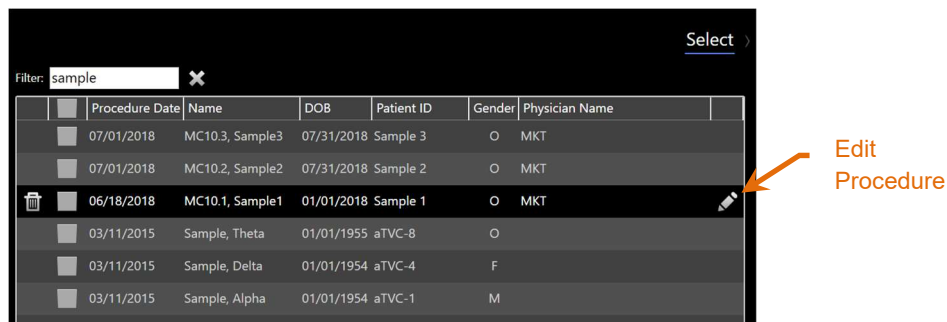
NOTE: Custom Export is only available for a single procedure.

12.1.1 Scan History

Updates made to scans after the procedure completes will be recorded in the Scan History. This will include changes to Scan Name, Mark additions or deletions, and Export or Archive actions.

12.1.2 Filtering Procedure List

The catalogue of saved procedures may become long between routine archiving and removal of data from the system. Use a filter term to reduce the displayed number of entries within the procedure list to facilitate selection.




	<input type="checkbox"/>	Procedure Date	Name	DOB	Patient ID	Gender	Physician Name	
	<input type="checkbox"/>	07/01/2018	MC10.3, Sample3	07/31/2018	Sample 3	O	MKT	
	<input type="checkbox"/>	07/01/2018	MC10.2, Sample2	07/31/2018	Sample 2	O	MKT	
	<input checked="" type="checkbox"/>	06/18/2018	MC10.1, Sample1	01/01/2018	Sample 1	O	MKT	
	<input type="checkbox"/>	03/11/2015	Sample, Theta	01/01/1955	aTVC-8	O		
	<input type="checkbox"/>	03/11/2015	Sample, Delta	01/01/1954	aTVC-4	F		
	<input type="checkbox"/>	03/11/2015	Sample, Alpha	01/01/1954	aTVC-1	M		


Figure 12-3: Select Phase with Filter applied to the Procedure and Scans lists for entries containing “Sample”.

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Enter a short amount of text within the filter control, the list will be reduced to a more manageable number of entries.

The system will search all Procedure ID, Patient Names, Patient ID, Physician Names, Catheter Lot Numbers, Scan Names, or Scan Notes for these characters.

Touch Clear, , to return to the complete procedure listing.

12.1.3 Edit Procedure

The procedure and patient information may be edited to correct or change information.

In the procedure list with the current selection, touch the Edit icon, , to open the edit procedure prompt.

The current procedure details will show in the Edit Procedure prompt. Use the available controls to update the fields.

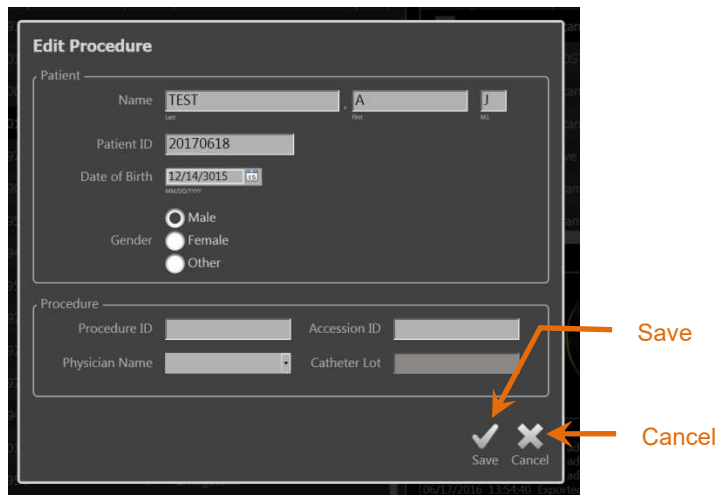


Figure 12-4: Select Phase with the Edit Procedure window open.

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Touch “Save”, , to commit the changes and close the prompt. Touch “Cancel”,



, to close the prompt without saving the changes.

NOTE: Edits made to the procedure will affect all scans associated with the procedure on the system. This includes unchecked scans.

NOTE: View the procedure to edit scan details within the selected procedure.

12.1.4 Print Report

Comprehensive reports for single or multiple procedure selections may be printed from the Makoto Integrated Intravascular Imaging System™ with a configured compatible printer.

NOTE: Contact your local Sales Representative or Infraredx Customer Service for more information about compatible printers and configuration.

Comprehensive reports will contain a summary of all the scans performed in a procedure including regions created and Marks and measurements performed. Print a comprehensive report by selecting a procedure by checking the box next to the entry in


the procedure list, and then touch the Print Procedure Report control, .

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Figure 12-5: Select Phase with Print Mark Report control highlighted.

Selecting a Mark or Screen Capture and touching Print, , will send a one page Mark Report or the screen capture to the printer.

NOTE: The content of a Mark Report is contained within the Comprehensive Report for the procedure.

12.1.5 Viewing

To view, edit, analyze and delete scans contained with the currently selected procedure

touch the “**View**” control, ,. This will load all the scans from the currently selected procedure into the View Phase of Review Mode.

The procedure and scans may be navigated, viewed, analyzed, edited and deleted in a manner similar to the Scan Phase of Acquisition Mode.

See Section 10 Reviewing, Measuring, and Annotating Scans for more information and guidance.

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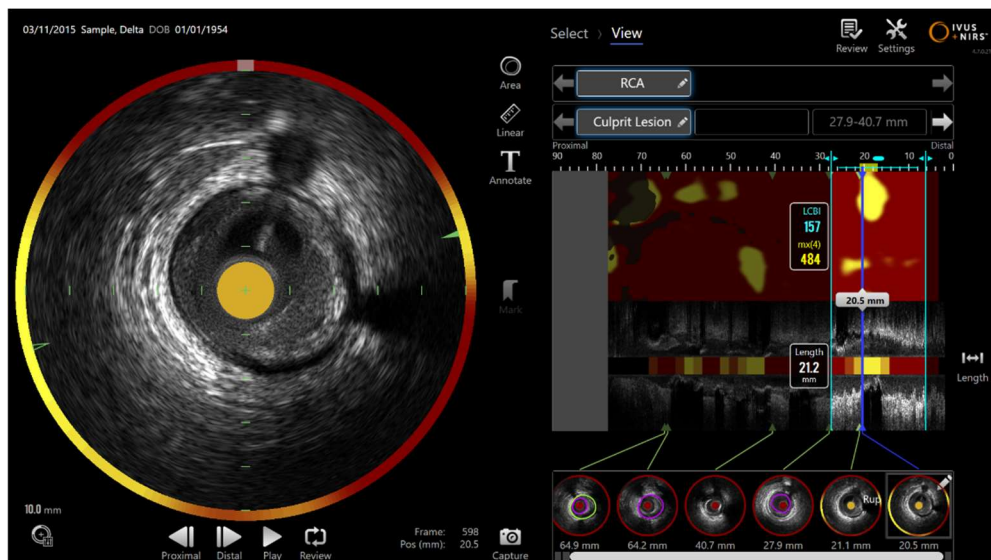


Figure 12-6: View Phase of Review Mode.

NOTE: Changes to Marks, regions, measurements, and annotations during the View Phase will become part of the saved procedure data when returning to the Select Phase.

Touch **Select**, **Select**, in the Progress Strip control or the Makoto™ Mode Toggle control to return to the Select Phase of Review Mode.

12.2 Exporting and Archiving

The Makoto Integrated Intravascular Imaging System™ provides several methods and formats for exporting data from the system. There are two configurable expedited methods for exporting and one method for a customized export.

Single or multiple procedure selections may be exported from the system for the purposes of archiving or other use. After making the desired procedure selections, use the Export Destination controls to initiate the data transfer.

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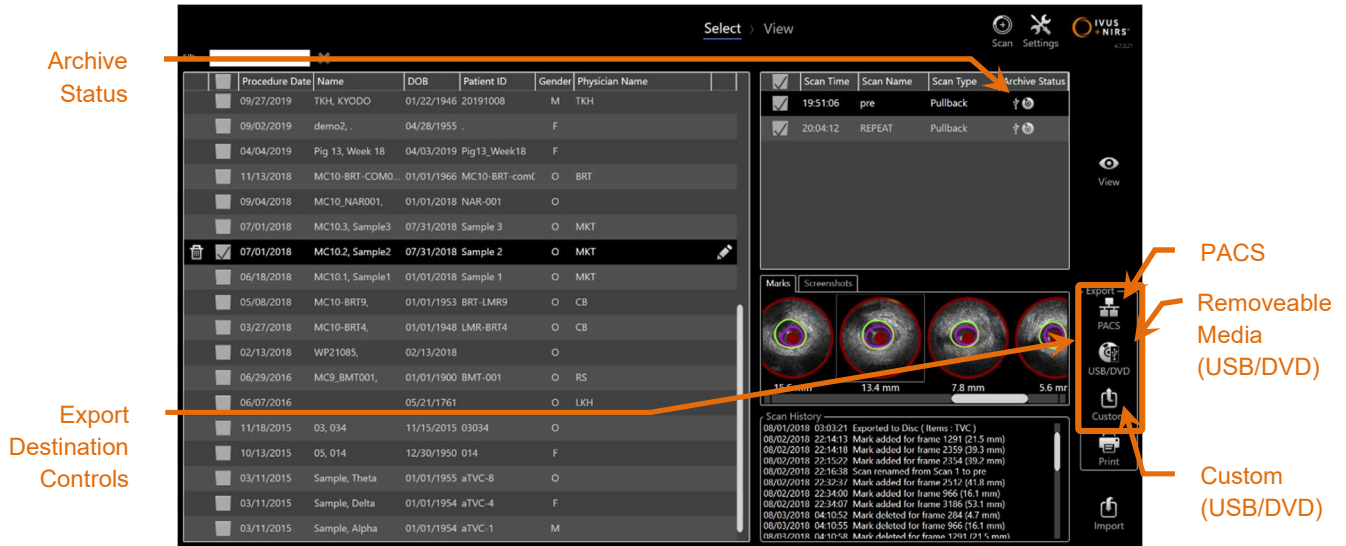


Figure 12-7: Select Phase with Export Destination controls highlighted.

Upon completion of the export the Scan List will update with the archive destination in the Archive Status column.

12.2.1 Configuring Export Destinations

Default export formats and compression can be configured for the PACS and Removable Media (USB/DVD) destinations.

Please see Sections 13.4 and 13.9 for more information on how to configure these defaults.

12.2.2 PACS Export




Ensure that cables originating from or connecting to the Makoto Integrated Intravascular Imaging System™ lay flat on the floor.

Data from the Makoto Integrated Intravascular Imaging System™ may be stored in the hospital PACS system if the systems have been properly configured. PACS systems will accept data that has been formatted using the DICOM standard.

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The system is designed to be connected to a protected hospital network for the purpose of direct transfer of Makoto Integrated Intravascular Imaging System™ data to a network storage solution such as PACS. Connect a compatible shielded Cat5e or Cat6 cable to the PACS connector or Infraredx Mobile Integration cable to the X-Ray connector on the right side of the Makoto™ Console.

Configure the PACS connection parameters using the guidance provided in Section 13 System Settings.

Touch the PACS control, , to begin the transfer of checked procedures to the configured destination.



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 Integrated Intravascular Imaging System™ to an IT network.

12.2.3 Removable Media (USB/DVD) Export

Data from the Makoto Integrated Intravascular Imaging System™ may be exported to removable media, either USB or Blu-Ray/DVD/CD writeable media.

The system will automatically check for available removable media in the system USB ports and optical media drive.

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Review the procedure and scan selections and the total export size. Confirm export file type formats.

If the desired export size is less than the available space on the export destination media, touch the desired media to begin the export. If the estimated export size is too great for the media, review the formats and procedure selections to reduce the size of the export.

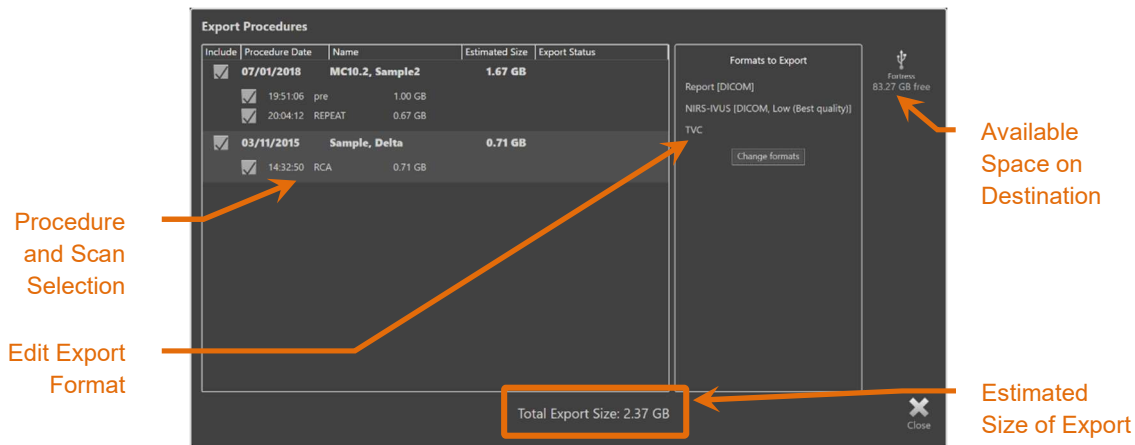


Figure 12-8: Export to Removable Media prompt.

Uncheck individual scans or whole procedures to reduce export size.

See Section 13.9 for more information on setting and changing the default export formats.

NOTE: An open session optical media disc can be created that will accept multiple exports by unchecking “Finalize disc” in the USB/DVD export options outlined in Section 13.9.

12.2.4 Custom Export

Data from the Makoto Integrated Intravascular Imaging System™ may be exported to removable media in customized ways. This method of export will require selection, or confirmation, of the data formats and storage destination. This method will also permit the user to remove identifiers from the data set as desired.

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
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Identifying information contained within the text of annotations on frames or scans will not be modified.

NOTE: Custom Export is useful for non-routine export of data or for research applications that require anonymization.

NOTE: Custom Export is only available for single procedure export.

Select the desired procedure and scans by touching their entries in the Procedure and Scan lists. Touch the Custom Export control, , to bring up the Custom Export window.

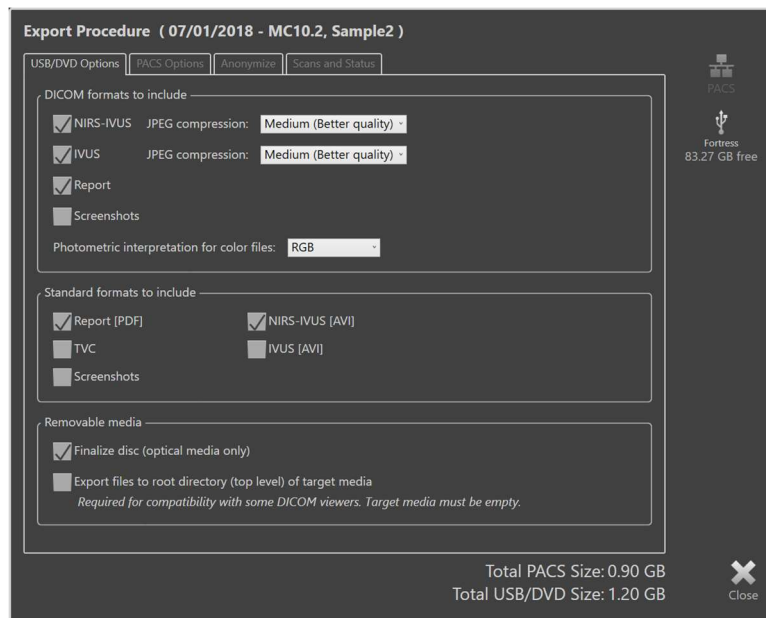


Figure 12-9: Custom Export window for setting data types and formats for export to removable media.

Either confirm the last data format settings used for removable media or adjust as needed for this export. See Section 13.4 for more information about data types and formats.

See Section 13.9 for more information about finalizing optical media.

If the intended DICOM player requires the DICOMDIR to be written to root level of the desired removable media, then check the “Export files to root directory (top level) of target media” option. This option requires the target media to be empty.

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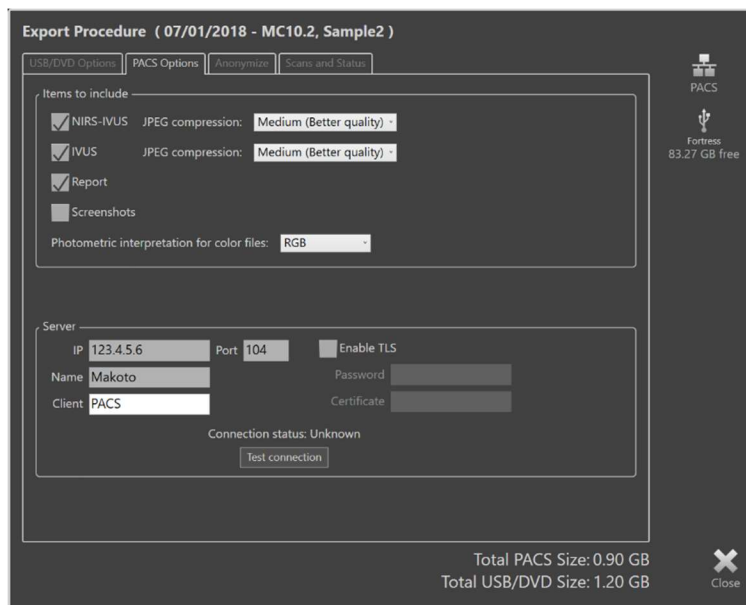


Figure 12-10: Custom Export window for configuring alternative network storage location.

If the Custom Export data will be sent via network then either confirm or adjust the DICOM data files and compression settings. Configure an alternate PACS server to send the custom data.

NOTE: The PACS items to include and PACS settings for a Custom Export will not affect standard PACS export settings.

NOTE: Many analysis programs that can analyze Makoto™ System data accept network transfer of DICOM information. Use the Custom Export to configure the network address of analysis workstations if they are different than the hospital medical record PACS.

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Export Procedure (07/01/2018 - MC10.2, Sample2)

USB/DVD Options | PACS Options | **Anonymize** | Scans and Status

☒ Anonymize procedure information

Patient

Name: S (Last) T (First) MI (Middle Initial)

Patient ID: abcdefg

Date of Birth: 01/01/2021

Gender: ☐ Male ☐ Female ☐ Other

Procedure

Procedure ID: Accession ID:

Physician Name: Catheter Lot:

Procedure Date: 07/01/2018

Total PACS Size: 0.90 GB
Total USB/DVD Size: 1.20 GB

Close

Figure 12-11: Custom Export window for anonymization of the procedure record.

Make the data anonymous by utilizing the “Anonymize” functions. Check the anonymize box and enter the desired alternate information.

NOTE: Anonymization will not change the original data remaining on the system.

NOTE: Anonymization features will not affect the procedure time, any notes, comments, or annotations made within the scans.

NOTE: Anonymization features will obscure patient name and date of birth information, but will not affect the other content of screen captures.

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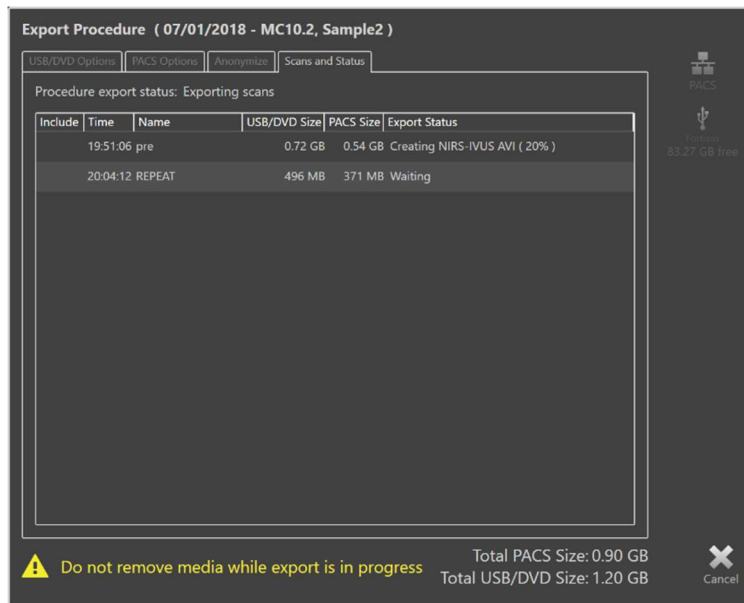


Figure 12-12: Custom Export window with scan export to USB in progress.

Review the size of the data to be exported to ensure that it will fit on the destination media. Make adjustments to your selections as required.

Touch the removable media destination to begin transfer to the destination in the file types, formats and compressions that have been configured.

12.3 Importing Data

Procedure and Scan data may be imported onto the Makoto Integrated Intravascular Imaging System™ for viewing, editing, measuring, and re-export.

NOTE: Data archived in TVC Format may be imported onto any Makoto Integrated Intravascular Imaging System™ of a compatible model number for later viewing.

The Makoto Integrated Intravascular Imaging System™ will accept TVC Format data (*.tvc from TVC-MC10 or TVC-MC9) or TVC Export data (*.zip from TVC-MC8 or TVC-MC8x) generated by this system or another TVC Imaging System. This data may be imported from Blu-Ray, DVD or USB sources.

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12.3.1 Importing Conflicts

If the data already exists or the imported scan procedural or patient data are similar to data already on the system, then additional input from the user may be required in order to complete the action.

Conflict resolution will occur after all import attempts have been processed. In this way, all conflicts can be resolved at one time greatly facilitating batch import.

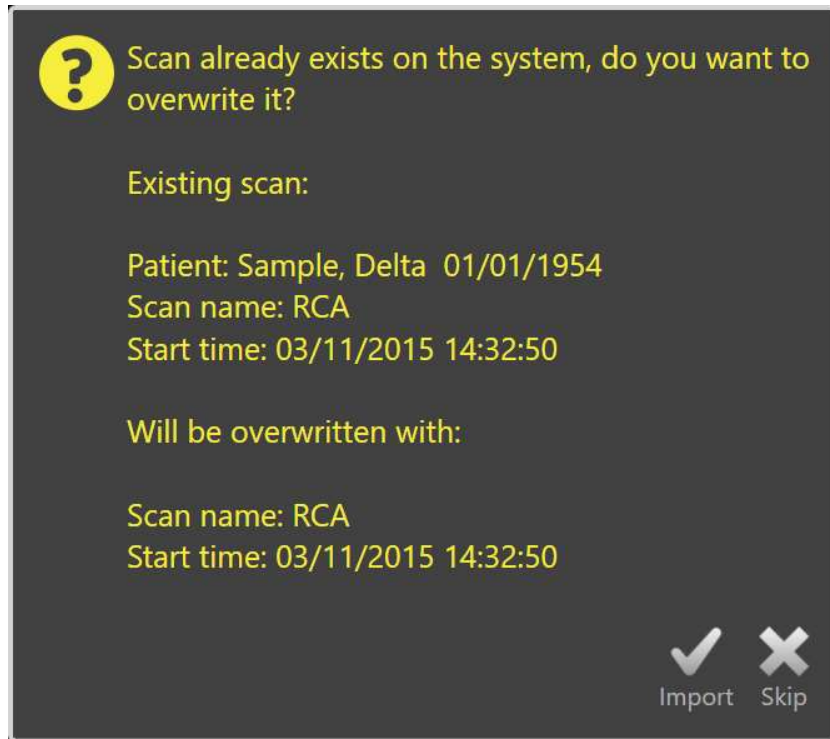


Figure 12-13: Import Conflict prompt. Proceed with resolution and overwrite or cancel import of this conflicting file.

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When the import conflict prompt appears, choose:

Import To proceed with conflict resolution. If there are no changes in procedure or patient data, then the existing file on the system will be overwritten. If there are differences in procedure or patient data then the user will be prompted to decide on the appropriate information.

Or

Skip This conflicting import will be skipped and the user will be prompted to resolve other conflicts with the import batch.

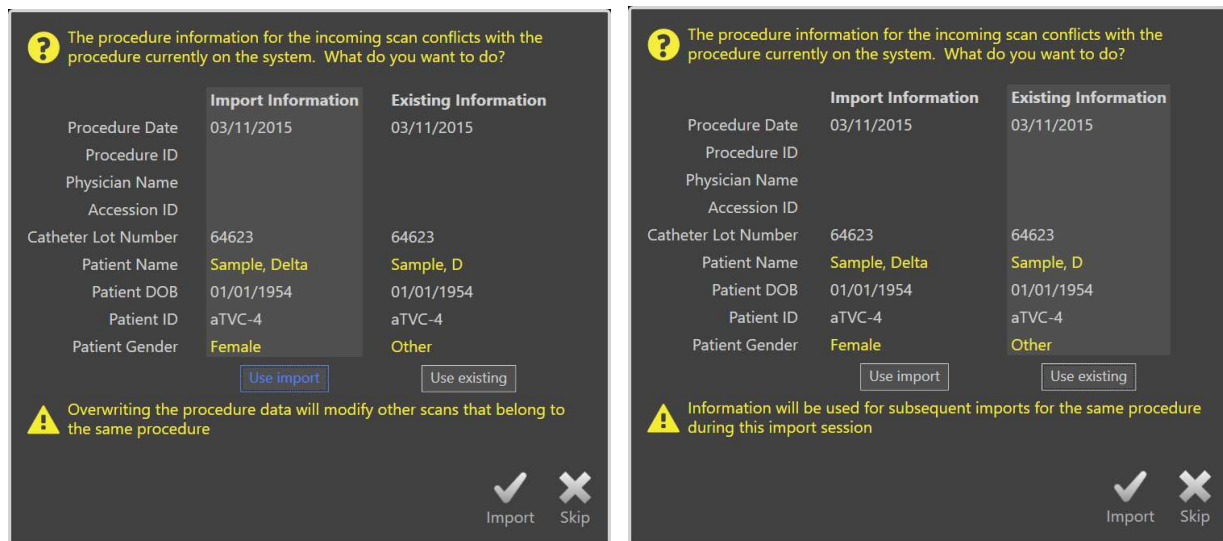


Figure 12-14: Import conflict resolution prompt.

If the user chooses to resolve the conflict with the import and procedure or patient information has changed, the user must choose:

Use Import To use the procedure and patient information from the imported file. This decision will apply to other scans imported for this procedure during this batch import AND will update any scans already on the system belonging to the same procedure.

Or

Use Existing To use the procedure and patient information already in system memory to update the imported file. This decision will apply to other scans imported for this procedure during this batch import.

Or

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Skip This conflicting import will be skipped and the user will be prompted to resolve other conflicts with the import batch.

Selecting Import will proceed with importing this procedure data based on the selection.

12.4 Deleting Scans & Procedures

Procedures and Scans stored on the system may be deleted to make more space available in the local memory.

Entire procedures may be deleted, one at a time, from the Select Phase of Review

Mode. Touch the procedure to select it, then touch the Delete control, . This will require confirmation of the action as deletion cannot be undone.



Deletion of data from the system is permanent and CANNOT be undone.

Scans may be deleted during the View Phase or the Scan Phase by deleting the scans individually by opening the Scan Edit window. See Section 10.2.9 Delete Scan for more information and guidance on this feature.

NOTE: The last scan in a procedure cannot be deleted during the View Phase. Return to the Select Phase and delete the procedure to completely remove the procedure from the system.

NOTE: Deleting a scan will delete all associated screen captures and measurements.

The Makoto Integrated Intravascular Imaging System™ is not designed to be a permanent data storage location. The customer is strongly encouraged to develop a data back-up and archiving plan that includes periodic deletion of data from the system.

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The Makoto Integrated Intravascular Imaging System™ is not intended as a permanent data storage or archive location.

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13 System Settings

Local settings of the Makoto Integrated Intravascular Imaging System™ may be adjusted to meet the needs of the user. The user may configure network communication settings, default export formats, adjust display parameters and access system diagnostic utilities.

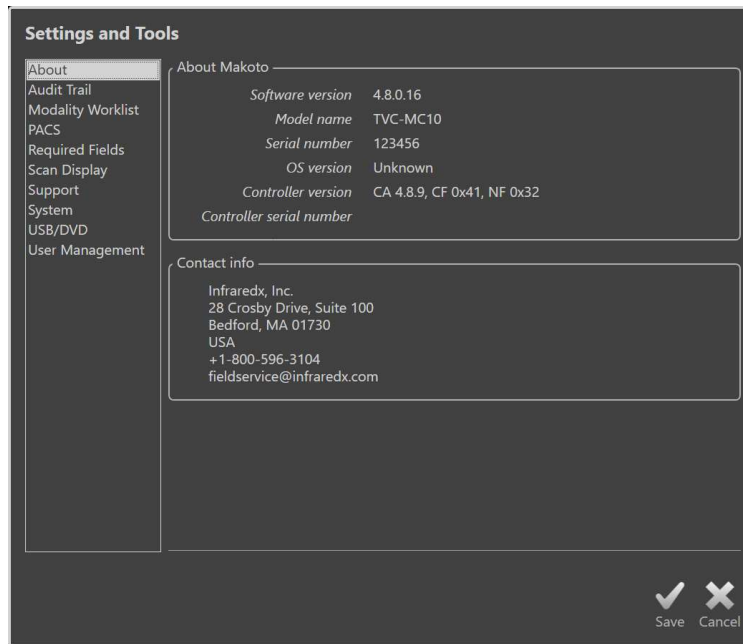



Figure 13-1: System Settings, About section. TVC-MC10 model shown.

NOTE:

The user must 'Save', , the changes to settings for them to take effect.

NOTE:

The figures in this section are visible to users with Administrator permissions. Some Settings are restricted due to the active user's permission levels.

13.1 About

This System Settings section will provide information about model number of the system as well as current installed software version numbers.

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Contact information for the customer's sales and/or service provider is available in this location.

13.2 Audit Trail

This section is available to Administrator users. This section provides a display of log in, log out, and user management events for each user of the system during the specified date ranges. The system login/logout audit log may be exported to desired available removable media in *.csv format.

13.3 Modality Worklist

The Modality Worklist network location and connection credentials can be configured by completing the fields in this section.

Settings and Tools

About
Audit Trail
Modality Worklist
PACS
Required Fields
Scan Display
Support
System
USB/DVD
User Management

Server

IP 128.1.1.1 Port 104 ☐ Enable TLS

Name Makoto Password

Client PACS Certificate

Connection status: Unknown

Test connection

Save Cancel

Figure 13-2: System Settings, Modality Worklist.


13.3.1 Modality Worklist Server Connection Settings

To use the Modality Worklist semi-automatic procedure setup options, the network address of the Worklist server must be configured. To configure the address enter the following information:

IP	The internet protocol, version 4, address of the Worklist server.
Port	The communication port on which the Worklist server expects communication. This is typically port 104.

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Name	The Worklist server network name.
Client	The name by which the Makoto Integrated Intravascular Imaging System™ will be identified on the network.
Secure TLS	Check or uncheck whether the Worklist server requires secure credentials to access. If checked, provide the necessary password and certificate.

Touch the Test Connection, , to ensure that the Worklist server and Makoto Integrated Intravascular Imaging System™ can communicate. Contact your service representative or Infraredx customer service for assistance in configuration.

13.4 PACS

In this section of System Settings, configure the data types, PACS server location and credentials.

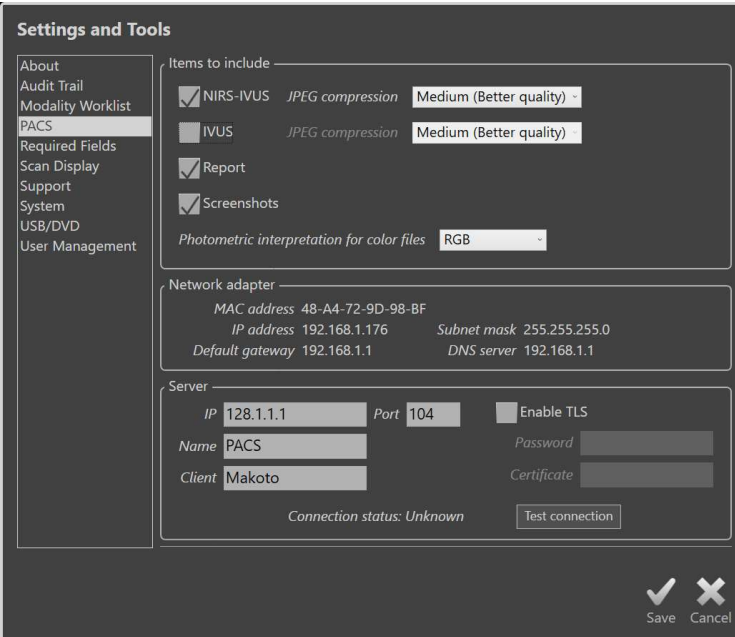


Figure 13-3: System Settings, PACS section.

13.4.1 Items to Include

There are several types of data and reports that can be generated from the Makoto Integrated Intravascular Imaging System™.

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These file types and formats are described in the table below:

Table 1: Available data file types and formats

File Type	Available Formats		Description
	DICOM	Standard	
NIRS-IVUS	Yes	*.avi	A loop of the recorded transverse frames of NIRS and IVUS data. Live IVUS and Frame recordings will produce only IVUS or grayscale images.
IVUS	Yes	*.avi	A loop of the recorded transverse frames of IVUS data only.
Report	Yes	*.pdf	A report that summarizes patient information, procedure details, annotations, measurements, regions and Marks.
TVC	No	*.tvc	A file that contains the NIRS and IVUS data in the native system format.
Screen Shot	Yes	*.png	Screen captures generated by the system and recorded by the user.

13.4.2 JPEG Compression

The compression settings of the DICOM data format can be adjusted to improve image quality or reduce data file size.

The Makoto Integrated Intravascular Imaging System™ offers JPEG compression to produce low, medium, or high compression image files.

Table 2. DICOM Compression Settings

Compression Setting	Image Quality (qualitative)	Image Quality Setting (1-100)	File Size (qualitative)
Low	Best	100	Large
Medium	Better	80	Medium
High	Good	50	Small

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13.4.3 Photometric Interpretation for Color DICOM Files

The DICOM standard provides for different methods of encoding color image information. On the Makoto Integrated Intravascular Imaging System™ choose from either “RGB” or “YBR Full 422”.


13.4.4 Network Adaptor

Information related to the Makoto Integrated Imaging System™ network adapters that may be useful for connecting the system to the hospital network can be found in this section.

13.4.5 PACS Server Connection Settings

To use the PACS export option, the network address of the PACS server must be configured. To configure the address, enter the following information:

IP	The internet protocol, version 4 (IPv4), address of the PACS.
Port	The communication port on which the PACS expects communication. This is typically port 104.
Name	The PACS server network name.
Client	The name by which the Makoto Integrated Intravascular Imaging System™ will be identified on the network.
Enable TLS	Check or uncheck whether the PACS requires secure credentials to access. If checked, provide the necessary password and certificate.

Touch the Test Connection, , to ensure that the PACS and Makoto Integrated Intravascular Imaging System™ can communicate. Contact your Service Representative or Infraredx Customer Service for assistance in configuration.

13.5 Required Fields

The system Setup Phase can be configured to require particular fields be completed prior to closing procedures or editing the information related to completed procedures. The required fields can be set by selecting the field from the “Not Required” list and then clicking or touching the “Add >>” button. Select fields in the “Required” list and click or touch “<< Remove” to reduce the requirements.

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Settings and Tools

- About
- Audit Trail
- Modality Worklist
- PACS
- Required Fields**
- Scan Display
- Support
- System
- USB/DVD
- User Management

Information required to close a procedure

Not required	Required
Patient Last Name	Patient Date of Birth
Patient ID	Patient Gender
Procedure ID	
Physician Name	

Add >> << Remove

Save Cancel

Figure 13-4: System Settings, Required Fields section.

13.6 Scan Display

The Scan Display section of System Settings permits customization of some visual aspects of the Scan Phase and View Phases.

Settings and Tools

- About
- Audit Trail
- Modality Worklist
- PACS
- Required Fields
- Scan Display**
- Support
- System
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Global

☒ Show transverse measurements

Lumen review range +/- 1 frames

Scan defaults

☒ Show longitudinal Block Level Chemogram

☒ Show transverse Chemogram Block

mx LCBI window size 4 mm

Save Cancel

Figure 13-5: System Settings, Scan Display section.

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13.6.1 Transverse Measurements

Use this toggle to view or conceal transverse measurements and results on the display. Collapsing the measurement results will also hide the measurement contours. When opening scans for review, the measurements will be hidden and the results will be collapsed.

13.6.2 Lumen Review Range of Frames

Use this control to vary the range of frames that will be played when Lumen Review function is activated, see Section 10.3.2 Lumen Review.

13.6.3 Longitudinal Block Level Chemogram Visibility

The visibility of the Block Level Chemogram may be updated based on the user preference. These changes will apply as a default to all new recorded scans. The visibility of the Block Level Chemogram on individual scans may be set by editing the scan properties, Section 10.2 Editing Scans.

NOTE: To adjust the visibility of the Longitudinal Block Level Chemogram on an individual scan see Section 10.2 **Editing Scans**.

13.6.4 Transverse Chemogram Block Visibility

The visibility of the Chemogram Block in the center of the transverse IVUS may be updated based on the user preference. These changes will apply as a default to all new recorded scans. The visibility of the Chemogram Block on individual scans may be set by editing the scan properties, Section 10.2 Editing Scans.

NOTE: To adjust the visibility of the Chemogram Block on the transverse IVUS image on an individual scan see Section 10.2 **Editing Scans**.

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13.6.5 mx LCBI Window Size

Use this control to vary the size of the default scan max LCBI window size on the display. Max LCBI results in reports will generate using the current setting for the max LCBI window size. This value may be set using the slide control provided in a range from 1 mm to 10 mm, in 1 mm increments.

NOTE: To adjust the mxLCBI window on an individual scan see Section 10.2 **Editing Scans**.

13.7 Support

This section of System Settings provides controls for exporting system log files. These files provide useful information to service personnel in diagnosis of system performance issues.

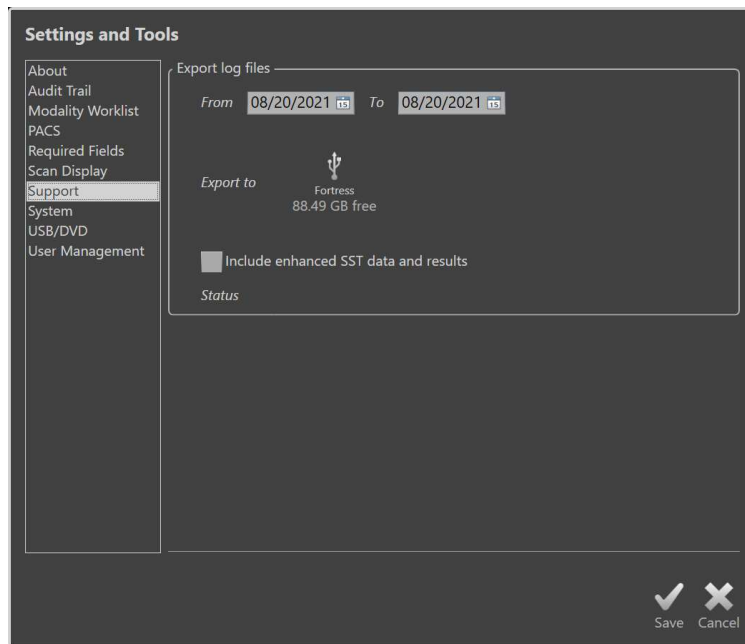


Figure 13-6: System Settings, Support section.

Set the desired date range using the provided controls, decide on inclusion of enhanced SST data and results files, and then choose the destination where the files will be copied.

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The files generated by this utility do not contain any protected health information.

13.8 System

This set of Settings parameters are used to configure system operation or labeling parameters. Some changes to these settings will require a re-start of the system to enable.

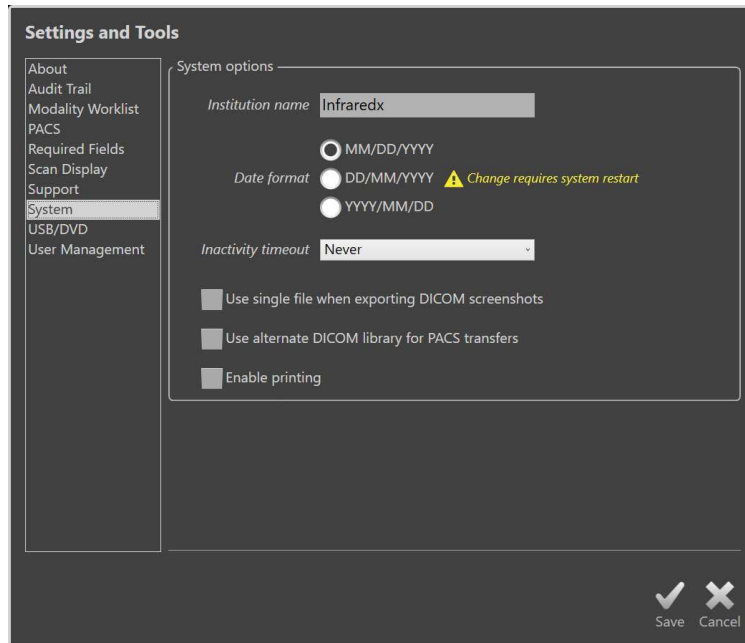


Figure 13-7 System Settings, System options section.

13.8.1 Institution Name

Use this field to configure the name of the institution as it will appear within the header of DICOM files or other reports generated by the system.

13.8.2 Date Format

Use this option to configure the date format displayed by the system on screen and in reports.

13.8.3 Inactivity Timeout

Use this option to configure the amount of time that the system must remain idle before the system automatically logs out the active user.

The system will not automatically log out during an active procedure.

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13.8.4 Single File DICOM Screen Shots

Use this option to consolidate all the recorded screen shots for a scan into a single DICOM frame stack of images.

13.8.5 DICOM Transfer Method

The Makoto Integrated Imaging System™ maintains ability to transfer or communicate DICOM files to a PACS in two ways. The primary method is enabled by default. Some PACS systems are limited in the PACS communication methods that will be accepted. Check this option to use the alternate communication method for PACS transfers.

This communication method does not impact the content of the DICOM file being transferred.

13.8.6 Enable Printing

Use this option to enable the Print button on marked frames and the Select Phase of Review Mode. A compatible printer must be enabled to print reports from the Makoto. Contact the Makoto™ Service provider for assistance in configuring a compatible printer.

13.9 USB/DVD (Removable Media)

The default data format options to be saved to removable media may be configured in this section of System Settings.

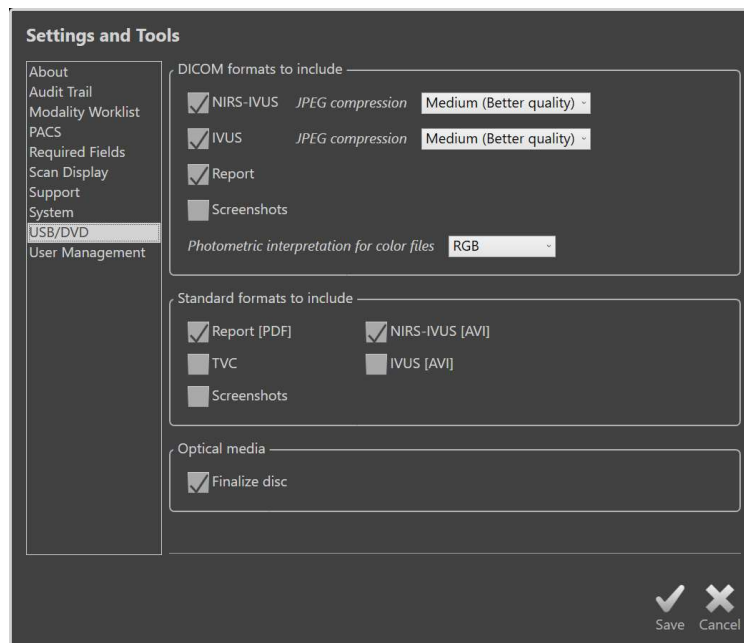


Figure 13-8: System Settings, USB/DVD section.

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13.9.1 DICOM Formats to Include

DICOM formats available, described in Table 1 above, are also available for export to removable media. Export of DICOM and standard file formats may be combined into a single export action.

13.9.2 Standard Formats to Include

In addition to the data file types only available in DICOM format, additional data file types in standard format (non-DICOM) may be selected.

The standard formats may be more suitable for presentation creation or viewing when DICOM tools are not available.

13.9.2.1 AVI Compression

The avi compression settings of the IVUS or IVUS+NIRS data is set to the following codecs: XviD.

13.9.3 Optical Media

Multi-session recording is supported when exporting to optical media (CD, DVD, Blu-Ray). Uncheck “Finalize disc” to permit additional exports to the same media.

13.10 User Management

This section is available to Administrator users. This section of settings is for managing user lists, editing permissions of users, setting or changing passwords or replicating user profiles on other Makoto Integrated Imaging Systems™.

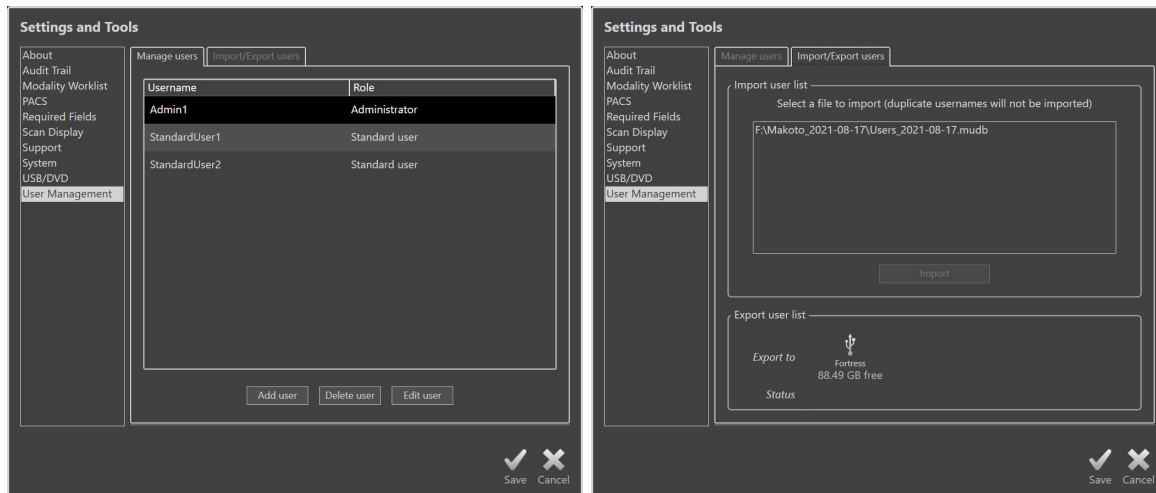


Figure 13-9. System Settings, User Management section. Manage Users (left) and Import/Export Users (right).

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13.10.1 Manage Users

A list of registered can be viewed and edited. Administrators are permitted to add, delete, or edit user profiles.

13.10.1.1 Administrator Profile

This profile is established to create and maintain other established user profiles. The Administrator profile can configure all system settings accessible to the institution including PACS and Modality Worklist connectivity. The Administrator profile has access to all patient data on the system and may import and export data.

13.10.1.2 Standard Profile

This is the profile used by typical users of the Makoto Integrated Imaging System™. These users must provide valid login credentials. This profile may have limited access to some configuration options of the system. Patient data can be viewed and may be imported or exported to configured destinations.

13.10.1.3 Anonymous Profile

This is the profile used when a valid Login is not completed due to use of the “Skip” function. This profile does not have permission to view other procedure or patient data on the system other than the data collected during the current active session. Configuration of system settings and data export options are limited.

13.10.1.4 Service Profile

A factory set profile for Service Engineers is pre-configured. This profile accessible to authorized service personnel for the purposes of configuring the Makoto for the institution or restoring Administrator User profiles.

13.10.2 Import/Export Users

13.10.2.1 Import Users

Connected media will be searched for valid Makoto™ User Data Base files. Available files will be presented. To import a user database file from another Makoto Integrated Imaging System™, select the desired database from the available list by clicking or touching the file name and then click or touch “Import”. Any new users found in the data base file will be added to the system.

13.10.2.2 Export Users

Touch the removable media destination to make a back up of the user profiles contained on the system. This file may be used to replicate the user profiles onto other Makoto Integrated Imaging Systems™ to ensure common user credentials across all Makoto™ maintained by the Institution.

14 Video Export & X-Ray System Integration

The Makoto Integrated Intravascular Imaging System™ may transmit video, data, or share control with a connected, compatible fluoroscopy X-ray system.

Utilization of the features outlined in this section may result in additional cable connections from fixed locations to the Makoto™ Console.



WARNING

Ensure that cables originating from or connecting to the Makoto Integrated Intravascular Imaging System™ lay flat on the floor.

14.1 Digital Video Output

Video signal may be exported from the Makoto™ System by connecting an external monitor to the system with a DVI-D cable. Connecting the DVI-D cable to the Video Out connector will export a 1920x1080 pixel image replicating the Physician Monitor display.

Optionally, the exported video resolution can be configured to 1600x1200 pixel (4:3 aspect ratio), please contact your Service Representative or Infraredx Customer Service for assistance.

15 Glossary of Terms

Block Level Chemogram	A simplified representation of the Chemogram information segmented into discrete blocks that are not dependent on rotation position information.
Chemogram	A map in the form of a graphical representation indicating the likelihood that lipid core containing plaques of interest are present.
Chemogram Block	A single segment in the block level Chemogram.
Chemogram Halo	A representation of the portion of a Chemogram located at a particular transverse IVUS frame that is displayed with a color ring around the transverse IVUS that is rotationally registered.
Console	The main component of the Makoto Integrated Intravascular Imaging System™; it contains the laser, software, power supply and computer.
Console User Interface	Provides the user an interactive interface to collect or review data using onscreen control buttons.
Good Spectra Indicator	Graphical display to represent the number of valid spectra recorded during a pullback acquisition.
Guide Catheter Mask	Included in the software package to automatically detect a guide catheter. This feature can be turned on and off by the physician.
Guidewire Map	A map that allows the physician to identify possible artifacts, including those caused by the presence of a guidewire.
Letterbox	An appearance of displayed information where a black border appears above and below the image content to fill a screen and not distort the image contents.
Lipid Core Burden Index	A measure of the overall proportion of lipid core in the scanned artery segment on a scale of 0 to 1000 (low to high lipid core burden).

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Composite Image	The Makoto Integrated Intravascular Imaging System™ display configuration that contains the Chemogram, longitudinal IVUS, and transverse IVUS with Chemogram halo.
Umbilical	The cable connecting the Makoto™ Controller to the Makoto™ Console.
XviD	A video file compression codec that produces small manageable video files that play on many viewers.

16 Maintenance

16.1 System Information

The system consists of three major components: a console, a controller (pullback/rotation sub-system), and the catheter. These components are connected optically, electrically, and mechanically.

The system is compatible with the following accessories:

Shielded Cat5e Cable	(REF PN2690)
Shielded Cat6 Cable	(REF PN6485)
Shielded DVI-D Video Cable	(REF PN2665)
DVI-D, Optical Extension, Fiber	(REF PN0370)
Detachable DVI Module	(REF PN6497)
Medical Grade Power Supply	(REF PN0407)

The Makoto Integrated Intravascular Imaging Systems™ (TVC-MC10, TVC-MC10i) manufactured by Infraredx are designed for use with the following catheter models:

Dualpro™ IVUS+NIRS Imaging Catheter	(REF TVC-C195-42)
Infraredx Clarispro™ HD-IVUS Imaging Catheter	(REF TVC-E195-42)

The Makoto Integrated Intravascular Imaging System™ console and Makoto™ Controller specifications are listed below. The imaging catheter specifications can be found in the associated catheter instructions for use documentation that is included in the catheter package.

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16.1.1 Physical

- Stationary Console (excluding cables)
 - Size: 9.5in x22.75in x22.25in (W x H x D) = (24 x 58 x 57)cm
 - Weight: 71lb = 32kg
- Workstation (excluding cables)
 - Monitor
 - Screen Size: 15.6" diagonal touch screen monitor (1920x1080p) = 39cm
 - Weight: 10lb = 4.5kg
 - Integration Interface Module
 - Size: 9.25in x3.5in x11.75in (W x H x D) = (23 x 8 x 30)cm
 - Weight: 5lb = 2.25kg
- Local Junction Box (excluding cables)
 - Size: 6in x3in x8in (W x H x D) = (15 x 8 x 20)cm
 - Weight: 3lb = 1.5kg
- Controller (excluding cables)
 - Size: 5in x6in x17in (W x H x D) = (13 x 16 x 44)cm
- Controller Storage
 - Size and weight of the storage solution may vary depending on configuration installed.
- Integration Cables
 - These items will vary depending on x-ray vendor, functions enabled, and installation location of the Stationary Console.

16.1.2 Environmental

- The console shall operate in room temperature from 60° to 90°F (15° to 32°C).
- The console shall operate in room humidity from 20% to 80% (non-condensing).
- The console shall be stored and transported in a temperature range of 10° to 120°F (-12° to 50°C).
- The console shall be stored and transported in a relative humidity of 10% to 85% (non-condensing).
- The compatible catheters shall be operated and stored at room temperature from 60° to 86°F (15° to 30°C).
- The compatible catheters have no relevant relative humidity requirement for operation or storage. Product should be kept dry.
- The compatible catheters shall be transported in a temperature range of -22° to 140°F (-30° to 60°C).
- The compatible catheters shall be transported in a relative humidity of <85% (non-condensing).

16.1.3 Electrical

- The device operates from a nominal line voltage of 100 VAC, 120VAC, 220 VAC, or 240VAC, 50 – 60 Hz, single phase. The power entry module must be manually configured for the appropriate input voltage and fusing. For operation at 100VAC or 120VAC, two 5 A fast blow high breaking capacity, 3AG fuses are used. For operation at 240 VAC, two 3 A, fast blow high breaking capacity, 3AG fuses are used.
- The device operates with a three power cords (1-Stationary Console, 1-Integration Interface Module, 1-Workstation Monitor).
- Power connection is hospital grade.
- The device is a Class I electrical device.

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- Protection Type CF Applied Part.
- The system is capable of transmitting and receiving wireless communication via Bluetooth®2.0 communication protocol.

16.1.4 Optical

- The Makoto Integrated Intravascular Imaging System™ contains a near infrared Class 1M laser.
- Laser light is transmitted from the console to the connected catheter by way of the Makoto™ Controller and connecting cables.

16.1.5 Makoto™ Controller

- Rotation speed = 960, 1800 rpm, counterclockwise viewing the connection socket.
- Longitudinal speed = 0.5, 1.0, 2.0, 10.0 mm/s.
- Full range of longitudinal movement = 155 mm (minimum).
- The Makoto™ Controller functions inside an intermediary sterile Makoto™ Controller Sterile Barrier.

16.2 Installation Responsibilities

This section describes the installation site requirements and the potential relocation of the system.

16.2.1 Customer Responsibilities

The Makoto Integrated Intravascular Imaging System™ is intended to be installed in a catheterization laboratory or similarly equipped facility. Before installation, the intended site must be prepared as described in this section. The site must have sufficient space to accommodate the system, must provide the proper electrical power configuration and receptacles, and must meet the additional environmental specifications outlined below.

It is the responsibility of the customer to ensure that the installation configuration of the Makoto Integrated Intravascular Imaging System™ (TVC-MC10i) complies with applicable requirements as described in IEC 60601-1.

16.2.2 Manufacturer Responsibilities

Installation of the Makoto Integrated Intravascular Imaging System™ is performed by a service representative. Following installation, Infraredx personnel or authorized representative will instruct designated catheterization laboratory personnel on the basic operation and care of the system; this instruction supplements the more detailed information presented in this manual.

16.3 Installation Requirements

16.3.1 Facilities Requirements

The Makoto Integrated Intravascular Imaging System™ is designed to be used in a typical certified catheterization laboratory or similarly equipped facility.

The emissions characteristics of this equipment make it suitable for use in industrial areas or hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

It may be necessary to install cables within existing cable routing or conduits. In some cases, it may be necessary to modify an existing facility to install necessary cabling or mount components.

16.3.2 Space Requirements

Sufficient floor space is required for the system. Approximately 15 inches (40 cm) of clearance is required between the rear panel of the system and the wall behind it to provide room for the power cord and to allow circulation of air from the cooling vents.

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16.3.3 Electrical Requirements

The Makoto Integrated Intravascular Imaging System™ is designed to work with the standard electrical wiring available in a catheterization laboratory.

The Makoto™ Stationary Console, Makoto™ Integration Interface Module, and touch screen monitor require power. The Makoto™ Stationary Console and Local Junction Box are equipped with an equipotential ground stud located on the units.



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.



DO NOT obstruct access to the power plug of the installed Makoto™ Stationary Console.

16.4 Environmental Requirements/Precautions

16.4.1 Air Quality

Ensure that the atmosphere is non-corrosive, with no salts or acids in suspension in the air. Acids, corrosives, and volatile materials are likely to attack electrical wiring and the surfaces of optical components.

Keep airborne dust particles to a minimum. Dust particles can cause permanent damage to optical surfaces. Metallic dust can be destructive to electrical equipment.

There is an air filter in the console. This filter will be inspected and cleaned or replaced as necessary during routine maintenance visits.

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16.5 General & Contact Information

In general, the Makoto Integrated Intravascular Imaging System™ requires no special maintenance by the user. Routine care of the Makoto™ Controller as well as cleaning and disinfection of the exterior of the system are covered in the Section 16.5.2 Cleaning and Disinfection.

Fault or warning indicators are described in Section 16.6 Warning and Fault Indicators with the recommended responses.

All other maintenance and service must be performed by a qualified service representative. Routine preventive maintenance of the system should be performed by a qualified service representative at least every 12 months. At each of these visits, the service representative checks and adjusts the functionality of the system as necessary.

16.5.1 Contact Information:

For all service, maintenance, and replacement part requests please contact your local sales and service provider or call Infraredx, Inc. at: +1-800-596-3104.

16.5.2 Cleaning and Disinfection

The exterior of the Makoto Integrated Imaging System™ and Makoto™ Controller may be cleaned using a soft cloth moistened with a solution of mild soap and water. Harsh detergents should not be used. If it becomes necessary to disinfect the exterior of the Makoto™ Console or Makoto™ Controller, a soft cloth moistened with hospital-grade disinfectant may be used.



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.

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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.

16.6 Warning and Fault Indicators

During Makoto Integrated Intravascular Imaging System™ use, the data acquisition software checks the electrical communication link with the Makoto™ Controller and the laser light source. If the devices are not attached or communication with either device is not functioning properly, then the software alerts the user with a fault message that appears at the top of the screen.

If this fault is encountered then contact your local service provider or Infraredx customer service.

Beyond the warnings and fault indicators listed above, there are no other warning or fault indicators on the Makoto Integrated Intravascular Imaging System™.

16.7 Troubleshooting

Symptom	Possible Causes	Remedies
System will not power on	System not plugged in	Plug in system, See Section 6.
	Fuses not functioning	Contact service provider, see Section 13.1.
System will not remain powered	CPU battery is drained.	Plug system into power source between uses.
	Supplied power is unstable.	Try a different power outlet or socket. Contact service provider, see Section 13.1.
No virtual keyboard appears at login	Virtual keyboard is disabled.	Click or touch Skip to bypass login. Click or touch Options, enable Virtual Keyboard, then Log Out.
No virtual keyboard appears when text boxes are selected.	Virtual keyboard is disabled.	Touch or click Options, enable virtual keyboard,

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Symptom	Possible Causes	Remedies
Unable to Login	User name not registered.	Contact Administrator to register user.
	User name typed incorrectly	Enter username and password again.
	Incorrect password provided	Enter password again or contact Administrator to reset password.
No image on console monitor	Monitors turned off	Locate and press power button on bottom of physician monitor.
		Locate and press power button on rear of technician monitor.
	Monitors not powered	Secure power cable in monitor.
		Secure the power plug of the monitor at power socket.
		Contact service provider, see Section 13.1.
	Video feed disconnected	Secure connections of video cables to monitor.
	Internal video distribution subsystem not functioning	Contact service provider, see Section 13.1.
System software does not start, error message received	A component of the system has failed to respond during start up sequences.	Turn system off and then on. If problem persists then contact service provider, see Section 13.1.
	Operating system cannot open a necessary configuration or data file.	Turn system off and then on. If problem persists then contact service provider, see Section 13.1.

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Symptom	Possible Causes	Remedies
Touch Screen Not Responding	USB cable is loose.	Check connection of USB cable.
	Mouse is moving	Stabilize mouse or turn mouse over.
	System not properly configured for 1600x1200 video output	Contact service provider, see Section 13.1.
Review Mode Toggle disabled	Active procedure in progress with data recorded	Close procedure, see Section 11.
		Delete all scans, see Section 10.2.9.
Data Export disabled	No procedures selected	Select procedures, see Section 12.2.
	Insufficient user permissions	Contact Administrator.
Custom Export disabled	Multiple procedures selected	Reduce selections to 1 procedure, see Section 12.2.4.
	Insufficient user permissions	Contact Administrator
No procedures in Select Phase	All data removed from system.	Perform more procedures, see Section 7.
		Import data, see Section 12.3.
	Filter found no procedures or scans that apply.	Clear Filter, see Section 12.1.2.
	Insufficient user permissions	Contact Administrator
Not recognizing USB storage device	Incompatible device	Use alternate USB storage device
	Encrypted device attempting to load data or program onto Imaging System.	Use alternate USB storage device.

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Symptom	Possible Causes	Remedies
No IVUS image visible	Black Level set too high or other improper image adjustment.	Return to Factory image settings or adjust Black Level, see Section 10.8.4
	Insufficient priming of catheter	Flush catheter with additional heparinized saline or Consult catheter instructions for use.
	Catheter transducer not functioning	Exchange catheter.
IVUS Image is dim or flickers	Image settings require adjustment	Return to Factory image settings or adjust individual image settings, see Section 10.8.4
	Insufficient priming of catheter	Flush catheter with additional heparinized saline or Consult catheter instructions for use.
Guidewire Map is uniformly white.	Catheter optical fiber damaged.	Exchange catheter
Guidewire Map is uniformly black.	Catheter model does not produce chemograms.	Check catheter model and product description to confirm that NIRS data is generated, see Section 4.7.

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Symptom	Possible Causes	Remedies
Dualpro™ or Infraredx Clarispro™ Catheter will not load or connect	Controller is not in the LOAD position	Use the distal motion controls on the Makoto™ Controller until the display reads LOAD.
		Controller out of calibration. Contact service provider, see Section 13.1.
	Catheter handle is not aligned with controller socket	Orient the catheter handle with colored button up prior to insertion in the Makoto™ Controller catheter socket.
	Catheter rotating imaging core is not aligned with catheter handle.	Using the cap, turn the core so that the core colors match the color of the buttons on the handle.
Dualpro™ or Infraredx Clarispro™ Catheter will not unload or disconnect (inside rotating core stays connected after handle is removed)	Controller is not in the READY position at time of disconnection	Reconnect catheter handle and advance the controller to the READY position prior to attempting disconnection
	Catheter handle buttons are depressed during removal.	Reconnect catheter handle, adjust grip to avoid pressing the colored buttons on the catheter handle during disconnection.
		Remove sterile barrier gasket from controller socket. Insert handle through gasket and connect to controller socket inside the barrier. Attempt catheter removal again.

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Symptom	Possible Causes	Remedies
Chemogram fails to generate	Live IVUS acquisition performed.	No Chemograms are generated during Live IVUS acquisitions. Consult Section 9.1.
	Pullback distance insufficient	Repeat automated pullback acquisition with increased length, consult Section 9.2.2.
	Excessive low optical signal recorded during scanning.	Return to READY, unload then load the catheter again. Retry scan.
	Catheter fiber optics damaged	Exchange catheter, try again.
	System optical component failure.	Contact service provider, see Section 13.1.
	Catheter model does not produce chemograms.	Check catheter model and product description to confirm that NIRS data is generated, see Section 4.7.
Chemogram generates unexpectedly	HD-IVUS catheter model number read incorrectly or failed to read by RFID subsystem.	Replace catheter with new HD-IVUS catheter and try again.
Chemogram is covered with dark patches.	Biologic source of artifact: reflection of excessive thrombus	Exclude chemogram analysis in this region or repeat automated acquisition. See Section 9.3.
	Non-Biologic source of artifact: reflection of dense spacing of overlapping stents or covered stents.	Exclude chemogram analysis in this region or repeat automated acquisition. See Section 9.3.

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Symptom	Possible Causes	Remedies
	Biologic source of artifact: excessive blood depth	Exclude chemogram analysis in this region or repeat automated acquisition. See Section 9.3.
	Controller fiber optics dirty.	Contact service provider, see Section 13.1.
	Controller malfunction.	Contact service provider, see Section 13.1.
	Catheter fiber optics dirty.	Exchange catheter, try again.
	Catheter fiber optics damaged.	Exchange catheter, try again.
Controller will not return imaging core to READY position or move distally	Attempting to advance imaging core into a kinked transmission window	Follow on screen guidance. Straighten kinks attempt again. If problem persists, exchange catheter, try again.
	Catheter imaging core is bound or damaged.	Carefully remove catheter handle, then imaging core by pulling on the catheter shaft. Follow on screen guidance to exchange catheter.
Controller inner carriage is not moving when motor is running and translation buttons are pressed.	Controller has worn drive mechanism.	Contact service provider, see Section 13.1.
Catheter Lot Number is not automatically recorded	Catheter not programmed with lot number information	Enter the lot number found on the catheter packaging manually.
	Catheter lot number is read incorrectly.	Enter the lot number found on the catheter packaging manually.

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16.8 Spare Parts

For ordering information, please call your local service provider or Infraredx, Inc. by dialing:

+1-800-596-3104.

16.9 System Lifetime

The Makoto™ console and controller lifetime is 3 years. Infraredx recommends performing preventative maintenance, service repairs and system upgrades as needed.

16.10 Decommissioning the Makoto™ Imaging System

For information on safely decommissioning the system, please call your local service provider or Infraredx, Inc. by dialing:

+1-800-596-3104.

16.11 Product Disposal

Infraredx is committed to protecting the natural environment, and ensuring continued safe and effective use of this product through proper preventative maintenance, service repairs and system upgrade. Therefore Infraredx products are designed and manufactured to comply with relevant guidelines for environmental protection. As long as the product is used and maintained properly, it presents no environmental risks. However, the product may contain materials which could be harmful to the environment if disposed of incorrectly. Use of such materials is essential for the product's functions and its compliance to the statutory and other requirements.

16.11.1 Final Disposal of the Product

Final disposal is when the user disposes of the product in such a way that it can no longer be used for its intended purposes. The return, proper disposal and recovery of the medical device take place in accordance to the respective requirements of national legislation. Assuming no parts of the system housing are opened and the system is used properly, there are no risks to people or the environment.



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.

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17 Appendices

17.1 Appendix A: Warranty and Related Information

Most service support requirements that occur during the first year of your ownership of the Makoto Integrated Intravascular Imaging System™ are covered by our warranty, as explained in the following sections. For support not specifically covered under the terms of the Infraredx warranty, we will provide support on a per-call basis. Please contact the Infraredx Customer Service Department at +1-800-596-3104 for equipment support for your Makoto Integrated Intravascular Imaging System™, or for information on available service support programs.

Warranty

Infraredx warrants that all standard components of its Makoto Integrated Intravascular Imaging System™ will be free of defects in material and workmanship for a period of one (1) year. Infraredx will repair or replace, at its discretion, all defective components during this warranty period. Any such replacement may include refurbished parts or components. After the termination of the initial warranty period or any purchased extended warranty, repair services may be purchased from Infraredx at its published rates. Infraredx warrants that the software designated for use with the instrument will execute its programming instructions when properly installed. Infraredx will provide any software corrections or “bug-fixes” if and when they become available, without charge, for a period of one (1) year after installation. The warranty period will begin on the date of initial installation for hardware and software installed by Infraredx personnel unless the installation date has been delayed at your request.

The above warranties shall not apply to defects resulting from misuse, negligence or accident, including, without limitation: operation by untrained operators; operation outside of the environmental specifications for the instrument or accessories; improper or inadequate maintenance by the user; installation of software or interfacing not supplied by Infraredx; making of modifications to the instrument or the software not authorized by Infraredx; making of repairs by anyone other than Infraredx or an authorized repair agent of Infraredx.

Warranty Shipments, Returns, and Adjustments

A warranty claim must be made promptly and must be received by Infraredx during the applicable warranty period. Should it become necessary to return a product for repair and/or adjustment, a Return Merchandise Authorization (RMA) must be obtained from the Infraredx Customer Service Department (+1-800-596-3104). Infraredx will provide instructions as to how and where products should be shipped.

Any product or component returned for examination or for warranty repair shall be sent insured and prepaid via the means of transportation specified by Infraredx Customer Service.

Shipping charges for all products or components replaced or repaired under warranty shall be the sole responsibility of the buyer. In all cases, Infraredx has sole responsibility for determining the cause and nature of a product or component's failure, and Infraredx's determination with regard thereto will be final.

Decontamination of Returned Equipment

To comply with United States postal and transportation laws, equipment returned to Infraredx must be properly decontaminated with a chemical germicide that is approved for use as a hospital disinfectant. If equipment is received without having been decontaminated, Infraredx will charge cleaning costs to the customer.

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Limitations

This warranty does not cover the Dualpro™ IVUS+NIRS or Infraredx Clarispro™ HD-IVUS Catheter, and related test components, or other OEM equipment that is not included in the Makoto Integrated Intravascular Imaging System™. This warranty does not cover normal calibration, cleaning, or maintenance of the system. Any product returned to Infraredx without prior authorization shall be returned at sender's expense. Infraredx reserves the right to change or discontinue this product, its specifications, or price without prior notice.

Indemnification

Buyer agrees to indemnify and hold Infraredx harmless from and against any and all actions, suits, liabilities, claims, fines, damages, losses or expenses including reasonable attorney's fees and expenses of litigation (the "Losses") incurred by or imposed in connection with any and all actions, suits, claims or demands, brought by third parties including, without limitation, those arising from violation of local, state, or federal laws relating to the product or its use including, without limitation, Losses related to improper inspection, the injury of any person or the injury or destruction of any property, selection of patients, application, operation, or use of Infraredx products, including multiple use of single-use items, except for such Losses resulting from the sole and exclusive negligence of Infraredx, its employees and duly authorized agents. No agent, employee, or representative of Infraredx has the authority to change any of the foregoing, or assume or bind Infraredx to any additional liability or responsibility in connection with the product.

Licenses

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Infraredx WARRANTS THAT REASONABLE CARE HAS BEEN USED IN THE DESIGN AND MANUFACTURE OF PRODUCT SOLD HEREUNDER. THE SOFTWARE IS PROVIDED "AS IS" AND Infraredx DOES NOT WARRANT THAT ITS OPERATION WILL BE UNINTERRUPTED, ERROR OR BUG FREE. THE ENTIRE RISK AS TO SATISFACTORY QUALITY, PERFORMANCE, ACCURACY, AND EFFORT (INCLUDING LACK OF NEGLIGENCE) IS WITH YOU. ALSO, THERE IS NO WARRANTY AGAINST INTERFERENCE WITH YOUR ENJOYMENT OF THE SOFTWARE OR AGAINST INFRINGEMENT. **THIS WARRANTY AND THE REMEDIES SET FORTH ABOVE ARE IN LIEU OF AND EXCLUDE ALL OTHER WARRANTIES NOT EXPRESSLY SET FORTH HEREIN, WHETHER EXPRESSED OR IMPLIED BY OPERATION OF LAW OR OTHERWISE, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.**

HANDLING, STORAGE, CLEANING AND STERILIZATION OF THE PRODUCT AS WELL AS OTHER FACTORS RELATING TO THE PATIENT, DIAGNOSIS, TREATMENT, SURGICAL PROCEDURES, AND OTHER MATTERS BEYOND INFRAREDx's CONTROL DIRECTLY AFFECT THE PRODUCT AND THE RESULTS OBTAINED FROM ITS USE. INFRAREDx **SHALL** NOT BE LIABLE FOR ANY

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INCIDENTAL OR CONSEQUENTIAL LOSS, DAMAGE, OR EXPENSE DIRECTLY OR INDIRECTLY ARISING FROM THE USE OF THE PRODUCT (INCLUDING WITHOUT LIMITATION LOSS OF USE, LOST BUSINESS, REVENUE, PROFITS, DATA OR GOODWILL) EVEN IF INFRAREDx IS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. INFRAREDx NEITHER ASSUMES, NOR AUTHORIZES ANY OTHER PERSON TO ASSUME FOR IT, ANY OTHER OR ADDITIONAL LIABILITY OR RESPONSIBILITY IN CONNECTION WITH THE PRODUCT.

INFRAREDx ASSUMES NO LIABILITY WITH RESPECT TO DEVICES THAT ARE REUSED, REPROCESSED, OR RESTERILIZED AND MAKES NO WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING BUT NOT LIMITED TO MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO SUCH DEVICES.

Export Restrictions

Unless otherwise agreed to by Infraredx, if you export the Makoto Integrated Intravascular Imaging System™ you shall assume all responsibility for obtaining any required export authorization and shall comply with all the applicable laws, rules, and regulations of all governmental authorities, including, without limitation, the Export Administration Act. You shall not export or re-export technical data supplied by Infraredx or the direct product of such data in violation of applicable export regulations. You acknowledge that the software is of US-origin. You agree to comply with all applicable international and national laws that apply to the software, including the U.S. Export Administration Regulations, as well as end-user, end-use and country destination restrictions issued by the U.S. and other governments.

17.2 Appendix B: Summary of Ex Vivo and Clinical Studies

The Infraredx near-infrared (NIR) imaging system was developed to identify lipid core plaques of interest (LCPs) in coronary arteries. The LCP detection algorithm for this system was developed from data collected in autopsy hearts in an *ex vivo* study (CDEV3). In parallel, NIR measurements of coronary arteries were collected *in vivo* in a clinical pivotal study (SPECTACL). The *ex vivo* study prospectively assessed the accuracy of the NIR readings compared to histology, while the clinical study prospectively assessed the equivalence of the *in vivo* and *ex vivo* measurements. Later a prospective *in vivo* clinical outcomes study (LRP Study) was performed to prospectively assess the ability of NIR readings to identify patients and vessel segments at risk of major adverse cardiac events (MACE).

17.2.1 Ex Vivo Study (CDEV3)

Study Objective

The objective of the *ex vivo* study was to calibrate and prospectively validate the Infraredx NIR imaging system for the detection of LCPs. Calibration and validation of the system was accomplished using coronary arteries from autopsy human hearts in which pre-defined histologic criteria served as the comparator method.

Study Design

Calibration and validation of the Infraredx system was performed by acquiring co-registered spectroscopic and histologic data from 84 human hearts, 33 of which were used in the development of the calibration and 51 in the final validation. The calibration dataset was used to construct a multivariate discrimination model to detect the presence of LCP from NIR scan measurements. This model was then prospectively validated by testing its LCP detection performance on the validation dataset.

Each arterial segment in the calibration and validation was mounted in a fixture designed to permit perfusion with blood and precise registration of the site of NIR measurement with subsequent histologic sections. All scans were performed with an automated pullback and rotation device that pulled the optical tip along the length of the artery at 0.5 mm/s with a rotation speed of 240 rpm. Individual spectra were collected at a rate of approximately 40 Hz. With an average segment length of nearly 50 mm, this configuration resulted in an average of close to 4000 points of tissue interrogated per segment.

LCP was defined as fibroatheroma with lipid core greater than 60 degrees in non-contiguous circumferential extent, greater than 200 microns thick on average, and covered by a fibrous cap having a mean thickness of 0 to 450 microns. One histologic section was analyzed for every 2 mm cross-section (block) of artery. Histologic features of the arteries were classified by a pathologist according to the “modified AHA classification” scheme (Virmani R, Kolodgie FD, Burke AP, Farb A, Schwartz SM. Lessons From Sudden Coronary Death : A Comprehensive Morphological Classification Scheme for Atherosclerotic Lesions. *Arterioscler Thromb Vasc Biol.* 2000; 20(5):1262-1275).

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Table 1. Donor Demographics, Medical History, and Cause of Death

Characteristics	(n=51)
Demographic Profile	
Male, n (%)	36 (71)
Mean +/- SD age, years	65.9 ± 15
Medical History, n (%)	
Hypertension	31 (61)
Chronic smoker	21 (41)
Diabetes mellitus	17 (33)
Prior presentation CHF	16 (31)
Prior MI	11 (22)
Prior CABG	4 (8)
Cause of Death, n (%)	
Cardiovascular related	40 (78)
Non-cardiovascular related	8 (16)
Unknown	3 (6)

Study Endpoints

The diagnostic accuracy of the Infraredx system was assessed in three study endpoints using the area under the curve (AUC) of the Receiver Operating Characteristic (ROC) curve for two clinical uses: localized detection of LCP and determination of overall lipid core burden of a scanned artery segment.

Primary Endpoint: Image Accuracy in Detecting LCP without regard to cap thickness

Localized detection accuracy was assessed for all adequate 2 mm blocks of scanned artery using ROC analysis of the block Chemogram intensity values versus the paired histologic comparisons for blocks having a lumen diameter less than or equal to 3.0 mm. The block Chemogram intensity is the 90th percentile intensity of the Chemogram pixels in a 2 mm block of scanned artery, which visually corresponds to the 10% most yellow pixels in the block. The histologic comparison was presence or absence of LCP in each 2 mm block. Percent positive and negative agreement of the thresholded block Chemogram values were computed as the threshold was varied over all possible thresholds to sweep out the ROC curve, and the area under the ROC curve (AUC) was computed. For the primary endpoint, no restriction was imposed on the plaque cap thickness in the LCP definition.

Secondary Endpoint 1: Image Accuracy in Detecting LCP with cap thickness < 0.45 mm

This secondary endpoint used the same hypothesis and analysis methods as the primary endpoint but restricted the LCP definition to those with a cap thickness less than 0.45 mm on average. LCPs with cap thickness greater than or equal to 0.45 mm were analyzed as part of the negative group.

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Secondary Endpoint 2: Lipid Core Burden Index Accuracy

This secondary endpoint of the CDEV3 validation study supported a secondary use of the system: overall assessment of lipid core burden in a scanned artery segment using the Lipid Core Burden Index (LCBI). Accuracy of this measure was assessed for all adequate scanned artery segments using ROC analysis of the LCBI values versus the paired histologic comparisons. All lumen diameters were included in the analysis. LCBI is the fraction of Chemogram pixels of a scanned segment with intensity greater than 0.6, which visually corresponds to a transition from red to dark orange color on the Chemogram. The histologic comparison was presence or absence of any-sized fibroatheroma in the scanned segment. Percent positive and negative agreement of the threshold LCBI values were computed as the threshold was varied over all possible thresholds to sweep out the ROC curve, and the area under the ROC curve (AUC) was computed.

Study Results

The overall system AUC for detecting LCP without regard to cap thickness was found to be 0.80 (95% confidence interval 0.76 – 0.85) in arteries with lumen diameters less than or equal to 3.0 mm. When detecting LCP with caps less than 0.45 mm thick, the AUC was also 0.80 (95% confidence interval 0.76 – 0.84). The AUC for detecting the presence of any fibroatheroma along an artery segment using the LCBI was 0.86 (97.5% confidence interval 0.80 – 0.91) for all artery diameters. Table 2 summarizes the diagnostic accuracy results for the 3 study endpoints. **Figure 17-1** shows the corresponding percent agreement values as functions of the Block Chemogram intensity threshold (Primary Endpoint and Secondary Endpoint 1) or LCBI threshold (Secondary Endpoint 2).

Table 2: Accuracy Results for the Three Ex Vivo Study Endpoints

Study Endpoint	AUC
Primary Endpoint: Image accuracy in detecting LCP without regard to cap thickness ¹	0.80 (95% CI: 0.76-0.85)
Secondary Endpoint 1: Image accuracy in detecting LCP with cap thickness < 0.45 mm ¹	0.80 (95% CI: 0.76-0.84)
Secondary Endpoint 2: Lipid core burden index accuracy ²	0.86 (97.5% CI: 0.80-0.91)

¹ 51 hearts, 122 segments, 1909 2mm blocks; average lumen diameter <= 3 mm

² 51 hearts, 120 segments

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17.2.2 Clinical Pivotal Study (SPECTACL)

Study Objective

The overall study objective of SPECTACL was to assess the similarity of measurements obtained under clinical conditions to those acquired from autopsy specimens. Histopathologic comparisons were not available for the clinical patients, thereby precluding the direct evaluation of the accuracy of the *in vivo* NIR arterial images. Thus, the study used the spectral data underlying the images to demonstrate that the information acquired *in vivo* was similar to the information used in the *ex vivo* study.

Study Design

SPECTACL was a prospective multi-center clinical trial of patients undergoing elective or non-emergent percutaneous coronary intervention of a *de novo* native coronary artery lesion. Patients with stable or progressive angina, as well as patients with stabilized acute coronary syndrome, were enrolled. The SPECTACL clinical study was designed to show that the spectral features of data acquired in patients were substantially similar to the spectral features of data collected in the *ex vivo* study.

Study Period, Clinical Sites, and Enrollment

The SPECTACL pivotal study was carried out over a 21-month period at 6 clinical sites in the United States and Canada. A total of 106 patients were enrolled in the study during this period. NIR images were not obtained in 17 of these patients, resulting in data from 89 patients for analysis. Reasons for failure to acquire NIR images included inability to track vessel (7), device failure (7), procedural error (2), and improper accessory setup (1).

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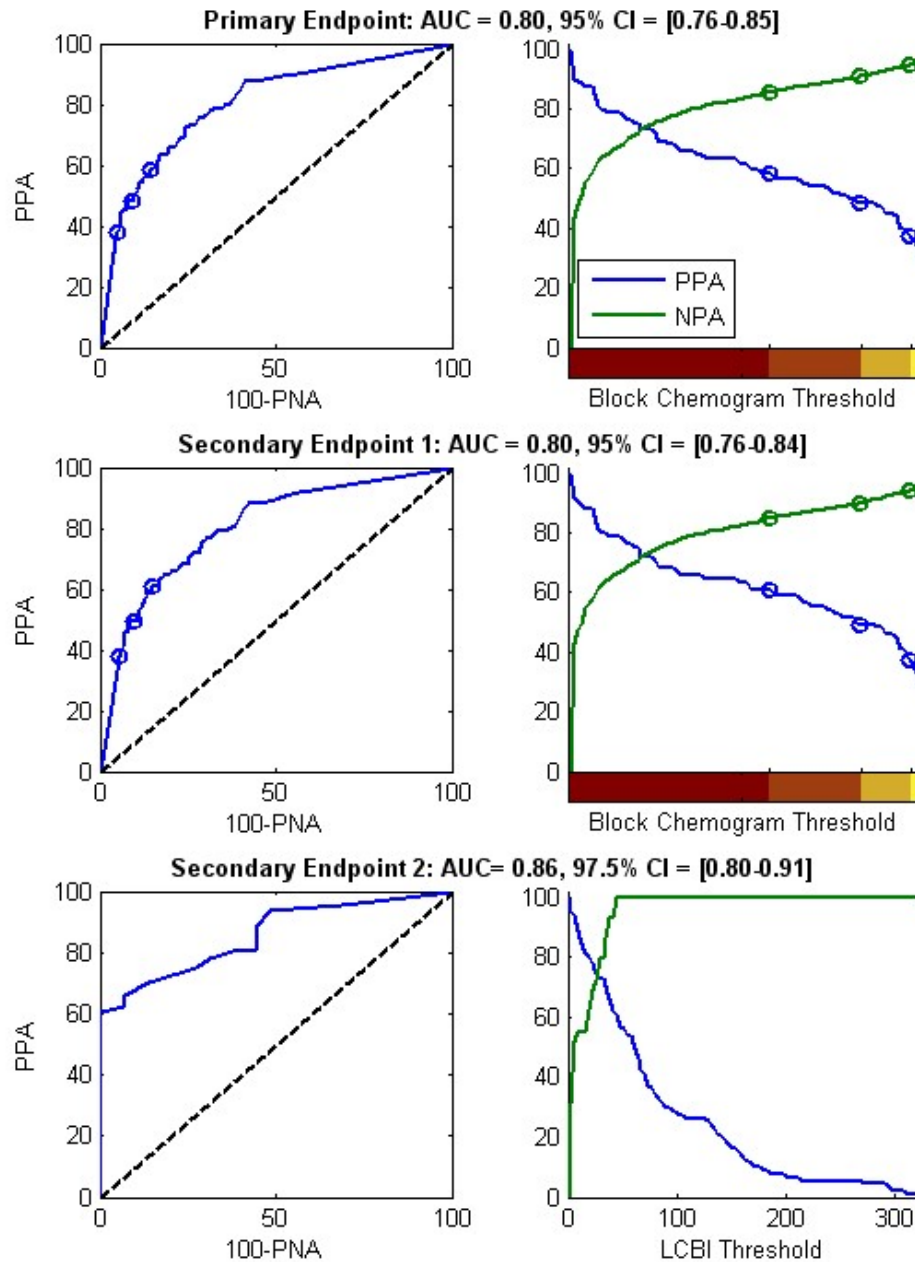


Figure 17-1. ROC curves (left column) and percent positive and negative agreement curves versus test threshold (right column) for the 3 study endpoints. A: *Primary endpoint - No cap thickness threshold*. Accuracy of the Chemogram versus histology in 2 mm blocks (51 hearts, 122 segments and 1909 2 mm blocks). The three color thresholds on the Block Chemogram (delineating red, dark orange, light orange and yellow) result in the positive and negative agreement percentages denoted by the circles. B: *Secondary endpoint 1 - A cap thickness threshold of 450 microns*. C: *Secondary Endpoint 2 - Accuracy of the Lipid Core Burden Index (LCBI) versus histology (51 hearts, 120 segments)*. PPA: percent positive agreement. PNA: percent negative agreement.

Among the 89 patients, data for 30 of the patients were un-blinded during the course of the clinical study for algorithm development. As a result, NIR images from 59 patients remained for a prospective evaluation of similarity of *in vivo* and *ex vivo* NIR measurements.

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Table 3: Ex vivo Demographics and Clinical Characteristics

Demographics	n=18 hearts (%)
Age (years)	
Mean +/- SD age	65 ± 14
Gender	
Male	13 (72)
Race	
Caucasian	17 (94)
African American	0
Asian	1 (6)
Pacific Islander	0
Native American	0
Other	0
Clinical History	
Family history of coronary artery disease	9 (50)
Hypertension	14 (78)
Diabetes mellitus	6 (33)
Tobacco Use	9 (50)
Prior myocardial infarction	1 (6)
Cerebral vascular accident/Transient ischemic attack	9 (50)
Congestive heart failure	3 (17)
Cause of Death	
<i>Cardiovascular related</i>	11 (61)
<i>Non-cardiovascular related</i>	3 (17)
<i>Unknown</i>	4 (22)

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Table 4: In vivo Patient Demographics, Clinical History, and Clinical Presentation

Demographics	n = 106 (%) ¹	n = 48 (%) ²
Age (years)		
Mean +/- SD	61.7 ± 10.0	61.4 ± 9.2
Gender		
Male	86 (81)	38 (79)
Race		
Caucasian	95 (90)	40 (83)
African American	5 (5)	2 (4)
Asian	1 (1)	1 (2)
Pacific Islander	0 (0)	0 (0)
Native American	0 (0)	0 (0)
Other	4 (4)	4 (8)
Unknown/Unreported	1 (1)	1 (2)

¹ Total number of enrolled patients

² Number of patients in prospective validation set with spectrally adequate pullbacks (see **Study Results**)

Clinical History	n = 106 (%)	n=48 (%)
Hyperlipidemia	70 (66)	36(75)
Hypertension	74 (70)	36(75)
Diabetes mellitus	23 (22)	11(23)
Prior myocardial infarction	16 (15)	5(10)
Prior percutaneous intervention	28 (26)	13(27)
Coronary artery bypass graft	3 (3)	0(0)
Cerebral vascular	0 (0)	0(0)
accident/Transient ischemic		
attack		
Peripheral vascular disease	4 (4)	2(4)
Family history of coronary artery	46 (43)	19(40)
disease		
Chest pain in last 7 days	67 (63)	33(69)
Stable angina	54 (51)	27(56)
Congestive heart failure	6 (6)	0(0)

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Clinical Presentation	n = 106	n=48
Post myocardial infarction	15 (14)	8(17)
Unstable angina	10 (9)	7(15)
Stable angina	40 (38)	16(33)
Positive functional study	25 (24)	14(29)
Atypical chest pain	9 (8)	0(0)
Congestive heart failure	1 (1)	0(0)
Other	6 (6)	3(6)

Safety

While the SPECTACL study was not powered to assess the safety of the Infraredx instrument, adverse event monitoring ensured that the safety profile was similar to that seen with similar catheters. Since the Infraredx catheter is similar to the IVUS catheter in physical characteristics and use, it was expected that the rates and types of adverse events associated with the Infraredx device in the SPECTACL study would be similar to the well-documented experience with IVUS catheters in a similar PCI patient group.

Study Endpoint

The SPECTACL primary endpoint was judged prospectively by assessing the fraction of patients with a pullback similar to the autopsy data in the LCP algorithm training set. Individual patient pullbacks were deemed similar to the *ex vivo* measurements if greater than 80% of the spectra of adequate quality in the pullback met thresholds on similarity metrics, as described below.

Spectral Adequacy

Spectrally inadequate pullbacks were considered to be of poor quality as a result of obstructions or data acquisition errors and were excluded from similarity analysis. The spectral adequacy of individual spectra was determined on the basis of several outlier metrics. These metrics were designed to identify obstructions in the path of the optical beam that could distort the spectral measurement. Obstruction outliers included:

- Spectra collected with the guide wire obstructing the arterial wall.
- Spectra collected with the optical tip inside the guide catheter.
- Spectra flagged by the oscillation metric (e.g. poor optical connections, micro-bubbles in priming saline of primed catheters).
- Spectra flagged by the wall visibility metric (arterial wall not visible due to too much intervening blood).

For the purpose of assessing data quality, a pullback was subdivided into contiguous 2 mm blocks and each was evaluated for spectral adequacy. A block was judged to be spectrally adequate if greater than 75% of the spectra within the block were adequate. A pullback, in turn, was determined to be spectrally adequate if greater than 75% of the blocks within the pullback were adequate.

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Spectral Similarity

Two multivariate metrics were used for assessing the similarity between a spectrum and those in the model calibration set: the Mahalanobis distance (MD) and the spectral F-ratio (SFR). The former is a measure of the covariance-weighted distance between a point and the centroid of a set of points in multi-dimensional space. For a prediction spectrum x and the mean spectrum y of the calibration set, the MD metric is given by (in squared units)

$$MD = (x - y)' S^{-1} (x - y), \quad (1)$$

where S^{-1} is the inverse of the covariance matrix of the training set. Since the data in the system application are bimodal (positive or negative for LCP), separate MDs were calculated relative to each class. That is, one MD was computed with respect to the subset of calibration spectra with positive LCP reference (MD+), and the other was calculated with respect to the subset of calibration spectra with negative LCP reference (MD-). A given validation spectrum is assigned the smaller of the two distances (MD+ or MD-).

The SFR is a measure of the sum of squared residuals of the validation spectrum to the average sum of squared residuals of the calibration set. The spectral residual is the difference between the estimated spectrum constructed in a lower dimensional projection space spanned by the model and the actual measured spectrum. For spectral residuals e_{val} and e_{cal} corresponding to the validation and calibration spectra, respectively, the SFR is given by

$$SFR = m(\sum_{k=1}^n e_{val,k}^2) / (\sum_{i=1}^m \sum_{k=1}^n e_{cal,i,k}^2), \quad (2)$$

for m calibration spectra and n wavelengths in a spectrum.

A pullback was judged similar if at least 80% of the adequate spectra in the pullback were below the thresholds for both the MD and SFR metrics. MD and SFR thresholds were established in the ex vivo calibration as part of the algorithm parameters.

Hypothesis Testing

The null hypothesis to be tested was:

$$H_0: p \leq 0.67$$

$$H_a: p > 0.67$$

where p is the proportion of patients showing spectral similarity between clinical recordings and the autopsy dataset. The null hypothesis was to be rejected, and therefore the primary endpoint met, if the lower bound of the 95% confidence interval exceeded 0.67.

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Study Results

A total of 59 patient pullbacks (one pullback per patient) were assessed in the validation. Eleven pullbacks were judged to be of inadequate spectral quality due to poor optical connection, excessive bubbles in the saline of primed catheters, blood flow disturbances, or obscuration of the arterial wall by excessive blood. Among the 48 pullbacks of adequate quality, 40 were found to be spectrally similar to the ex vivo spectra for a success rate of 0.83 (95% confidence interval, 0.70-0.93). This success rate satisfied the primary endpoint of the SPECTACL pivotal study by demonstrating that the lower bound on the 95% confidence interval exceeded 0.67. Figure 17-2 plots the percent similarity of each of the 48 pullbacks. The dashed horizontal line represents the median spectral similarity value (96%) of the pullbacks. The solid horizontal line indicates the lower bound for judging the spectral similarity of a pullback.

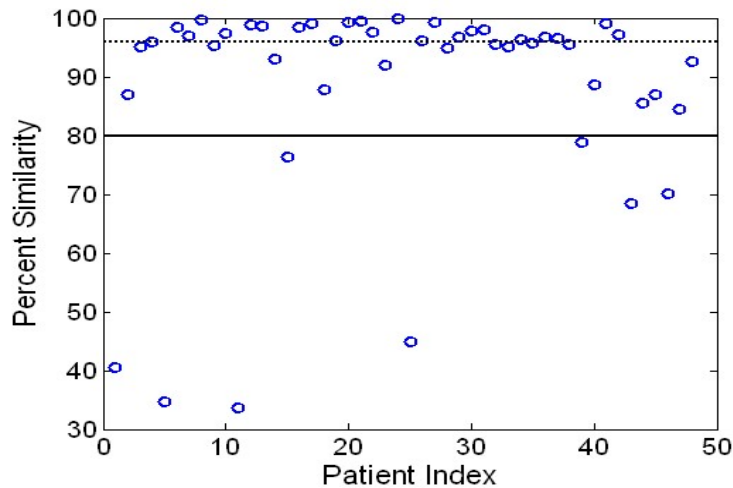


Figure 17-2: Percent similarity of adequate pullbacks. Dashed line is median percent similarity (96%). Percent similarity is defined as the percentage of spectra in a pullback that are within both the MD and SFR metric thresholds. Solid black line is 80% minimum threshold for defining a spectrally similar pullback. Forty of the 48 pullbacks (0.83) have a percent similarity above the threshold. Comparison of the SPECTACL study *in vivo* spectra is made relative to CDEV3 *ex vivo* calibration spectra (18 hearts).

An additional plot illustrating the similarity of the spectra collected in patients with those measured in autopsy specimens is given in Figure 17-3. The figure plots the MD metric for a random 1% of the spectra in each of the CDEV3 calibration (18 hearts), SPECTACL and CDEV3 validation data sets. The significant overlap among the different sets of data illustrates the similarity between ex vivo and in vivo spectra measured with the Infraredx NIR imaging system.

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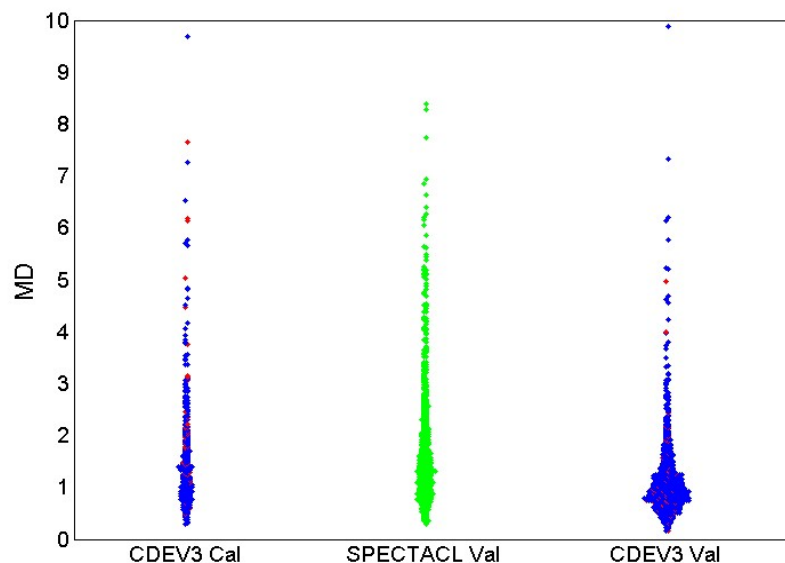


Figure 17-3: Similarity between CDEV3 ex vivo and SPECTACL in vivo spectra by MD. Red indicates positive for LCP by histology; blue indicates negative for LCP by histology; green indicates no histology. CDEV3 Cal = calibration model data (18 hearts, 51 segments, 790 spectra); SPECTACL Val = clinical pivotal study data (48 patients, 48 segments, 1770 spectra); CDEV3 Val = validation data (51 hearts, 126 segments, 3416 spectra). Each cluster represents 1% of the spectra selected at random from each set.

Safety

During the SPECTACL pivotal study, NIR spectra were collected in 89 patients. Combined with an additional 10 patients scanned in a prior feasibility study, the NIR imaging catheter was inserted in a total of 99 patients. No adverse events were determined to be related to the device as a result of these procedures.

17.2.3 Clinical Outcomes Study (LRP Study)

Study Objective

The overall study objective of the Lipid-Rich Plaque (LRP) Study was to determine in patients undergoing multi-vessel NIRS-IVUS imaging, the relationship between LRPs detected by intracoronary NIRS at non-stenotic sites and the prediction of subsequent coronary events from new culprit lesions at both the patient level (vulnerable patients) and the segment level (vulnerable plaque).

Study Design

The LRP Study was a multicenter, prospective study of patients with stable ischemic heart disease or a stabilized acute coronary syndrome (ACS) examined with angiography and NIRS-IVUS imaging for one or more suspected culprit lesions. After

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successful percutaneous coronary intervention (PCI) of all angiographically flow-limiting lesions, intravascular imaging with the combined NIRS-IVUS catheter was performed in at least two vessels and a minimum length of 50mm of coronary artery. The NIRS-IVUS data was then sent to a central core lab to determine presence or absence of LRPs.

All enrolled patients with a large LRP ($\text{maxLCBI}_{4\text{mm}} \geq 250$) as detected by NIRS were contacted at 2, 6, 12, and 24 months to determine if a new coronary event had occurred. A randomly selected half of the patients with a small, or no LRP ($\text{maxLCBI}_{4\text{mm}} < 250$), received an identical follow-up.

Study Period, Clinical Sites, and Enrollment

The LRP study enrollment took place over 25 months at 44 clinical sites in the United States and Europe. A total of 1563 patients were enrolled in the study during this period. NIRS data was not analyzable in 11 of these patients, resulting in data from 1552 patients for primary analysis. The primary analysis included 1271 patients that were assigned to the follow-up group.

Study Hypotheses and Endpoints

The study was designed to test two primary hypotheses with related endpoints.

Vulnerable Patient Hypothesis - During a 24-month follow-up after NIRS-IVUS imaging, there will be an association between the baseline value of $\text{maxLCBI}_{4\text{mm}}$ (over all coronary artery segments included in the analysis) and the incidence of non-index culprit MACE (NC-MACE) events.

Vulnerable Patient Endpoint – To test the association between $\text{maxLCBI}_{4\text{mm}}$ in all imaged arteries and future non-culprit MACE. First a univariate proportional hazards regression model in which $\text{maxLCBI}_{4\text{mm}}$ is the only independent variable and NC-MACE is the outcome was analyzed. The null hypothesis was tested by the Wald test that the regression coefficient in a proportional hazards regression model was significantly different from 0. This analysis determined whether $\text{maxLCBI}_{4\text{mm}}$ is a risk factor for NC-MACE.

This univariate analysis was the definitive test of the primary Vulnerable Patient Hypothesis. In supportive analyses, validity of the proportional hazards assumption was assessed. The proportional hazard assumptions were assessed prior to running the model; if rejected, however, the Lin-Wei estimator would have been utilized for inference.

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After the univariate analysis was determined to be positive, an additional multivariate analysis to assess the incremental prognostic value of NIRS detection of LRPs beyond conventional measures of risk was performed by fitting proportional hazards regression models that include the maxLCBI_{4mm} value and other identified prognostic variables unrelated to NIRS IVUS imaging.

To identify the variables to be included in the multivariate model, a step-up regression blinded to the NIRS and IVUS data was performed to identify the prognostic factors (including, but not limited to ACS, diabetes, renal insufficiency, hypertension, age>65, male gender, elevated cholesterol at baseline, and elevated cholesterol during the follow-up period) other than NIRS or IVUS data associated with the NC-MACE outcome. With this model, maxLCBI_{4mm} was added to assess its incremental prognostic value.

Vulnerable Plaque Hypothesis -During a 24-month follow-up, there will be an association between the maxLCBI_{4mm} of a proximal, mid, or distal segment of a coronary artery and the incidence of a follow-up culprit lesion in that segment leading to a NC-MACE event.

Vulnerable Plaque Endpoint – To test the association between maxLCBI_{4mm} in a segment and incidence of future NC- MACE in the same segment.

In the Vulnerable Plaque Hypothesis, each individual coronary artery segment is treated as a separate unit of observation. A study participant may provide results for an average of up to 12 segments.

To test this hypothesis, a proportional hazards regression model was fit with maxLCBI_{4mm} in the coronary artery segment as the measure of exposure and NC-MACE during 24 months caused by a new culprit lesion in that segment as the outcome. This analysis was performed with adjustment for the potential clustering effect within patient utilizing the Wei, Lin and Weissfeld (WLW) methodology. The primary vulnerable plaque analysis was the univariate analysis determining whether maxLCBI_{4mm} is a statistically significant risk factor for NC-MACE events.

Key Secondary Endpoints – There were key secondary endpoints analyzed for both the vulnerable patient and the vulnerable plaque analysis.

(1) To test the association between a threshold of maxLCBI_{4mm} > 400 in a patient and incidence of future NC-MACE events.

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(2) To test the association between a threshold of $\text{maxLCBI}_{4\text{mm}} > 400$ in a coronary artery segment and incidence of future NC-MACE event located within that segment.

Results

The 1271 patients in the follow up group had an average follow-up of 732 ± 27 days.

Baseline Characteristics

The baseline characteristics of the study cohort were typical for patients referred for PCI and are displayed in *Table 5*. The median age was 64 years, 69.5% were male, and 36.7% had diabetes mellitus. Stable angina with or without positive stress testing was the predominant clinical presentation of the patients. PCI was performed in 87.5% of the patients.

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Table 5: Demographics, Clinical and Presentation Characteristics of the Patients

Variable	Value	n or %
Age (years)	64 ± 10.3	1271
Median	64	
Interquartile range	57-71	
Male sex	883/1271	69.5%
Diabetes	464/1266	36.7%
Diabetes requiring insulin	162/1243	13%
Smoking history (any)	687/1249	55%
Current smokers	282/1249	22.6%
Hypertension	1019/1267	80.4%
Hyperlipidemia	1013/1261	80.3%
Family history of coronary artery disease	782/1386	56.4%
Prior myocardial infarction	294/1253	23.5%
Prior PCI	569/1267	44.9%
Clinical presentation		
Stabilized STEMI	32/1271	2.5%
Non-STEMI	182/1271	14.3%
Unstable angina	468/1271	36.8%
Stable angina or positive stress test	589/1271	46.3%
BMI	30.2 ± 6.5	1262
Cholesterol panel*		
Total cholesterol mg/dl	163.5 ± 45.6	875
LDL mg/dl	91.7 ± 40.4	846
HDL mg/dl	44.7 ± 15.2	867
Triglycerides mg/dl	152.3 ± 127.5	859
Number of diseased vessels	1 ± 0.7	1227
<70% in any epicardial artery	268/1227	21.8%
One	702/1227	57.2%
Two	228/1227	18.6%
Three	29/1227	2.4%
PCI performed at Index [#]	1111/1270	87.5%

*Aggregated (baseline cholesterol values or first cholesterol values within 24 months if patient was on statin therapy at enrollment).

[#]Summary of PCI details in *Table 6* and *Table 7*

Baseline Imaging

In the followed population, the mean number of arteries scanned per patient was 2.1 ± 0.5 with ≥ 50 mm of eligible vessel in 89.5% of the vessels. Overall the total scanned artery length was 139 ± 45.2 mm and the total analyzable NIRS data in non-stented vessel was 97.8 ± 43.4 mm (**Table 6**). The mean maxLCBI_{4mm} of these scanned vessels was 359.2 ± 175.1 , and 38.8% of the scanned arteries had maxLCBI_{4mm} more

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than 400. In the enrolled population (1552) the mean maxLCBI_{4mm} of these scanned vessels was 318.7 ± 184.4 and 31.9% of the scanned arteries had maxLCBI_{4mm} > 400. The mean length of the Ware segment was 21.2 ± 9.1 mm with most scanned Ware segments in the left anterior descending artery. The mean Ware maxLCBI_{4mm} was 165 ± 177.1 and in 11.5% of the patients the maxLCBI_{4mm} was greater than 400. In the enrolled population of Ware segments (6884), the mean Ware segment maxLCBI_{4mm} was 147.5 ± 169.7 .

Table 6: Core Laboratory Data, Patient

Variable	Patient Level	
	Value	n or %
Patient-level maxLCBI _{4mm} in a blinded artery scan	738/1271	58.1%
Patient-level maxLCBI _{4mm} in an un-blinded artery scan	533/1271	41.9%
Artery Imaged		
LM	5/1271	0.4%
LAD	1148/1271	90.3%
RCA	546/1271	43.0%
LCX	967/1271	76.1%
≥ 50mm of Eligible Vessel	1137/1271	89.5%
Number of Vessels Scanned	2.1 ± 0.5	1271
Total Artery Length Scanned, mm	139 ± 45.2	1271
Total Eligible Vessel Length, mm*	97.8 ± 43.4	1271
Patient-level maxLCBI _{4mm}	359.2 ± 175.1	1271
Median	353	
Interquartile range	257-476	
Patient-level maxLCBI _{4mm} > 400	493/1271	38.8%
Number of Ware segments	5.2 ± 1.8	1271

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Table 7: Core Laboratory Data, Vessel Segments

Variable	Ware Segment Level# Value	n or %
Scanned Artery		
LM	6/5755	0.1%
LAD	2656/5755	46.2%
RCA	1277/5755	22.2%
LCX	1807/5755	31.4%
Segment Location		
Proximal	2248/5755	39.1%
Mid	1927/5755	33.5%
Distal	1246/5755	21.7%
Far Distal	334/5755	5.8%
Ware Segment Length		
=30 mm	2159/5755	37.5%
<30 mm	3482/5755	60.5%
>30 mm	114/5755	2%
Ware Segment Length (mm)	21.2 ± 9.1	5755
Plaque-level maxLCBI _{4mm}	165 ± 177.1	5755
Median	113	
Interquartile range	0-283	
Plaque-level maxLCBI _{4mm} > 400	664/5755	11.5%

Major Adverse Cardiac Events

During the follow-up of the 24 months, 3 event types were followed. The cumulative incidence function for non-culprit MACE was 8.8% (n = 103), culprit or previously stented MACE was 8.7% (n = 104), and events with indeterminate coronary location was 2.3% (n = 28), Figure 17-4.

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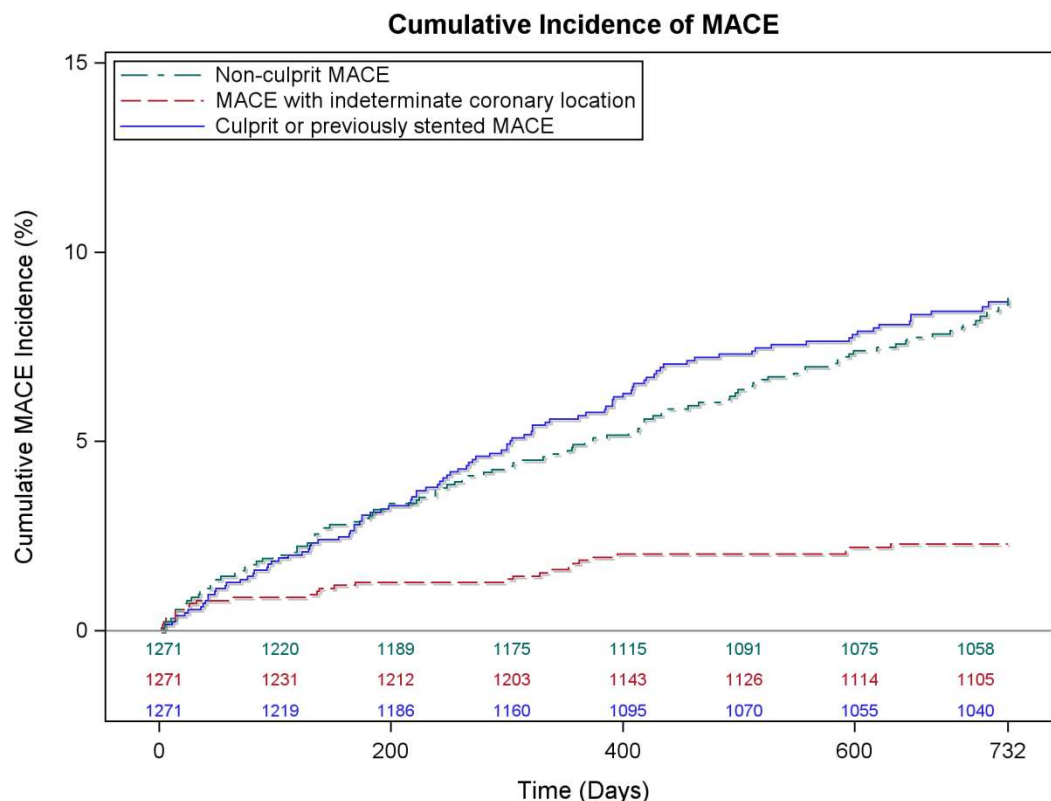


Figure 17-4: Cumulative incidence function by MACE type. Non-culprit MACE – 8.8%; Culprit or previously stented MACE – 8.7%; MACE with indeterminate coronary location – 2.3%.

Vulnerable Patient and Vulnerable Plaque Level Endpoints

The independent correlates of non-culprit MACE during the follow-up are displayed in Table 3. For the maxLCBI_{4mm} as a continuous variable, the adjusted hazard ratio was 1.17 (95% CI [1.04-1.31], p=0.005) for experiencing NC- MACE event within 24 months with each 100 unit increase in maxLCBI_{4mm}. Patients with maxLCBI_{4mm} greater than 400 had an adjusted hazard ratio of 1.84 (95% [1.22-2.77], p=0.003) to experience NC-MACE relative to patients with less than or equal to 400.

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Table 8: Co-primary endpoint proportional hazards models

Vulnerable Patient Level Unadjusted and Adjusted Cox Proportional Hazards Model		
Variable	Hazard Ratio [95% CI]	
	maxLCBI _{4mm} continuous	maxLCBI _{4mm} > 400
Unadjusted LCBI alone		
maxLCBI _{4mm}	1.21 [1.09-1.35]	2.18 [1.48-3.23]
Multivariable-Adjusted Model		
maxLCBI _{4mm}	1.17 [1.04-1.31]	1.84 [1.22-2.77]
Age	0.99 [0.97-1.01]	0.99 [0.97-1.01]
Male sex	0.81 [0.53-1.23]	0.83 [0.54-1.26]
Diabetes	1.29 [0.85-1.97]	1.29 [0.85-1.97]
Hypertension	2.13 [1.04-4.34]	2.11 [1.04-4.31]
Chronic renal insufficiency	2.00 [1.15-3.49]	2.00 [1.15-3.49]
History of smoking	1.44 [0.95-2.18]	1.45 [0.96-2.19]
Prior PCI	1.45 [0.97-2.18]	1.43 [0.96-2.15]
Presentation with ACS	1.22 [0.72-2.06]	1.23 [0.73-2.08]
Vulnerable Plaque Level Unadjusted and Adjusted Cox Proportional Hazards Models*		
Variable	Hazard Ratio [95% CI]	
Unadjusted LCBI alone		
maxLCBI _{4mm} - continuous	1.45 [1.28-1.64]	
maxLCBI _{4mm} >400	4.12 [2.32-7.32]	
Multivariable-Adjusted Model		
maxLCBI _{4mm} >400	4.31 [2.37-7.83]	

*Patient cluster adjusted via Wei Lin Weissfeld methodology

The estimated cumulative incidence functions for patients above and below the pre-specified maxLCBI_{4mm} threshold of 400 is presented in Figure 17-5.

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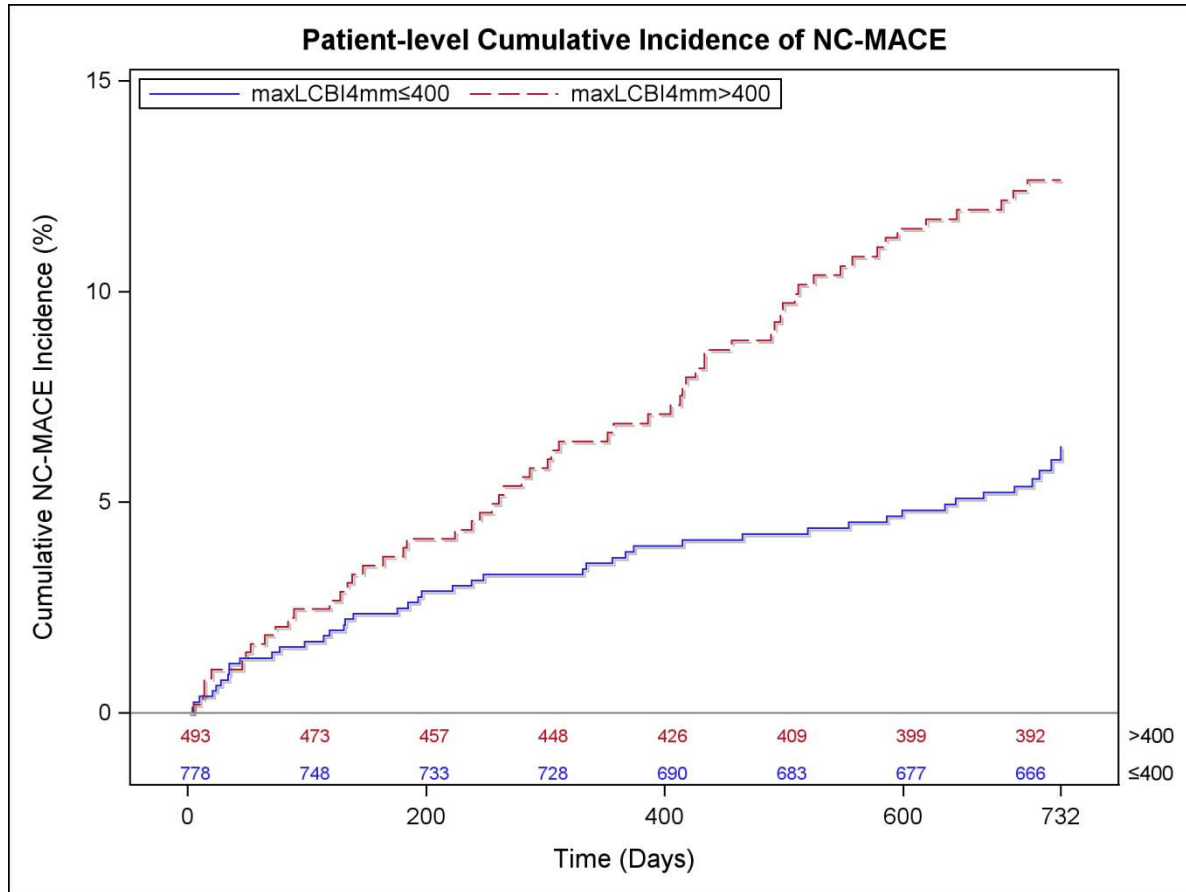


Figure 17-5: Patient level cumulative incidence of NC-MACE; Less than or equal to 400 – 5.8%; Greater than 400 – 12.6%, P<0.001.

Table 9 shows the cumulative incidence of NC-MACE at the patient follow-up time points of 2, 6, 12, and 24 months.

Table 9: Patient-Level Cumulative Incidence of NC-MACE (%)

	2 months	6 months	12 months	24 months
Patients with large LRP (maxLCBI _{4mm} ≥ 400) (Vulnerable patients)	1.3	2.5	3.7	5.8
Patients with small or no LRP (maxLCBI _{4mm} < 400)	1.6	3.7	6.9	12.6

For the plaque level, the unadjusted hazard ratio for experiencing a subsequent event in a coronary segment within 24 months was 1.45 (95% CI [1.28-1.64], P <0.001) with each 100 unit increase in maxLCBI_{4mm}. A coronary segment with maxLCBI_{4mm} greater than 400 had an unadjusted hazard ratio of 4.12 (95% CI [2.32-7.32], P<0.001).The

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cumulative incidence functions for Ware segments above and below the pre-specified maxLCBI_{4mm} threshold of 400 is shown in **Figure 17-6**.

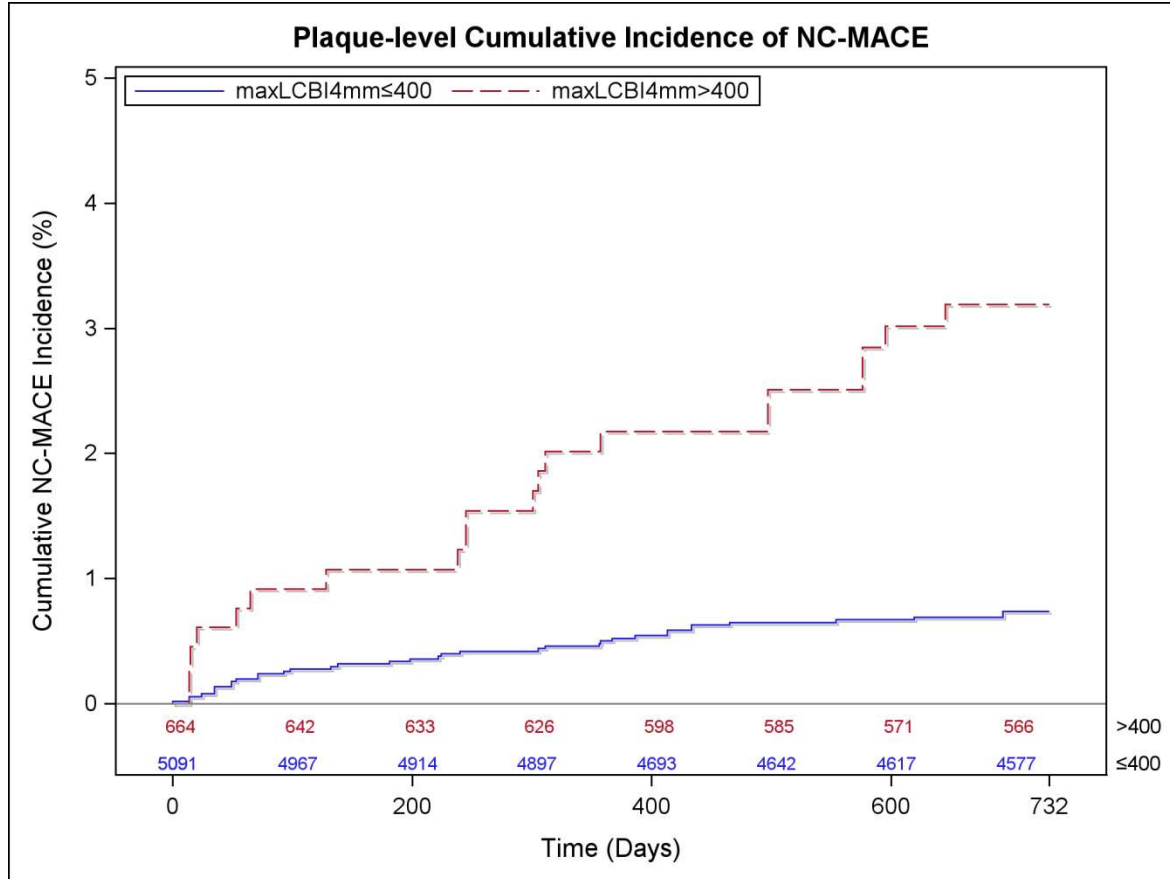


Figure 17-6: Plaque level cumulative incidence of NC-MACE; Less than or equal to 400 – 0.7%; Greater than 400 – 3.2%, P<0.001.

Safety

During the LRP Study, NIRS-IVUS imaging was performed in 1563. Six patients (0.3%) were adjudicated by a clinical events committee to be related to the device.

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17.3 Appendix C: Reference Literature

- 1 Gardner CM, Tan H, Hull EL, et al. Detection of lipid core coronary plaques in autopsy specimens with a novel catheter-based near-infrared spectroscopy system. JACC Cardiovasc Imaging 2008; 1: 638–48.
- 2 Waxman S, Dixon SR, L'Allier P, et al. In vivo validation of a catheter-based near-infrared spectroscopy system for detection of lipid core coronary plaques: initial results of the SPECTACL study. JACC Cardiovasc Imaging 2009; 2: 858–68.
- 3 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. Lancet 2019; 394: 1629–37.
- 4 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. Lancet.2021;397:985-995.

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17.4 Appendix D: Acoustic Output (I) Compliance to IEC 60601-2-37:2007

System Model: Makoto Integrated Intravascular Imaging System™ (TVC-MC10i)
Transducer: Dualpro™ IVUS+NIRS Imaging Catheter (TVC-C195-42) or Infraredx
Claripro™ HD-IVUS Imaging Catheter (TVC-E195-42), 50 MHz

Operating Mode: B mode

Application(s): Vascular

Probes Model	TI Type	TI Value (unitless)	MI (unitless)
TVC-C195-42	TIS	0.43	0.36
TVC-E195-42	TIS	0.43	0.36

This data reports the worst case. As neither MI nor TI are greater than 1.0, no further tables need to be filled-in.

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17.5 Appendix E: Acoustic Output (II) Reporting Table for Track 1

System Model: Makoto Integrated Intravascular Imaging System™ (TVC-MC10i)
 Transducer Model: Dualpro™ IVUS+NIRS Imaging Catheter (TVC-C195-42) or Infraredx Clarispro™ HD-IVUS Imaging Catheter (TVC-E195-42), 50 MHz
 Operating Mode: B-Mode
 Application: Intravascular

Acoustic Output			MI	I _{spta.3} (mW/cm ²)	I _{sppa.3} (W/cm ²)
Global Maximum Value			0.36	98	257
Associated acoustic parameter	P _{r,a}	(Mpa)	2.6		
	W	(mW)		1.73	1.73
	f _c	(MHz)	51.97	51.97	51.97
	Z _{sp}	(cm)	0.1		0.1
	Beam Dimensions	x-6 (cm)			0.0123
		y-6 (cm)			0.0317
	PD	usec	.1356		0.1356
	PRF	Hz	61440		61440
	EDS	Az. (cm)		0.31	
		Elev. (cm)		0.05	
Operating control conditions	No operator settings affect acoustic output				

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17.6 Appendix F: Ultrasound Indications for Use Table

System Model: Makoto Integrated Intravascular Imaging System™ (TVC-MC10i)
Transducer Model: Dualpro™ IVUS+NIRS Imaging Catheter (TVC-C195-42) or Infraredx Clarispro™ HD-IVUS Imaging Catheter (TVC-E195-42), 50 MHZ

Clinical Application		Mode of Operation						
General	Specific	B	M	PWD	CWD	Color Doppler	Combined (Specify)	Other* (Specify)
Ophthalmic	Ophthalmic							
Fetal Imaging & Other	Fetal							
	Abdominal							
	Intra-Operative (Specify)							
	Intra-operative (Neuro)							
	Laparoscopic							
	Pediatric							
	Small Organ (Specify)							
	Neonatal Cephalic							
	Adult Cephalic							
	Trans-rectal							
	Trans-vaginal							
	Trans-urethral							
	Trans-esoph. (non-Card.)							

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	Musculo-skeletal (Conventional)							
	Musculo-skeletal (Superficial)							
	Intravascular							
	Other							
Cardiac	Cardiac Adult	X						
	Cardiac Pediatric							
	Intravascular (Cardiac)	X						
	Trans-esoph. (Cardiac)							
	Intra-Cardiac							
	Other (Specify)							
Peripheral Vessel	Peripheral vessel							
	Other (Specify)							

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17.7 Appendix G: Measurement Precision and Accuracy

IVUS Measurement	Specification/Acceptance Criteria	Test Result*
IVUS/NIR co-registration Precision	The standard deviation of angular offsets between the NIR and IVUS channels is less than or equal to 25 degrees.	6 degrees
	The standard deviation of longitudinal offsets between NIR and IVUS channels is less than 0.5 mm.	0.17 mm
IVUS Measurement Precision	For lumen diameters less than 5 mm, the standard deviation in the measured lumen diameter is less than or equal to 0.125 mm.	0.10 mm
	For lumen diameters less than or equal to 4 mm with vessel diameters less than or equal to 7.5 mm, the standard deviation of the measured plaque cross sectional area (CSA) due to uncertainties in the vessel (EEM) and lumen boundaries and the effects of NURD shall be less than or equal to 2.79 mm ²	1.56 mm ²
IVUS Measurement Accuracy	For lumen diameters less than or equal to 4 mm with vessel diameters less than or equal to 7.5 mm, the error in the accuracy of the measured plaque cross sectional area (CSA) due to uncertainties in the vessel (EEM) and lumen boundaries and the effects of NURD shall be less than or equal to -9%, +14% of measured value ± 0.10 mm ² .	1.74 %
	For lumen diameters between 1.8 mm and 5 mm inclusive, the error in the accuracy of measured lumen area due to uncertainties in the lumen boundary where the ultrasound only traverses through blood shall be less than or equal to $\pm 5\%$ of the measurement ± 0.10 mm ² .	1.89 %
Imaging Depth	The design of the system shall be compatible with measurement of structures at depth up to 8 mm and areas up to 200 mm ² .	Pass

* Average of the result at minimum (0.5 mm/s) and maximum (2.0 mm/s) automated pullback acquisition speeds.

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17.8 Appendix H: Electromagnetic Compliance

Guidance and manufacturer's declaration – electromagnetic emissions			
The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i is intended for use in the electromagnetic environment specified below. The customer or the user of the TVC-MC10i should assure that it is used in such an environment.			
Emissions test	Test Level	Compliance	Electromagnetic environment – guidance
Conducted emissions IEC/EN 61000-4-6	150KHz to 30MHz, Class A	150KHz to 30MHz, Class A	The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
Radiated emissions IEC/EN 61000-4-3	30MHz to 1.8GHz, Class A	30MHz to 1.8GHz, Class A	
Harmonics IEC/EN 61000-3-2:2001/A2:2014	Class A Device	Per Clause 5 of standard	The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Flicker IEC/EN 61000-3-3:2013	Per Clause 5 of standard	Per Clause 5 of standard	

RFID Specifications (Transmission / Reception):

- Frequency: 902.8MHz to 927.2MHz
- Effective Radiated Power: <0.2W

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Guidance and manufacturer's declaration – electromagnetic immunity			
The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i is intended for use in the electromagnetic environment specified below. The customer or the user of the TVC-MC10i should assure that it is used in such an environment.			
Immunity test	Test level	Compliance level	Electromagnetic environment - guidance
Electrostatic discharge (ESD) IEC/EN 61000-4-2	±2, 4, 8 kV contact discharge ±2, 4, 8 & 15kV air discharge	±2, 4, 8 kV contact discharge ±2, 4, 8 & 15kV air discharge	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst IEC/EN 61000-4-4	±2 kV for AC Mains ±1 kV I/O Lines 5/50 5KHz & 100KHz	±2 kV for AC Mains ±1 kV I/O Lines 5/50 5KHz & 100KHz	Mains power quality should be that of a typical commercial or hospital environment.
Surge Line to Line (AC Power) IEC/EN 61000-4-5	±.5 kV line to line ±2 kV line to Ground	±.5 kV line to line ±2 kV line to Ground	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips & Interruptions IEC/EN 61000-4-11	0% U_T 0.5 cycle 0% U_T 1 cycle 70% U_T 25 cycles 0% U_T 5 s	0% U_T 0.5 cycle 0% U_T 1 cycle 70% U_T 25 cycles 0% U_T 5 s	If the user of the Model TVC-MC10i requires continued operation during power mains interruptions, it is recommended that the TVC-MC10i be powered from an uninterruptible power supply or a battery.
Magnetic Immunity IEC/EN 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Note: U_T is the AC mains voltage prior to application of the test level.			

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Guidance and manufacturer's declaration – electromagnetic immunity			
The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i is intended for use in the electromagnetic environment specified below. The customer or the user of the TVC-MC10i should assure that it is used in such an environment.			
Immunity test	Test level	Compliance level	Electromagnetic environment - guidance
Radiated Immunity IEC/EN 61000-4-3 Proximity field from RF wireless communication equipment IEC/EN 61000-4-3	80 MHz to 2.7 GHz, 3 V/m Spot frequencies 385MHz – 5.75GHz, Pulse Modulation See Section 5.3.7 or Table 9 from the standard excerpted below.	80 MHz to 2.7 GHz, 3 V/m Spot frequencies 385MHz – 5.75GHz, Pulse Modulation See Section 5.3.7 or Table 9 from the standard excerpted below.	Portable and mobile RF communications equipment should be used no closer to any part of the Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. Recommended separation distance Minimum separation distances for higher Immunity Test Levels shall be calculated using the following equation: $E = \left(\frac{6}{d}\right) \sqrt{P}$ where P is the maximum output power of the transmitter in watts (W), d is the distance in m, and E is the immunity test level in V/m.
Conducted Immunity (AC Power) (I/O Lines) IEC/EN 61000-4-6	0.015 - 80 MHz 3 V _{RMS} & 6 V _{RMS} in ISM Band, 1KHz, AC Mains	0.015 - 80 MHz 3 V _{RMS} & 6 V _{RMS} in ISM Band, 1KHz, AC Mains	Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

Recommended separation distances between portable and mobile RF communications equipment and the Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i

The Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Model TVC-MC10i can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Makoto Integrated Intravascular Imaging System™ Model TVC-MC10i as recommended below,

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according to the maximum output power of the communications equipment. This table is excerpted from IEC/EN 61000-4-3

Test specifications for Enclosure Port Immunity to RF wireless communications equipment						
Test Frequency (MHz)	Band ^{a)}	Service ^{a)}	Modulation ^{b)}	Maximum power (W)	Distance (m)	Immunity Test Level (V/m)
385	380-390	TETRA 400	Pulse Modulation ^{b)} 18 MHz	1.8	0.3	27
450	430-470	GMRS 460, FRS 460	FM ^{c)} ± 5 kHz deviation 1 kHz sine	2	0.3	28
710	704-787	LTE Band 13, 17	Pulse Modulation ^{b)} 217 MHz	0.2	0.3	9
745						
780						
810	800-960	GSM 800/900, TETRA 800, IDEN 820, CDMA 850, LTE Band 5	Pulse Modulation ^{b)} 18 MHz	2	0.3	28
870						
930						
1720	1700-1990	GSM 1800; CDMA 1900; GSM 1900; DECT; LTE Band 1, 3, 4, 25; UMTS	Pulse Modulation ^{b)} 217 MHz	2	0.3	28
1845						
1970						
2450	2400-2570	Bluetooth, WLAN, 802.11 b/g/n, RFID 2450, LTE Band 7	Pulse Modulation ^{b)} 217 MHz	2	0.3	28
5240	5100-5800	WLAN, 802.11 a/n	Pulse Modulation ^{b)} 217 MHz	0.2	0.3	9
5500						
5785						
NOTE: If necessary to achieve the immunity Test Level, the distance between the transmitting antenna and the ME Equipment or ME System may be reduced to 1 m. The 1 m test distance is permitted by IEC 61000-4-3.						
a) For some services, only the uplink frequencies are included.						
b) The carrier shall be modulated using a 50 % duty cycle square wave signal.						
c) As an alternative to FM modulation, 50 % pulse modulation at 18 Hz may be used because while it does not represent actual modulation, it would be worst case.						