User's Manual

Beta-Cath™ 3.5F System

(For use with the β-Rail™ 3.5F Delivery Catheter or the β-Rail™ 3.5F XL Delivery Catheter)

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

D03745 Rev. C 8/04

Table of Contents

[1] The Beta-Cath™ System is not indicated for pullback (stepping).

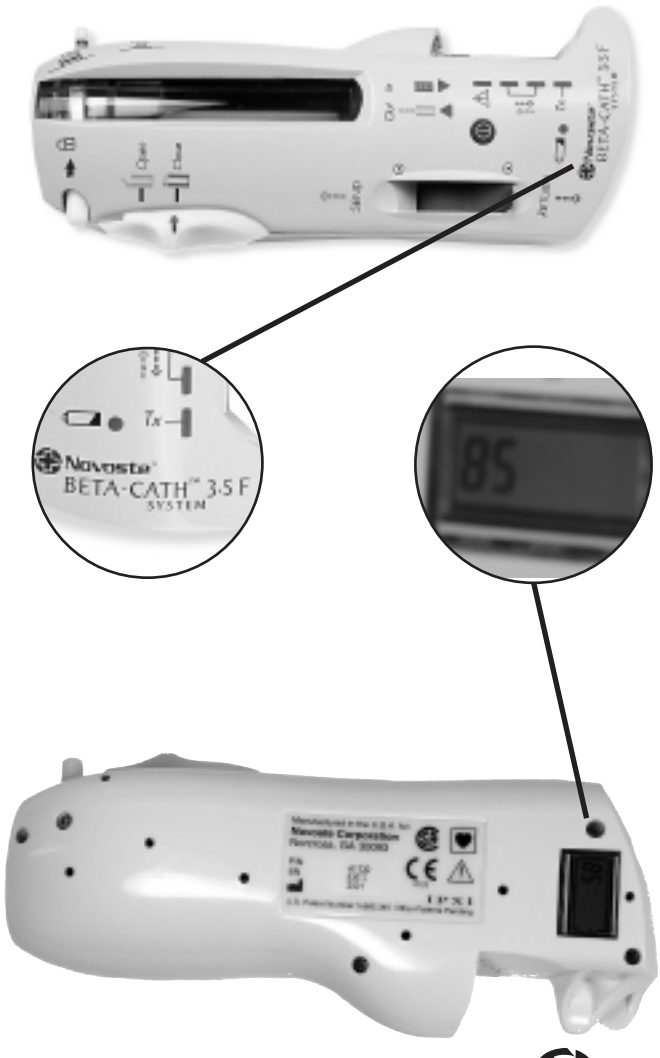
DETERMINE WHICH TRANSFER DEVICE YOU ARE USING

The instructions for the Beta-Cath™ 3.5F System User's Manual have been combined for two (2) Transfer Device Models. Before proceeding, please determine the Transfer Device that you will be using on a case-by-case basis by referring to the identifying photos shown below:

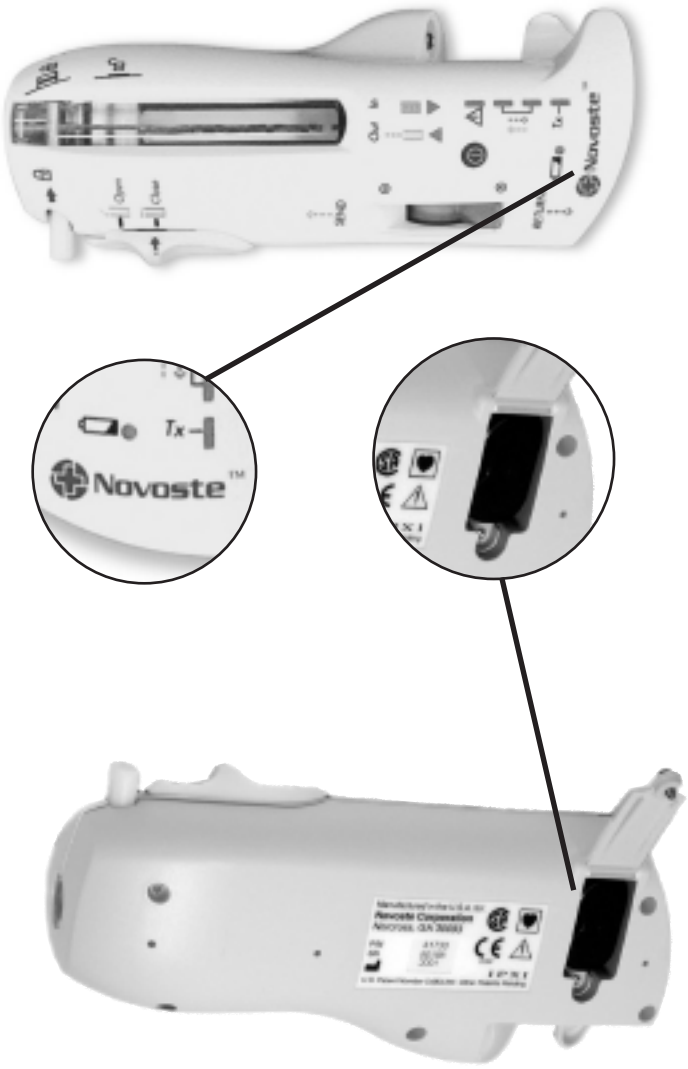
Please note that the operation of and treatment with both Transfer Devices is identical; the only differences between the two models are indicated below. Please refer to the System Description of the Transfer Device on page 3 for further information.

Unless otherwise indicated, references to "Transfer Device" in this User's Manual apply to both Models of the Transfer Device.

Standard Model



Exchangeable Battery Model



I. Introduction

How To Use This Manual

This manual is intended to guide clinicians that have completed the authorized formal training program for the Novoste™ Beta-Cath™ 3.5F System. Please contact Novoste to schedule a training session. Read this manual completely before system use and keep it readily available for reference. This manual contains recommended safety procedures as minimum safety guidelines developed from good clinical practices and the "As Low As Reasonably Achievable" (ALARA) radiation exposure philosophy.

Definitions:

Indications: Indications are the general descriptions of the disease or condition the device can be used to treat, prevent, cure or mitigate including a description of the patient population for which the device is intended.

Contraindications: Contraindications are conditions under which the device should NOT be used because the risk of use outweighs any possible benefit.

Special Considerations: Patient circumstances or conditions which merit additional attention by the physician.

Adverse Events: Undesirable effects reasonably associated with the use of the device. A serious adverse event refers to an adverse experience that is life threatening, results in permanent impairment of a body function, permanent damage to a body structure, necessitates medical/surgical intervention to preclude permanent impairment/damage to a body function/structure.

WARNING: A WARNING statement is used to alert the user to a potential serious outcome or harm (death, injury, or serious adverse events) to the user or to the patient associated with the use or misuses of the device.

PRECAUTIONS: A precaution statement alerts the user to exercise special care necessary for the safe and effective use of the device. Precautions may include actions to be taken to avoid effects on patients or users that may not be potentially life threatening or result in serious injury, but also alert the user to adverse effects on the device of use or misuse and the care necessary to avoid such effects.

Note: A note provides additional information to clarify a point in the text.

Notations In Manual:

Performed by Cardiologist or Designee	**CARD/D**
Performed by Radiation Oncologist or Designee	**RO/D**
Performed by Medical Physicist, Radiation Safety Officer or Designee	**MP/RSO/D**
Performed by Radiation Oncologist, Medical Physicist, Radiation Safety Officer or Designee	**RO/MP/RSO/D**

II. System Description

The Beta-Cath™ 3.5F System is an integrated system comprised of four components: the β-Rail™ 3.5F Delivery Catheter, Transfer Device, the Source Train, and the System Accessories. The System is designed so that the Transfer Device and the Delivery Catheter are exclusively compatible.

The β-Rail™ 3.5F Delivery Catheter provides the path through which the Source Train is delivered to and retrieved from the site of interventional injury.

Note: This manual is for use with the β-Rail™ 3.5F Delivery Catheter and the β-Rail™ 3.5F XL Delivery Catheter. The β-Rail™ 3.5F Delivery Catheter may only be used *inside* the sterile field, using the Sterile Bag. The β-Rail™ 3.5F XL Delivery Catheter may be used *inside* or *outside* the sterile field. When the β-Rail™ 3.5F Delivery Catheter is referenced, it applies to both the β-Rail™ 3.5F Delivery Catheter and β-Rail™ 3.5F XL Delivery Catheter, unless otherwise specified. Section H is specific to preparing the β-Rail™ 3.5F Delivery Catheter for use *inside* the sterile field, and Section I is specific to using the β-Rail™ 3.5F XL Delivery Catheter *outside* the sterile field.

The ergonomically designed Transfer Device stores and shields the Source Train when not in use, and controls the hydraulic delivery and return of the Source Train during the treatment procedure. The gray color-coded Novoste™ Transfer Device is exclusively compatible with the β-Rail™ 3.5F Delivery Catheter and β-Rail™ 3.5F XL Delivery Catheter.

The Transfer Device is available in two Models: the Standard Model, which has "Novoste Beta-Cath™ 3.5F System" stamped on the bottom of the front of the device, and a procedure counter on the bottom of the back of the device, and the Exchangeable Battery Model, which has "Novoste" stamped on the bottom of the front of the device, and an exchangeable battery compartment on the back of the device. Please refer to page 2 of this User's Manual for an illustration of the two Transfer Device Models.

Note: Because the two Transfer Device Models have different service cycles, it is important to identify which Model you are using. Specific instructions for the different Models may be found in Sections *IV. Transfer Device Controls & Indicators*, and *VI. System Specifications*. The operation of and treatment with both Transfer Device Models is identical; they only differ as noted in the Transfer Device Controls & Indicators section and System Specifications.

III. Essential Prescribing Information

Note: Unless otherwise indicated, references to "Transfer Device" in this User's Manual apply to <u>both</u> Transfer Device Models.

The Source Train consists of a wire jacketed series of individual, cylindrical, sealed sources containing Sr^{90}/Y^{90} and an inactive radiopaque marker at each end. The Source Train provides the radiation dose during the treatment procedure.

The System Accessories are the ancillary components of the Beta-Cath™ 3.5F System that (1) ensure sterility and facilitate operation of the system during a clinical procedure, (2) permit temporary storage of System components in the event of a disrupted clinical procedure, (3) facilitate handling of Source Train components if located outside of the System, (4) facilitate Medical Physicist's operations, and/or (5) enable transport of the System components and Medical Physicist's Kit.

Indications

The Beta-Cath™ 3.5F System is intended to deliver beta radiation to the site of successful Percutaneous Coronary Intervention (PCI) for the treatment of in-stent restenosis in native coronary arteries with discrete lesions (treatable with a 20 mm balloon for the 30 mm and 40 mm Systems and injury areas up to 40 mm for the 60 mm System) in a reference vessel diameter ranging from 2.7 mm to 4.0 mm.

Contraindications

- Unprotected left main disease (>50% narrowing).
- Patients in whom antiplatelet and/or anticoagulant therapy are contraindicated.

Warnings

- **Every attempt should be made to avoid re-stenting of the target lesion to minimize the risk of thrombosis.**

<u>Delivery Catheter & Source Train Placement</u>

- Use of an Internal Mammary (IM) Artery Guide Catheter may impede the path of the ACTIVE Source Train and may cause unintentional exposure of radiation and/or unintended results.
- Vessel trauma may result from the improper use of the Delivery Catheter. Follow the enclosed directions carefully. When the Delivery Catheter is in the body, it should be manipulated only under fluoroscopy. Never advance or withdraw the Delivery Catheter against resistance without first determining the reason for the resistance under fluoroscopy.
- Do not over-tighten the hemostatic valve as this may damage the Delivery Catheter and impede the path of the ACTIVE Source Train and may cause unintentional exposure of radiation and/or unintended results.
- Failure to open the hemostatic valve may prevent the radiation source train from returning to the device and may result in unnecessary radiation exposure to the patient or personnel.
- Failure to correctly position the Source Train at the interventional injury site may underexpose the targeted treatment area and expose tissue not targeted for treatment to unintentional radiation; unpredictable results may occur. Exceeding the prescribed radiation treatment time will result in a higher than intended dose. Migration or improper location of the Source Train may cause unintentional radiation exposure to occur and may decrease treatment efficacy.
- Failure to comply with the specific use of the Transfer Device controls may result in injury or unintended radiation exposure. Radiation is emitted from the Transfer Device when the Radiation Source Train is in the Source Chamber. To minimize hand dose, the Transfer Device is designed to be held on the underside and may also be set down when appropriate.

<u>Intravascular Radiation Procedure</u>

- If the fluid in the capped Fluid Collection Bag after the procedure is found to be contaminated after scanning, then the Transfer Device and capped Fluid Collection Bag should be placed in the Temporary Storage Container. Immediately inform Institutional Radiation Safety personnel, implement contamination control procedures and call your Novoste Representative.
- If, at any time, a Survey Meter reading of the Transfer Device, Delivery Catheter, Fluid Collection Bag, or Procedure Room is significantly different from initial baseline readings, stop all activity and re-survey the Transfer Device, Delivery Catheter, Fluid Collection Bag, or Procedure Room making sure the fluoroscopy is off. If the reading is not within the acceptable baseline range or background range there may potentially be a misplaced source; refer to Section Q, Emergency Source Recovery Procedure.
- **UNDER NO CIRCUMSTANCES** should an individual attempt to remove the Radiation Source Train from the Beta-Cath™ 3.5F System, grasp the catheter directly with hands (when an active Radiation Source Train is being used), cut the catheter, or pick up a source with his/her fingers, because unintended radiation exposure and injury may result. Required equipment is provided for this purpose in the Response Kit.

III. Essential Prescribing Information

- Should breach of ACTIVE Source Train containment occur:

    1. Notify personnel present of missing source(s).
    2. Follow institutional procedures regarding personnel allowed to enter or leave the room until the source is contained.
    3. Individuals involved in source recovery should wear disposable gloves, an extremity dosimeter on the hand expected to receive the highest dose and a whole body dosimeter on the front of the body between the neck and the waist.

PRECAUTIONS

- The Beta-Cath™ 3.5F System is designed to be used by a team of appropriately trained personnel. At a minimum, this team should include a Cardiologist, Radiation Oncologist, and Medical Physicist.

Beta-Cath™ 3.5F System Preparation

- Prior to any procedure, the equipment should be thoroughly examined to verify the proper function and integrity of the system.
- Handle the Transfer Device carefully and do not use if dropped. Do not use the Transfer Device if the controls and indicators are not functioning correctly or the LED light test is not observed. Do not begin a procedure if the Low Battery light is blinking. If the Low Battery Indicator starts blinking during a procedure, there will be enough battery power to complete the procedure.
- The Transfer Device is not sterile. A Sterile Bag is provided to maintain a sterile field during the procedure. The inside portion of the tape covering the Syringe Port Hole and the Proprietary Connector Port Hole of the sterile bag is not sterile; remove from the sterile field.
- Do not recharge, disassemble, expose to high temperatures or incinerate the provided Transfer Device battery. Keep in package until ready to use. Dispose of used battery properly.
- The Exchangeable Battery Model Transfer Device requires scheduled maintenance by Novoste Corporation within a period not to exceed twelve months. Refer to each Transfer Device's Calibration Certificate for its specified use period. Please contact your Novoste Representative to arrange for service.
- Use the Delivery Catheter and Procedure Accessory Pack before the expiration date noted on the package. Verify that the sterility of the devices has not been compromised by assuring the package integrity has been maintained. The Delivery Catheter and Procedure Accessory Pack items are intended for single use. Do not re-sterilize and/or reuse these items. Do not use if sterile package is damaged.
- Use only **Sterile Water for Irrigation**, which may also be referred to as sterile distilled non-pyrogenic water, in the Transfer Device. Do not use saline as a hydraulic fluid in the Transfer Device; corrosion may occur.
- Do not use the Delivery Catheter if there is evidence of damage. Damaged catheters may cause vessel trauma or unpredictable results during use.
- Do not use the Delivery Catheter if there is evidence of fluid leakage other than at the IST hub vent position.
- Use caution when connecting the Proprietary Connector to the Transfer Device. The Proprietary Connector of the Delivery Catheter is no longer sterile once disconnected from the Transfer Device.
- Use care when attaching components to the Transfer Device to ensure that the Sterile Bag does not get pinched in the process. Ensure a sufficient number of water-filled syringes are available before beginning treatment. Always reserve at least 10 ml of water for the return of the ACTIVE Source Train to prevent unintentional radiation exposure.
- If the self-diagnostic test is not observed, do not use the device and call your Novoste Representative for service.
- Do not begin a procedure if the Low Battery light is blinking. If the Low Battery Indicator starts blinking during a procedure, there will be enough battery power to complete the procedure. Should this occur when using the Standard Model only, call your Novoste Representative for service after the procedure. For the Exchangeable Battery Model only, replace the battery per instructions found on page 31 of this User's Manual.
- Do not force the connector lock latch into position. If resistance is felt, reposition the 3.5F compatible Flushing Adapter to ensure proper engagement with the Transfer Device.
- Do not force the connector lock latch into position. If resistance is felt, reposition the proprietary connector to ensure proper engagement with the Transfer Device.

III. Essential Prescribing Information

PRECAUTIONS *Continued*

- Ensure that the Gate Control Switch is completely closed, as incomplete closure may render the Gate inoperable.

- The Standard Model Transfer Device requires scheduled maintenance by Novoste Corporation every 125 procedures or every six months, whichever event occurs first. Please contact your Novoste Representative to arrange for service.

Intravascular Radiation Procedure

- The individual performing the wipe and leak tests for radioactive material should use good contamination control techniques.

- If the transferable contamination exceeds 200 dpm/100 cm^2 (or the level determined by local regulation or institutional policy) or the leak test results exceed 11,100 dpm (or the level determined by local regulation or institutional policy) on any sample, place the contaminated object(s) in a plastic bag and label "Caution: Radioactive Material." Immediately inform institutional Radiation Safety personnel, implement containment control procedures and call your Novoste Representative. Should this occur, do not continue with this procedure.

- Use only the 3.5F compatible Flushing Adapter provided with the Beta-Cath™ 3.5F System. Use of any other Beta-Cath™ Flushing Adapter will result in an improper fit and an inability to properly perform the Leak Test Procedure.

- Always advance the Delivery Catheter with the IST in position within the Delivery Catheter. Never advance or withdraw the Delivery Catheter against resistance. Do not advance the Delivery Catheter over the floppy portion of the guidewire as the guidewire may prolapse when the Delivery Catheter is withdrawn. If this occurs, attempt to resolve the prolapse by gently pulling back on the guidewire while simultaneously advancing the catheter. If the prolapse persists, disengage the Delivery Catheter from the guidewire by continuing to advance the Delivery Catheter while gently pulling back on the guidewire.

- Exercise care when withdrawing the Delivery Catheter through any area of increased restriction, such as a stent, guide catheter tip, or hemostatic valve. Always withdraw the Delivery Catheter slowly and observe under fluoroscopy, whenever possible.

- The Transfer Device contains radioactive material. Use of this device is restricted to persons licensed in the handling of radioactive materials. Personnel handling this device must follow the regulations, policies and procedures for their institution on the safety and hazards associated with radioactive materials.

- Utilize a manual Blood Pressure Cuff to monitor patient status during the radiation treatment because arterial wave form pressure may be dampened while the Delivery Catheter is in place.

- Illumination of the Red Pressure Indicator ⚠ light during a procedure indicates excessive pressure is being used; reduce applied pressure to return to the Amber ▼▲ Pressure Indicator area.

- Do not turn the Transfer Device power On or attempt to OPEN the Gate Control Switch during the Drying Procedure.

- Failure to perform adequate visual and radiation surveys post-procedure to verify source accountability may subject patients and/or personnel to unintended radiation exposure.

Emergency Source Recovery

- Under the undefined handling conditions outside the System, the ACTIVE Source Train jacket may be damaged, allowing individual ACTIVE Sources to be released. Use care when locating and handling the Radioactive Source Train to ensure that all individual ACTIVE Sources remain intact (jacketed) and are recovered and returned to safe, shielded storage.

- The Response Kit contains two Source Recovery Tools for picking up and transfering a Source(s) to a safe location: a) the Source Recovery Probe and b) the spring-loaded Tweezers. The Source Recovery Probe is the preferred method as it minimizes potential damage to the Source(s) and permits the operator's hand to be placed further from the Source(s).

- The magnetic Source Recovery Probe should be held and operated near its release lever in order to avoid unnecessary radiation exposure.

- In the event a source becomes loose or needs to be transferred to a safe location, use the source recovery tools with extreme care in source recovery. Improper use could damage sources and could potentially release unsealed radioactive material. Use of the Source Recovery Probe is the preferred method as it minimizes potential damage to a source.

III. Essential Prescribing Information

Special Considerations

As with other vascular brachytherapy procedures, safety and effectiveness has not been demonstrated in the following populations:

- Patients undergoing or having prior chest radiotherapy.
- Patients unable to tolerate the recommended dwell time of the Source Train in the Delivery Catheter (3.5 Fr).
- The safety and effectiveness of the Beta-Cath™ 3.5F System have not been evaluated in reference vessel diameters < 2.7 mm.
- Patients requiring revascularization methods other than balloon angioplasty, directional and rotational atherectomy and excimer laser for revascularization of in-stent restenosis.
- Vessel or lesion morphologies that would preclude revascularization or placement of the β-Rail™ 3.5F Delivery Catheter.
- Patients presenting with:
  - thrombotic lesions;
  - multiple vessel lesions;
  - vein graft segments;
  - overlapping stents;
  - myocardial infarction less than or equal to 72 hours prior to the procedure; and/or
  - ejection fractions less than 30%.
- Patients who have received a heart transplant.
- Women of child-bearing potential who are pregnant or suspect pregnancy.

Adverse Events

The original Beta-Cath™ (5F) System was evaluated in the **STents And Radiation Therapy (START) Trial,** a multicenter, randomized, placebo-controlled trial involving 476 patients. The START Trial primarily studied the treatment of lesions treatable with a 20 mm Balloon and a 30 mm Source Train (95%), using the Beta-Cath™ (5F) System. The observed adverse events are summarized in the following table.

Major Adverse Events – In-Hospital and Out-of-Hospital (to 8 months)
All Patients Treated (N=476)

	Sr-90 (N=244 Patients)		Placebo (N=232 Patients)		All Randomized (N=476 Patients)	
Combined (In-and Out-of-Hospital) Complications to 240 Days	Number	%	Number	%	Number	%
Any MACE (Death, MI, Emergent CABG, TVR)	44	18.0%	60	25.9%	104	21.8%
Death	3	1.2%	1	0.4%	4	0.8%
Myocardial Infarction (Q or Non-Q)	4	1.6%	7	3.0%	11	2.3%
Q Wave MI	0	0.0%	0	0.0%	0	0.0%
Non-Q Wave MI	4	1.6%	7	3.0%	11	2.3%
Emergent CABG	1	0.4%	0	0.0%	1	0.2%
Target Lesion Revascularization	32	13.1%	52	22.4%	84	17.6%
TL-CABG	20	8.2%	24	10.3%	44	9.2%
TL-PTCA	12	4.9%	30	12.9%	42	8.8%
Target Vessel Revascularization not involving the TL*	11	4.5%	15	6.5%	26	5.5%
TV-CABG	2	0.8%	2	0.9%	4	0.8%
TV-PTCA	9	3.7%	13	5.6%	22	4.6%
Target Vessel Revascularization	39	16.0%	56	24.1%	95	20.0%
TV-CABG	21	8.6%	24	10.3%	45	9.5%
TV-PTCA	19	7.8%	34	14.7%	53	11.1%
Stent Thrombosis (to 30 days)	0	0.0%	1	0.4%	1	0.2%
Site Thrombosis (Days 31-240)	0	0.0%	0	0.0%	0	0.0%
Abrupt Closure	0	0.0%	1	0.4%	1	0.2%
Subacute Closure	0	0.0%	1	0.4%	1	0.2%
Bleeding Complications	4	1.6%	4	1.7%	8	1.7%
Vascular Complications	4	1.6%	3	1.3%	7	1.5%
CVA	1	0.4%	1	0.4%	2	0.4%

*Target vessel revascularization not involving the target lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization

III. Essential Prescribing Information

Adverse Events *Continued*

Three (3) patients who received radiation died during the START trial. The deaths occurred between 167 and 225 days. One (1) patient died due to coronary artery disease, congestive heart failure, and multi-system dysfunction. It could not be determined if the cause of death was device-related. The cause of death for the other two patients was determined not to be device-related.

There were 476 patients treated with the Beta-Cath™ (5F) System (BCS) in the Stents and Radiation Therapy (START) Trial. Device success, defined as successful delivery and treatment with the BCS, was achieved in 467 of the 476 patients (~98%). The table provided below outlines the details of the malfunctions reported as part of the treatment of the 476 patients. The 108 patient treatments with device malfunctions include 89 cases with minor device malfunctions, 10 cases with initial device malfunctions with subsequent treatment success, and 9 device failures preventing treatment success.

Summary of Device Malfunctions	# of Patients
Number of patients enrolled in START Trial	**476**
Number of Cases with Device Malfunctions	**108**
Number of Cases with unsuccessful delivery and treatment with the BCS	9
Number of cases reporting initial device malfunctions with subsequent treatment success	10
Number of minor malfunctions not affecting Ability to Treat	89
Number of Cases Resulting In Use of the Temporary Storage Container* (included in the Device Malfunctions category listed above)	**6**
Patients Unsuccessfully Treated and Involving Use of the Temporary Storage Container*	1

*(Bail-Out is defined as physician use of the Novoste™ Temporary Storage Container)

Additionally, the original Beta-Cath™ (5F) System was evaluated in the START 40/20 Trial, a multi-center registry involving 207 patients. The START 40/20 Trial studied the treatment of lesions treatable with a 20 mm balloon with a 40 mm Source Train. The observed adverse events are summarized in the following tables.

Major Adverse Events – In-Hospital and Out-of-Hospital (to 240 days)
All Patients Treated (N=439)
START 40/20 versus START Placebo

	START 40/20 (N=207 Patients)	START Placebo (N=232 Patients)	All Patients (N=439 Patients)	Difference [95% C.I]
Combined (In-and Out-of-Hospital) Complications to 240 Days				
Any MACE (Death, MI, Emergent CABG, TVR)	19.3% (40/207)	25.9% (60/232)	22.8% (100/439)	-6.5% [-14.3%, 1.3%]
Death	2.4% (5/207)	0.4% (1/232)	1.4% (6/439)	2.0% [-0.3%, 4.2%]
Myocardial Infarction (Q or Non-Q)	4.3% (9/207)	3.0% (7/232)	3.6% (16/439)	1.3% [-2.2%, 4.9%]
Q Wave MI	1.4% (3/207)	0.0% (0/232)	0.7% (3/439)	1.4% [-0.2%, 3.1%]
Non-Q Wave MI	2.9% (6/207)	3.0% (7/232)	3.0% (13/439)	-0.1% [-3.3%, 3.1%]
Emergent CABG	0.0% (0/207)	0.0% (0/232)	0.0 (0/439)	0.0% [-,-]
Target Lesion Revascularization	11.1% (23/207)	22.4% (52/232)	17.1% (75/439)	-11.3% [-18.2%, -4.4%]
TL-CABG	6.8% (14/207)	10.3% (24/232)	8.7% (38/439)	-3.6% [-8.8%, 1.6%]
TL-PTCA	5.3% (11/207)	12.9% (30/232)	9.3% (41/439)	-7.6% [-12.9%, -2.3%]
Target Vessel Revascularization not involving the TL*	8.2% (17/207)	6.5% (15/232)	7.3% (32/439)	1.7% [-3.2%, 6.6%]
TV-CABG	1.4% (3/207)	0.9% (2/232)	1.1% (5/439)	0.6% [-1.4%, 2.6%]
TV-PTCA	6.8% (14/207)	5.6% (13/232)	6.2% (27/439)	1.2% [-3.4%, 5.7%]
Target Vessel Revascularization	15.9% (33/207)	24.1% (56/232)	20.3% (89/439)	-8.2% [-15.6%, -0.8%]
TV-CABG	7.7% (16/207)	10.3% (24/232)	9.1% (40/439)	-2.6% [-8.0%, 2.7%]
TV-PTCA	9.2% (19/207)	14.7% (34/232)	12.1% (53/439)	-5.5% [-11.5%, 0.5%]
Stent Thrombosis (to 30 days)	0.0% (0/207)	0.4% (1/232)	0.2% (1/439)	-0.4% [-1.3%, 0.4%]
Site Thrombosis (Days 31-240)	1.0% (2/207)	0.0% (0/232)	0.5% (2/439)	1.0% [-0.4%, 2.3%]
Abrupt Closure	0.0% (0/207)	0.4% (1/232)	0.2% (1/439)	-0.4 [-1.3%, 0.4%]
Subacute Closure	0.0% (0/207)	0.4% (1/232)	0.2% (1/439)	-0.4% [-1.3%, 0.4%]
Bleeding Complications	3.4% (7/207)	1.7% (4/232)	2.5% (11/439)	1.7% [-1.3%, 4.6%]
Vascular Complications	1.0% (2/207)	1.3% (3/232)	1.1% (5/439)	-0.3% [-2.3%, 1.6%]
CVA	1.0% (2/207)	0.4% (1/232)	0.7% (3/439)	0.5% [-1.0%, 2.1%]

*Target vessel revascularization not involving the target lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization.

Major Adverse Events – In- and Out-of-Hospital (to 240 days)
All Patients Treated (N=451)
START 40/20 versus START Sr-90

	START 40/20 (N=207 Patients)	START Sr-90 (N=244 Patients)	All Patients (N=451 Patients)	Difference [95% C.I]
Combined (In-and Out-of-Hospital) Complications to 240 Days				
Any MACE (Death, MI, Emergent CABG, TVR)	19.3% (40/207)	18.0% (44/244)	18.6% (84/451)	1.3% [-5.9%, 8.5%]
Death	2.4% (5/207)	1.2% (3/244)	1.8% (8/451)	1.2% [-1.3%, 3.7%]
Myocardial Infarction (Q or Non-Q)	4.3% (9/207)	1.6% (4/244)	2.9% (13/451)	2.7% [-0.5%, 5.9%]
Q Wave MI	1.4% (3/207)	0.0% (0/244)	0.7% (3/451)	1.4% [-0.2%, 3.1%]
Non-Q Wave MI	2.9% (6/207)	1.6% (4/244)	2.2% (10/451)	1.3% [-1.5%, 4.0%]
Emergent CABG	0.0% (0/207)	0.4% (1/244)	0.2% (1/451)	-0.4% [-1.2%, 0.4%]
Target Lesion Revascularization	11.1% (23/207)	13.1% (32/244)	12.2% (55/451)	-2.0% [-8.0%, 4.0%]
TL-CABG	6.8% (14/207)	8.2% (20/244)	7.5% (34/451)	-1.4% [-6.3%, 3.4%]
TL-PTCA	5.3% (11/207)	4.9% (12/244)	5.1% (23/451)	0.4% [-3.7%, 4.5%]
Target Vessel Revascularization not involving the TL*	8.2% (17/207)	4.5% (11/244)	6.2% (28/451)	3.7% [-0.9%, 8.3%]
TV-CABG	1.4% (3/207)	0.8% (2/244)	1.1% (5/451)	0.6% [-1.4%, 2.6%]
TV-PTCA	6.8% (14/207)	3.7%(9/244)	5.1% (23/451)	3.1% [-1.1%, 7.2%]
Target Vessel Revascularization	15.9% (33/207)	16.0% (39/244)	16.0% (72/451)	-0.0% [-6.8%, 6.7%]
TV-CABG	7.7% (16/207)	8.6% (21/244)	8.2% (37/451)	-0.9%[-5.9%, 4.2%]
TV-PTCA	9.2% (19/207)	7.8% (19/244)	8.4% (38/451)	1.4% [-3.8%, 6.6%]
Stent Thrombosis (to 30 days)	0.0% (0/207)	0.0% (0/244)	0.0% (0/451)	0.0%[-,-]
Site Thrombosis (Days 31-240)	1.0% (2/207)	0.0% (0/244)	0.4% (2/451)	1.0% [-0.4%, 2.3%]
Abrupt Closure	0.0% (0/207)	0.0% (0/244)	0.0% (0/451)	0.0% [-,-]
Subacute Closure	0.0% (0/207)	0.0% (0/244)	0.0% (0/451)	0.0% [-,-]
Bleeding Complications	3.4% (7/207)	1.6% (4/244)	2.4% (11/451)	1.7% [-1.2%, 4.7%]
Vascular Complications	1.0% (2/207)	1.6% (4/244)	1.3% (6/451)	-0.7% [-2.8%, 1.4%]
CVA	1.0% (2/207)	0.4% (1/244)	0.7% (3/451)	0.6% [-1.0%, 2.1%]

*Target vessel revascularization not involving the target lesion was defined as target vessel revascularization at a site other than the target site with or without concomitant target lesion revascularization.

Five (5) patients who received radiation died during the START 40/20 trial. The deaths occurred between 17 and 200 days. Two (2) patients died of cardiac deaths related to the target lesion: one following non-QMI/heart failure complicating the index procedure and one of massive GI bleed/ischemic bowel complicating reintervention with Reopro® (Eli Lilly and Company) of the target lesion. The remaining three died of cardiac death not related to the target lesions or the device: one patient died from CHF and multi-system failure following a non-target lesion intervention; one patient died from complications surrounding an intracerebral bleed; and one patient died following aortic valve replacement and non-target vessel CABG.

There were 207 patients treated with the Beta-Cath™ (5F) System (BCS) in the Stents and Radiation Therapy 40/20 Trial. Device success, defined as successful delivery and treatment with the BCS, was achieved in 200 of the 207 patients (~97)%.

Summary of Device Malfunctions	# of Patients
Number of patients enrolled in START 40/20 Trial	**207**
Number of Cases with unsuccessful delivery and treatment with the BCS	7
Number of cases reporting initial device malfunctions with subsequent treatment success	3
Number of Cases Resulting In Use of the Temporary Storage Container* (included in the Device Malfunctions category listed above)	**8**
Patients Unsuccessfully Treated and Involving Use of the Temporary Storage Container*	1

*(Bail-Out is defined as physician use of the Novoste™ Temporary Storage Container)

The original Beta-Cath™ (5F) System was evaluated in a subset analysis of the European Surveillance **REgistry with the NOvoste Beta-Cath™ System (RENO) Registry**), a prospective commercial registry at 46 centers in Europe involving 1098 patients. This subset analysis included a comparison of 139 patients from the RENO registry (RENO-Long Subgroup) that had diffuse in-stent restenotic lesions in single vessels treated by longer than 40 mm of radiation source train as compared to a placebo control group (94 patients) obtained from the WRIST and LONG WRIST studies by selecting the cases which required longer or equal to 13 seeds of dummy sources and to the START trial results. Additionally, comparisons were made between the pullback[1] and 60mm source train groups of the RENO-Long Subgroup to ensure the outcomes could be pooled. Treatments with the Beta-Cath™ (5F) System included stepping (pullback) procedures utilizing either 30, 40 or 60 mm source trains or a single 60 mm source train. The observed adverse events are summarized in the following tables:

RENO-Long versus WRIST/Long-WRIST Control
Major Adverse Events - In-and Out-of-Hospital (to 6 months)
All Patients (N=233)

Combined In- and Out-Of-Hospital Events to 6-Months	RENO-Long (N=139)	WRIST/Long-WRIST Control (N=94)	Combined (N=233)
MACE	17.9% (24/134)	64.9% (61/94)	37.3% (85/228)
Death	2.2% (3/134)	2.1% (2/94)	2.2% (5/228)
MI (Q or Non-Q)	1.5% (2/134)	17.0% (16/94)	7.9% (18/228)
Q-wave MI	0.7% (1/134)	1.1% (1/94)	0.9% (2/228)
Non Q-wave MI	0.7% (1/134)	16.0% (15/94)	7.0% (16/228)
TVR	14.9% (20/134)	60.6% (57/94)	33.8% (77/228)
TV-PTCA	2.2% (3/134)	9.6% (9/94)	5.3% (12/228)
TV-CABG	12.7% (17/134)	56.4% (53/94)	30.7% (70/228)

[1] The Beta-Cath™ System is not indicated for pullback (stepping).

RENO-Long versus START Placebo
Major Adverse Events - In-and Out-of-Hospital
All Patients (N=371)

Combined In- and Out-Of-Hospital Events	RENO-Long (N=139)	START Placebo (N=232)	Combined (N=371)
MACE	17.9% (24/134)	25.9% (60/232)	23.0% (84/366)
Death	2.2% (3/134)	0.4% (1/232)	1.1% (4/366)
MI	1.5% (2/134)	3.0% (7/232)	2.5% (9/366)
Q-wave MI	0.7% (1/134)	0.0% (0/232)	0.3% (1/366)
Non Q-wave MI	0.7% (1/134)	3.0% (7/232)	2.2% (8/366)
TVR	14.9% (20/134)	24.1% (56/232)	20.8%(76/366)
TV-PTCA	12.7% (17/134)	14.7% (34/232)	13.9% (51/366)
TV-CABG	2.2% (3/134)	10.3% (24/232)	7.4% (27/366)

RENO-Long versus START Radiation
Major Adverse Events - In- and Out-of-Hospital
All Patients (N=383)

Combined In- and Out-Of-Hospital Events	RENO-Long (N=139)	START Radiation- (N=244)	Combined (N=383)
MACE	17.9% (24/134)	18.0% (44/244)	18.0% (68/378)
Death	2.2% (3/134)	1.2% (3/244)	1.6% (6/378)
MI	1.5% (2/134)	1.6% (4/244)	1.6% (6/378)
Q-wave MI	0.7% (1/134)	0.0% (0/244)	0.3% (1/378)
Non Q-wave MI	0.7% (1/134)	1.6% (4/244)	1.3% (5/378)
TVR	14.9% (20/134)	16.0% (39/244)	15.6% (59/378)
TV-PTCA	12.7% (17/134)	7.8% (19/244)	9.5% (36/378)
TV-CABG	2.2% (3/134)	8.6% (21/244)	6.3% (24.378)

Pullback[1] versus Non-pullback (60 mm)
Major Adverse Events - In- and Out-of-Hospital (to 6 months)
All Patients (N=139)

Combined In- and Out-Of-Hospital Events to 6 Months	Pullback (N=109)	Non-pullback (N=30)	Combined (N=139)
MACE	19.0% (20/105)	13.8% (4/29)	17.9% (24/134)
Death	2.9% (3/105)	0.0% (0/29)	2.2% (3/134)
MI	0.0% (0/105)	6.9% (2/29)	1.5% (2/134)
Q-wave MI	0.0% (0/105)	3.4% (1/29)	0.7% (1/134)
Non Q-wave MI	0.0% (0/105)	3.4% (1/29)	0.7% (1/134)
TVR	16.2% (17/105)	10.3% (3/29)	14.9% (20/134)
TV-PTCA	13.3% (14/105)	10.3% (3/29)	12.7% (17/134)
TV-CABG	2.9% (3/105)	0.0% (0/29)	2.2% (3/134)

The following adverse events were NOT observed during the clinical investigations, but are recognized as potential adverse events associated with the non-radioactive portion of vascular brachytherapy, including (but not limited to):

- Arrhythmia
- Arterial Damage, Dissection or Perforation
- Vascular Access Site Hematoma
- Contrast-Induced Nephrotoxicity
- Neurologic Complications
- Allergic Reactions
- Infection
- Stroke
- Thrombotic Occlusion
- Renal Insufficiency
- Coronary Artery Bypass Graft Surgery
- Slow Flow-Phenomenon
- AV Fistula
- Pseudoaneurysm
- Left Ventricular Dysfunction
- Systemic Atheroembolization
- Endocarditis
- Distal Embolizations
- Vasospasm
- Arterial Perforation
- Retroperitoneal Hematoma

Additional potential Adverse Events associated with the radiation portion of vascular brachytherapy include (but are not limited to):

- Radiation-Induced Malignancy
- Aneurysm
- Excessive Radiation Exposure to Patient/Staff
- Arterial Damage
- Coronary Artery Bypass Graft Surgery
- Thrombosis
- Restenosis
- Myocardial Infarction
- Death

[1] The Beta-Cath™ System is not indicated for pullback (stepping).

Antiplatelet Therapy

To minimize the risk of thrombosis when new stents are implanted in conjunction with radiation therapy, a minimum of three (3) months antiplatelet therapy is recommended with the 30 and 40 mm Beta-Cath™ 3.5F System, and a minimum of six (6) months with the 60 mm Beta-Cath™ 3.5F System. If a new stent is not implanted in conjunction with radiation therapy, antiplatelet therapy should be administered at the physician's discretion.

Novoste START Trial

The **START (STents And Radiation Therapy) Trial**, a multicenter, randomized, placebo-controlled trial, began in September 1998. The START Trial primarily studied the treatment of lesions treatable with a 20 mm Balloon with a 30 mm Source Train (95%), using the Beta-Cath™ (5F) System. The acute and 8-month clinical and angiographic results showed that the procedure success rate, defined as the attainment of a residual stenosis of <50%, without in-hospital major adverse cardiac events (MACE [death, Q wave and non-Q wave MI, emergent CABG, and target vessel revascularization]), was 97.1% (237/244) in the Sr-90 arm and 97.0% (225/232) in the Placebo arm (p=0.9237). The Kaplan-Meier estimate of freedom from MACE at 8 months was 81.4% in the Sr-90 arm and 72.2% in the Placebo arm (p=0.0393). The Kaplan-Meier estimate of freedom from target vessel failure (TVF), defined as target vessel revascularization, MI, or death, at 8 months was 81.4% in the Sr-90 arm and 72.2% in the Placebo arm (p=0.0393).

A total of 476 patients were enrolled at 50 US, Canadian, and European investigational sites in the placebo-controlled, triple-masked, multicenter START Trial. All 476 of the enrolled patients were randomized to receive either the active Beta-Cath™ (5F) System (n=244) or placebo Beta-Cath™ (5F) System (n=232). The primary endpoint of 8-month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass graft surgery (CABG), and revascularizations attributed to the target vessel (TVR). A clinical events committee, masked to the treatment assignment, adjudicated all major endpoints. Eligible patients, with angina or a positive functional study, were identified for elective treatment of in-stent restenosis in a native coronary artery lesion visually estimated to be between 2.7 and 4.0 mm in diameter and treatable with up to a 20 mm (length) angioplasty balloon. These patients underwent successful percutaneous coronary interventions (defined as revascularization by balloon angioplasty, directional and rotational atherectomy, and excimer laser) after which treatment with the randomized Beta-Cath™ (5F) System (active or placebo) was administered. After the vascular brachytherapy treatment, additional percutaneous coronary interventional techniques or devices were utilized as deemed necessary by the clinician. Placement of a new stent, while discouraged, occurred at the discretion of the clinician in 21% (n=101) of the cases.

Radiation was prescribed according to the following reference vessel diameter: $\geq 2.7 \leq 3.35$ mm received 18.4 Gy* and $> 3.35 \leq 4.0$ mm received 23 Gy* at a distance 2mm from the centerline of the source train.

*18.4 and 23 Gray reflect the NIST-recommended adjustments to the documented doses as described in Technical Report DSGN-0311-A and are equivalent to the 16 and 20 Gray documented doses described in the START Trial.

The Antiplatelet/Anticoagulant regimen administered for the 476 patients in the START Trial were as follows:

Antiplatelet/ Anticoagulant[1]	Duration (Days) 0-14	15-30	31-60	61-90	>90	Unconfirmed
Ticlopidine (250-500mg/day)	9	50	3	0	0	3
Clopidogrel (75mg/day)	23	121	42	55	12	10
Ticlopidine/Clopidogrel	0	0	0	1**	1***	1****

[1] 145 patients received no additional antiplatelet therapy other than aspirin.
**One patient received Ticlopidine for 30 days followed by Clopidogrel for 60 days.
***One patient received Ticlopidine for 14 days followed by Clopidogrel for 155 days.
****One patient received Ticlopidine for 7 days followed by Clopidogrel for an unconfirmed duration.

Clinical follow-up occurred at in-hospital, 1 month, and 8 months. Angiographic follow-up occurred at 8 months. The study randomization was successful as both treatment groups were found to be demographically equivalent. All randomized patients were included in the intent-to-treat analysis. The principal effectiveness and safety results are presented in Table 1 followed by the freedom from target vessel failure Kaplan-Meier curve, Figure 1. The mean lesion length studied was 16.1mm with approximately 30% of the lesions greater than 19 mm.

Table 1. Principal Effectiveness and Safety Results - START Trial
All Patients Treated (N=476)

Efficacy Measures	Sr-90 (N=244 Patients)	Placebo (N-232 Patients)	Relative Risk [95% C.I.]	Difference [95% C.I.]	P-value
8 Month Stent Segment Binary Restenosis Rate	14.2% (28/197)	41.2% (77/187)	0.3 [0.24, 0.51]	-27.0% [-35.5%, -18.4%]	0.0000
8 Month Analysis Segment Binary Restenosis Rate	28.8% (57/198)	45.2% (85/188)	0.6 [0.49, 0.83]	-16.4% [-25.9%, -6.9%]	0.0008
TLR-Free at 240 Days*	86.4%	75.6%	1.14 [1.03, 1.27]	10.8% [2.5%, 19.0%]	0.0090
TVR-Free at 240 Days*	83.5%	73.8%	1.13 [1.01, 1.27]	9.7% [1.1%, 18.3%]	0.0283
TVF-Free at 240 Days*	81.4%	72.2%	1.13 [1.00, 1.27]	9.2% [0.3%, 18.1%]	0.0393
MACE-Free at 240 Days*	81.4%	72.2%	1.13 [1.00, 1.27]	9.2% [0.3%, 18.1%]	0.0393
Target Lesion Success	99.6% (243/244)	99.1% (230/232)	1.0 [0.99, 1.02]	0.5%[-1.0%, 1.9%]	0.5332
Procedure Success	97.1% (237/244)	97.0% (225/232)	1.0 [0.97, 1.03]	0.1% [-2.9%, 3.2%]	0.9237
Device Success	98.4% (240/244)	97.8% (227/232)	1.0 [0.98, 1.03]	0.5% [-1.9%, 3.0%]	0.6796
Post-Procedure Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	2.17±0.42 (242)	2.15±0.42 (229)		0.02 [-0.06, 0.09]	0.6503
Range (min, max)	(1.12, 3.47)	(1.20, 3.40)			
Post-Procedure Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.94±0.39 (243)	1.94±0.41 (230)		-0.00 [-0.08, 0.07]	0.9058
Range (min, max)	(1.03, 3.02)	(0.98, 3.10)			
Post-Procedure Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	22.9%±13.5% (242)	22.9%±12.9% (229)		0.0% [-2.4, 2.4%]	0.9972
Range (min, max)	(-31.1%, 53.2%)	(-19.6%, 51.9%)			
Post-Procedure Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	31.4%±10.2% (243)	30.7%±11.0% (230)		0.7% [-1.2, 2.6%]	0.4800
Range (min, max)	(6.7%, 57.6%)	(5.8%, 62.5%)			
Follow-Up Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.96±0.66 (197)	1.47±0.60 (187)		0.49 [0.36, 0.62]	0.0000
Range (min, max)	(0.00, 3.45)	(0.00, 2.65)			
Follow-Up Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.65±0.64 (198)	1.41±0.58 (188)		0.24 [0.12, 0.36]	0.0001
Range (min, max)	(0.00, 3.18)	(0.00, 2.66)			
Follow-Up Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	30.4%±22.7% (197)	47.9%±20.8% (187)		-17.5% [-21.9, -13.1%]	0.0000
Range (min, max)	(-32.2%, 100.0%)	(-4.4%, 100.0%)			
Follow-Up Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	41.7%±20.7% (198)	50.1±19.7% (188)		-8.5% [-12.5, -4.4%]	0.0000
Range (min, max)	(-10.4%, 100.0%)	(13.4%, 100.0%)			
Safety Measures and Other Clinical Events to 240 days					
In-Hospital MACE	2.5% (6/244)	2.2% (5/232)	1.1[0.35, 3.69]	0.3% [-2.4%, 3.0%]	0.8255
Out-of-Hospital MACE to 240 Days	16.0% (39/244)	24.1% (56/232)	0.7 [0.46, 0.96]	-8.2% [-15.3%, -1.0%]	0.0261
In- and Out-of-Hospital MACE to 240 Days	18.0% (44/244)	25.9% (60/232)	0.7 [0.49, 0.98]	-7.8% [-15.2%, -0.4%]	0.0388
Aneurysm†	0.5% (1/198)	0.0% (0/188)	-[-,-]	0.5% [-0.5%, 1.5%]	0.3292
Stent Thrombosis (to 30 days)	0.0% (0/244)	0.4% (1/232)	0.0 [-,-]	-0.4% [-1.3%, 0.4%]	0.3046
Site Thrombosis (Days 31-240)	0.0% (0/244)	0.0% (0/232)	-[-,-]	0.0% [-,-]	-
Total Occlusions (Angiographic)	4.0% (8/198)	3.7% (7/188)	1.1 [0.40, 2.93]	0.3% [-3.5%, 4.2%]	0.8720

Numbers are % (counts/sample size) or Mean ± SD.
N/A = Not applicable.
Relative Risk = Sr-90/Placebo SE = sqrt{(1-p_1)/n_{11}+(1-p_2)/n_{21}} CI = RR*exp(±1.96*SE)
Difference = Sr-90 – Placebo SE = sqrt(p_1*q_1/n_1+p_2*q_2/n_2) CI = Diff±1.96*SE
CI = Confidence Interval

Target Lesion Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method. If QCA was not available, the visual estimate of diameter stenosis was used.

Procedure Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method and no in-hospital major adverse cardiac events (MACE). If QCA was not available, the visual estimate of diameter stenosis was used.

Device Success = Successful delivery of the Beta-Cath™ System.

Stent segment was defined as the area confined to the proximal and distal borders of the stent.

Analysis segment was defined as the segment that extends 5 mm proximal and distal to the radiated or injured landmark, whichever was longest in length.

*Survival estimates from Kaplan-Meier method. Standard error estimate from Peto formula.

TLR-free = Freedom from target lesion revascularization.

TVR-free = Freedom from target vessel revascularization.

TVF-free = Freedom from death, MI, and target vessel revascularization.

MACE-free = Freedom from death, MI, emergent CABG, and target vessel revascularization.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization from hospital discharge through the 240-day contact, as determined by the independent Clinical Events Committee.

Stent thrombosis was defined as angiographic thrombus or subacute closure within the target vessel at the time of the clinically driven angiographic restudy for documented ischemia (chest pain and ECG changes). Any death not attributed to a non-cardiac cause within the first 30 days was considered a surrogate for thrombosis in the absence of documented angiographic stent patency.

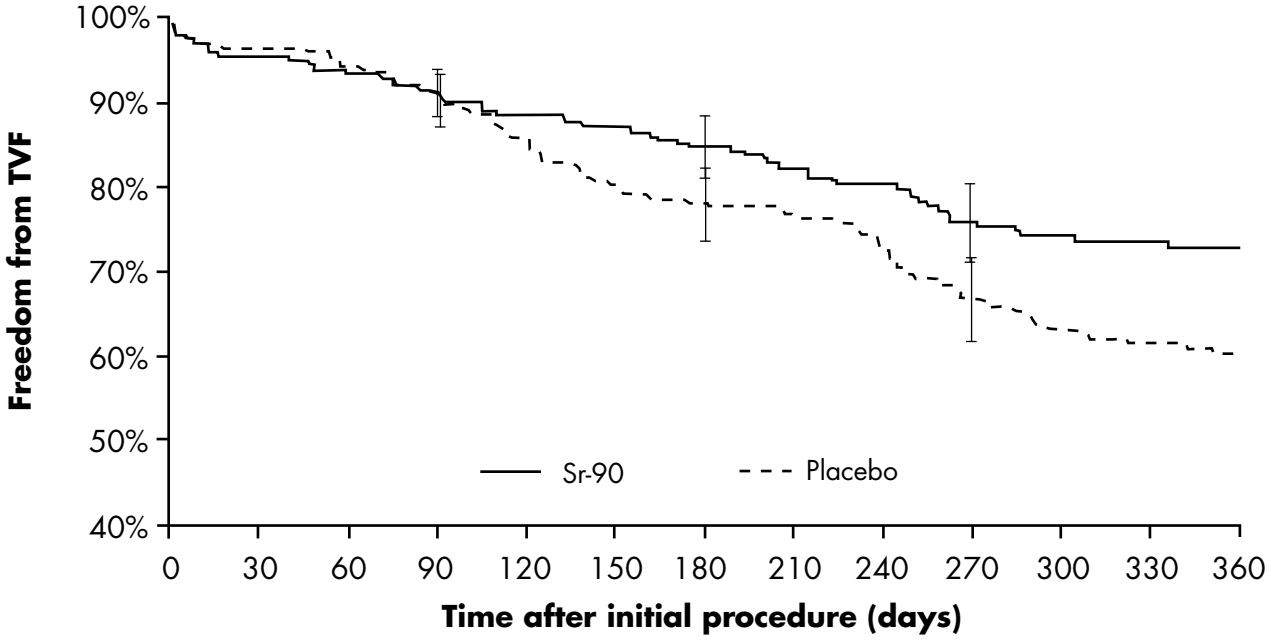
Site thrombosis was defined as myocardial infarction attributable to the target vessel with angiographic documentation (site-reported or by QCA) of thrombus or total occlusion at the target site >30 days after the index procedure in the absence of an intervening revascularization of the target vessel.

Aneurysm was defined as an expansion of the lumen by at least 20% compared with the normal lumen dimensions in the treatment region (analyzed segment) that extends with a wide or narrow mouth beyond the apparent normal contour.

†Baseline QCA for patient 15/3 revealed the presence of an aneurysm. The Angiographic Core Laboratory reported the absolute size of the aneurysm changed very little from baseline to follow-up and that the larger appearance at follow-up was due to the smaller reference vessel dimension rather than an increase in aneurysm size.

Total Occlusion = An MLD of zero at follow-up as assessed by QCA.

Figure 1:
Freedom from Target Vessel Failure (at 12 months)
Event – free Survival + 1.5SE; All Lesions Treated (n=476)
START Trial versus Placebo



Time after initial procedure (days)

	0	30	60	90	180	210	240	270	360
Sr-90									
# Entered	244	241	231	222	217	201	195	179	151
# Lost to Follow-up	1	1	4	0	1	0	12	19	145
# Incomplete	0	0	0	0	0	0	0	0	0
# At risk	243.5	240.5	229.0	222.0	216.5	201.0	189.0	169.5	78.5
# Events	2	9	5	5	15	6	4	9	5
# Events/Month		9	5	5	5	6	4	3	2
% Survived	99.2%	95.5%	93.4%	91.2%	84.9%	82.4%	80.7%	76.2%	73.6%
% SE	0.6%	1.4%	1.6%	1.9%	2.3%	2.5%	2.7%	3.0%	37.8%
Placebo									
# Entered	232	230	219	213	203	176	172	160	134
# Lost to Follow-up	0	5	1	1	0	0	4	14	122
# Incomplete	0	0	0	0	0	0	0	0	0
# At risk	232.0	227.5	218.5	212.5	203.0	176.0	170.0	153.0	73.0
# Events	2	6	5	9	27	4	8	12	12
# Events/Month		6	5	9	9	4	8	4	4
% Survived	99.1%	96.5%	94.3%	90.3%	78.3%	76.5%	72.9%	67.1%	60.9%
% SE	0.6%	1.3%	1.6%	2.0%	2.8%	2.9%	3.0%	3.3%	38.1%

Test Between Groups

Test	Chi-Square	Deg Frdm	P-Value
Wilcoxon	6.05	1	0.0139
Log-Rank	6.90	1	0.0086

The START 40/20 Trial

The START 40/20 (STents And Radiation Therapy) Trial, a multicenter, prospective registry trial, began in June 1999. The START 40/20 Trial studied the treatment of lesions treatable with a 20 mm balloon with a 40 mm Source Train, using the Beta-Cath™ (5F) System. The acute and 8-month clinical and angiographic results showed that the procedure success rate, defined as the attainment of a residual stenosis of <50%, without in-hospital major adverse cardiac events (MACE [death, Q-wave and non-Q-wave MI, emergent CABG, and target vessel revascularization]), was 93.7% (194/207). The Kaplan-Meier estimate of freedom from MACE at 8 months was 80.0%. The Kaplan-Meier estimate of freedom from target vessel failure (TVF), defined as target vessel revascularization, MI, or death, at 8 months was 80.0%. A total of 207 patients were enrolled at 22 US and European investigational sites in the START 40/20 Trial. All 207 of the enrolled patients received the active 40 mm Beta-Cath™ (5F) System. The primary end-point of 8-month clinical target vessel failure was defined as the composite of death, myocardial infarction (Q-wave and non-Q-wave), coronary artery bypass graft surgery (CABG), and revascularizations attributed to the target vessel (TVR). A clinical events committee adjudicated all major endpoints. Eligible patients, with angina or positive functional study, were identified for elective treatment of in-stent restenosis in a native coronary artery lesion visually estimated to be between 2.7 and 4.0 mm in diameter and treatable with up to a 20 mm (length) angioplasty balloon. These patients underwent successful percutaneous coronary interventions (defined as revascularization by balloon angioplasty, directional and rotational atherectomy, and excimer laser) after which treatment with the 40 mm Beta-Cath™ (5F) System was administered. After the vascular brachytherapy treatment, additional percutaneous coronary interventional techniques or devices were utilized as deemed necessary by the clinician. Placement of a new stent, while discouraged, occurred at the discretion of the clinician in 15.3% (n=31/207) of the cases. Radiation was prescribed according to the following reference vessel diameter: $> 2.7 \leq 3.35$ mm received 18.4 Gy* and $> 3.35 \leq 4.0$ mm received 23 Gy* at a distance 2 mm from the centerline of the source train.

*18.4 and 23 Gray reflect the NIST-recommended adjustments to the documented doses as described in Technical Report DSGN-0311-A and are equivalent to the 16 and 20 Gray documented doses described in the START 40/20 Trial.

The Antiplatelet/Anticoagulant regimen administered for the 207 patients in the START 40/20 Trial were as follows:

Antiplatelet/ Anticoagulant[1,2,3,4]	Duration (Days)				
	≤30 days	31-60	61-90	>90	Unconfirmed
Ticlopidine (250-500mg/day)	4	0	0	2	0
Clopidogrel (75mg/day)	38	2	72	37	10
Ticlopidine/Clopidogrel	0	1*	0	2**	0

[1] 11 patients received no antiplatelet therapy.
[2] 26 patients received no additional antiplatelet therapy other than aspirin.
[3] One patient had unconfirmed antiplatelet therapy.
[4] One patient received Coumadin® (Endo Products Inc.) for >90 days.
* One patient received Clopidogrel for 21 days followed by Ticlopidine for 14 days.
** One patient received Ticlopidine for 14 days followed by Clopidogrel for 30 days and one patient received Ticlopidine for 30 days followed by Clopidogrel for 90 days.

Clinical follow-up occurred at in-hospital, 1 month, and 8 months. Angiographic follow-up occurred at 8 months. The patients in the START 40/20 Trial were compared to the START Sr-90 and START Placebo groups. The principal effectiveness and safety results are presented in Tables 2 and 3 followed by the freedom from target vessel failure Kaplan-Meier curve, Figure 2. The mean lesion length studied was 17.4 mm.

Table 2. Principal Effectiveness and Safety Results
All Patients Treated (N=439)
START 40/20 versus START Placebo

Efficacy Measures	START 40/20 (N=207 Patients)	START Placebo (N=232 Patients)	Relative Risk [95% C.I.]	Difference [95% C.I.]	P-value
8 Month Stent Segment Binary Restenosis Rate	15.4% (23/149)	41.2% (77/187)	0.4 [0.25, 0.57]	-25.7% [-34.9%, -16.6%]	0.0000
8 Month Analysis Segment Binary Restenosis Rate	25.3% (38/150)	45.2% (85/188)	0.6 [0.41, 0.77]	-19.9% [-29.8%, -9.9%]	0.0002
TLR-Free at 240 Days*	88.2%	75.6%	1.17 [1.05, 1.29]	12.6% [4.4%, 20.8%]	0.0008
TVR-Free at 240 Days*	83.1%	73.8%	1.13 [1.01, 1.26]	9.3% [0.6%, 18.1%]	0.0174
TVF-Free at 240 Days*	80.0%	72.2%	1.11 [0.98, 1.25]	7.8% [-1.2%, 16.9%]	0.0559
MACE-Free at 240 Days*	80.0%	72.2%	1.11 [0.98, 1.25]	7.8% [-1.2%, 16.9%]	0.0559
Target Lesion Success	95.7% (198/207)	99.1% (230/232)	1.0 [0.93, 1.00]	-3.5% [-6.5%,-0.5%]	0.0197
Procedure Success	93.7% (194/207)	97.0% (225/232)	1.0 [0.93, 1.01]	-3.3% [-7.2%, 0.7%]	0.1017
Device Success	96.6% (200/207)	97.8% (227/232)	1.0 [0.96, 1.02]	-1.2% [-4.3%, 1.9%]	0.4315
Post-Procedure Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	2.09± 0.40 (196)	2.15± 0.42 (229)		-0.06 [-0.14, 0.02]	0.1292
Range (min, max)	(1.02, 3.33)	(1.20, 3.40)			
Post-Procedure Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.84± 0.39 (196)	1.94± 0.41 (230)		-0.10 [-0.18, -0.03]	0.0078
Range (min, max)	(0.61, 2.89)	(0.98, 3.10)			
Post-Procedure Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	23.8%± 15.7% (196)	22.9%± 12.9% (229)		0.8% [-1.9, 3.6%]	0.5432
Range (min, max)	(-13.4%, 66.0%)	(-19.6%, 51.9%)			
Post-Procedure Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	33.2%± 14.2% (196)	30.7± 11.0% (230)		2.4% [0.0, 4.9%]	0.0461
Range (min, max)	(-3.1%, 74.0%)	(5.8%, 62.5%)			
Follow-Up Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.85± 0.65 (149)	1.47± 0.60 (187)		0.38 [-0.24, 0.51]	0.0000
Range (min, max)	(0.00, 3.41)	(0.00, 2.65)			
Follow-Up Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.60± 0.58 (150)	1.41± 0.58 (186)		0.19 [0.06, 0.31]	0.0034
Range (min, max)	(0.00, 3.16)	(0.00, 2.66)			
Follow-Up Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	30.7%± 23.1% (149)	47.9± 20.8% (187)		-17.2% [-21.9, -12.5%]	0.0000
Range (min, max)	(-8.0%, 100.0%)	(-4.4%, 100.0%)			
Follow-Up Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	40.2%± 20.1% (150)	50.1± 19.7% (188)		-9.9% [-14.2, -5.7%]	0.0000
Range (min, max)	(2.4%, 100.0%)	(13.4%, 100.0%)			
Safety Measures and Other Clinical Events to 240 days					
In-Hospital MACE	1.9% (4/207)	2.2% (5/232)	0.9 [0.24, 3.29]	-0.2% [-2.9%, 2.4%]	0.8694
Out-of-Hospital MACE to 240 Days	17.9% (37/207)	24.1% (56/232)	0.7 [0.51, 1.07]	-6.3% [-14.3%, 1.3%]	0.1089
In- and Out-of-Hospital MACE to 240 Days	19.3% (40/207)	25.9% (60/232)	0.7 [0.52, 1.06]	-6.5% [-14.3%, 1.3%]	0.1030
Aneurysm	0.7% (1/150)	0.0% (0/188)	-[-,-]	0.7% [-0.6%, 2.0%]	0.2622
Stent Thrombosis (to 30 days)	0.0% (0/207)	0.4% (1/232)	0.0 [-,-}	0.4% [1.3%, 0.4%]	0.3443
Site Thrombosis (Days 31-240)	1.0% (2/207)	0.0% (0/232)	-[-,-]	1.0% [-0.4%, 2.3%]	0.1335
Total Occlusions (Angiographic)	3.3% (5/150)	3.7% (7/188)	0.9 [0.29, 2.76]	-0.4% [-4.3%, 3.6%]	0.8473

Numbers are % (counts/sample size) or Mean ± SD. CI = Confidence Interval

Relative Risk = START 40/20/START Placebo SE = sqrt{(1-p_1)/n_{11}+(1-p_2)/n_{21}} CI = RR*exp(±1.96*SE)

Difference = START 40/20 – START Placebo SE = sqrt($p1*q_1/n_1+p_2*q_2/n_2$) CI = Diff±1.96*SE

N/A = Not applicable.

Target Lesion Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method. If QCA was not available, the visual estimate of diameter stenosis was used.

Procedure Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method and no in-hospital major adverse cardiac events (MACE). If QCA was not available, the visual estimate of diameter stenosis was used.

Device Success = Successful delivery of the Beta-Cath™ System.

Stent segment was defined as the area confined to the proximal and distal borders of the stent.

Analysis segment was defined as the segment that extends 5 mm proximal and distal to the radiated or injured landmark, whichever was longest in length.

*Survival estimates from Kaplan-Meier method. Standard error estimate from Peto formula.
TLR-free = Freedom from target lesion revascularization.

TVR-free = Freedom from target vessel revascularization.

TVF-free = Freedom from death, MI, and target vessel revascularization.

MACE-free = Freedom from death, MI, emergent CABG, and target vessel revascularization.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization from hospital discharge through the 240-day contact, as determined by the independent Clinical Events Committee.

Stent thrombosis was defined as angiographic thrombus or subacute closure within the target vessel at the time of the clinically driven angiographic restudy for documented ischemia (chest pain and ECG changes). Any death not attributed to a non-cardiac cause within the first 30 days was considered a surrogate for thrombosis in the absence of documented angiographic stent patency.

Site thrombosis was defined as myocardial infarction attributable to the target vessel with angiographic documentation (site-reported or by QCA) of thrombus or total occlusion at the target site >30 days after the index procedure in the absence of an intervening revascularization of the target vessel.

Aneurysm was defined as an expansion of the lumen by at least 20% compared with the normal lumen dimensions in the treatment region (analyzed segment) that extends with a wide or narrow mouth beyond the apparent normal contour.

Total Occlusion = An MLD of zero at follow-up as assessed by QCA.

Table 3. Principal Effectiveness and Safety Results
All Patients Treated (N=451)
START 40/20 versus START Sr-90

Efficacy Measures	START 40/20 (N=207 Patients)	START Placebo (N=244 Patients)	Relative Risk [95% C.I.]	Difference [95% C.I.]	P-value
8 Month Stent Segment Binary Restenosis Rate	15.4% (23/149)	14.2% (28/197)	1.1 [0.65, 1.81]	1.2% [-6.4%, 8.8%]	0.7507
8 Month Analysis Segment Binary Restenosis Rate	25.3% (38/150)	28.8% (57/198)	0.9 [0.62, 1.25]	-3.5% [-12.8%, 5.9%]	0.4738
TLR-Free at 240 Days*	88.2%	86.4%	1.02 [0.94, 1.11]	1.8% [-5.2%, 8.8%]	0.4516
TVR-Free at 240 Days*	83.1%	83.5%	1.00 [0.91, 1.09]	-0.4% [-8.1%, 7.4%]	0.8750
TVF-Free at 240 Days*	80.0%	81.4%	0.98 [0.89, 1.09]	-1.4% [-9.5%, 6.8%]	0.8724
MACE-Free at 240 Days*	80.0%	81.4%	0.98 [0.89, 1.09]	-1.4% [-9.5%, 6.8%]	0.8724
Target Lesion Success	95.7% (198/207)	99.6% (243/244)	1.0 [0.93, 0.99]	-3.9% [-6.8%, -1.0%]	0.0047
Procedure Success	93.7% (194/207)	97.1% (237/244)	1.0 [0.93, 1.01]	-3.4% [-7.3%, 0.5%]	0.0795
Device Success	96.6% (200/207)	98.4% (240/244)	1.0 [0.95, 1.01]	-1.7% [-4.7%, 1.2%]	0.2320
Post-Procedure Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	2.09± 0.40 (196)	2.17± 0.42 (242)		-0.08 [-0.16, -0.00]	0.0489
Range (min, max)	(1.02, 3.33)	(1.12, 3.47)			
Post-Procedure Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.84± 0.39 (196)	1.94± 0.39 (243)		-0.10 [-0.17, -0.03]	0.0073
Range (min, max)	(0.61, 2.89)	(1.03, 3.02)			
Post-Procedure Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	23.8%± 15.7% (196)	22.9± 13.5% (243)		0.8% [-1.9, 3.6%]	0.5479
Range (min, max)	(-13.4%, 66.0%)	(-31.1%, 53.2%)			
Post-Procedure Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	33.2%± 14.2% (196)	31.4%± 10.2% (243)		1.8% [-0.5, 4.1%]	0.1329
Range (min, max)	(-3.1%, 74.0%)	(6.7%, 57.6%)			
Follow-Up Stent Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.85± 0.65 (149)	1.96± 0.66 (197)		-0.11 [0.25, 0.03]	0.1088
Range (min, max)	(0.00, 3.41)	(0.00, 3.45)			
Follow-Up Analysis Segment Minimal Lumen Diameter (MLD, in mm)					
Mean± SD (N)	1.60± 0.58 (150)	1.65± 0.64 (198)		-0.05 [-.18, 0.08]	0.4252
Range (min, max)	(0.00, 3.16)	(0.00, 3.18)			
Follow-Up Stent Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	30.7%± 23.1% (149)	30.4± 22.7% (197)		0.3% [-4.6, 5.2%]	0.8991
Range (min, max)	(-8.0%, 100.0%)	(-32.2%, 100.0%)			
Follow-Up Analysis Segment Percent Diameter Stenosis (% DS)					
Mean± SD (N)	40.2%± 20.1% (150)	41.7± 20.7% (198)		-1.5% [-5.8, 2.9%]	0.5046
Range (min, max)	(2.4%, 100.0)	(-10.4%, 100.0%)			
Safety Measures and Other Clinical Events to 240 days					
In-Hospital MACE	1.9% (4/207)	2.5% (6/244)	0.8 [0.22, 2.75]	-0.5% [-3.2%, 2.2%]	0.7051
Out-of-Hospital MACE to 240 Days	17.9% (37/207)	16.0% (39/244)	1.1 [0.74, 1.68]	1.9% [-5.1%, 8.8%]	0.5930
In- and Out-of-Hospital MACE to 240 Days	19.3% (40/207)	18.0% (44/244)	1.1 [0.73, 1.58}	1.3% [-5.9%, 8.5%]	0.7257
Aneurysm†	0.7% (1/150)	0.5% (1/198)	1.3 [0.08, 20.93]	0.2% [-1.5%, 1.8%]	0.8434
Stent Thrombosis (to 30 days)	0.0% (0/207)	0.0% (0/244)	- [-,-]	0.0% [-,-]	-
Site Thrombosis (Days 31-240)	1.0% (2/207)	0.0% (0/244)	- [-,-]	1.0% [-0.4%, 2.3%]	0.1238
Total Occlusions (Angiographic)	3.3% (5/150)	4.0% (8/198)	0.8 [0.28, 2.47]	-0.7% [-4.7%, 3.3%]	0.7305

Numbers are % (counts/sample size) or Mean ± SD. CI = Confidence Interval

Relative Risk = START 40/20 Sr-90/START Sr-90 SE = sqrt{(1-p_1)/n_{11}+(1-p_2)/n_{21}} CI = RR*exp(±1.96*SE)

Difference = START 40/20 Sr-90 – START Sr-90 SE = sqrt(p_1*q_1/n_1+p_2*q_2/n_2) CI = Diff±1.96*SE

N/A = Not applicable.

Target Lesion Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method. If QCA was not available, the visual estimate of diameter stenosis was used.

Procedure Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method and no in-hospital major adverse cardiac events (MACE). If QCA was not available, the visual estimate of diameter stenosis was used.

Device Success = Successful delivery of the Beta-Cath™ System.

Footnotes are continued on the following page.

Stent segment was defined as the area confined to the proximal and distal borders of the stent.

Analysis segment was defined as the segment that extends 5 mm proximal and distal to the radiated or injured landmark, whichever was longest in length.

*Survival estimates from Kaplan-Meier method. Standard error estimate from Peto formula.

TLR-free = Freedom from target lesion revascularization.

TVR-free = Freedom from target vessel revascularization.

TVF-free = Freedom from death, MI, and target vessel revascularization.

MACE-free = Freedom from death, MI, emergent CABG, and target vessel revascularization.

In-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization prior to discharge as determined by the independent Clinical Events Committee.

Out-of-Hospital MACE = Death, Q wave or non-Q wave MI, emergent CABG, or target vessel revascularization from hospital discharge through the 240-day contact, as determined by the independent Clinical Events Committee.

Stent thrombosis was defined as angiographic thrombus or subacute closure within the target vessel at the time of the clinically driven angiographic restudy for documented ischemia (chest pain and ECG changes). Any death not attributed to a non-cardiac cause within the first 30 days was considered a surrogate for thrombosis in the absence of documented angiographic stent patency.

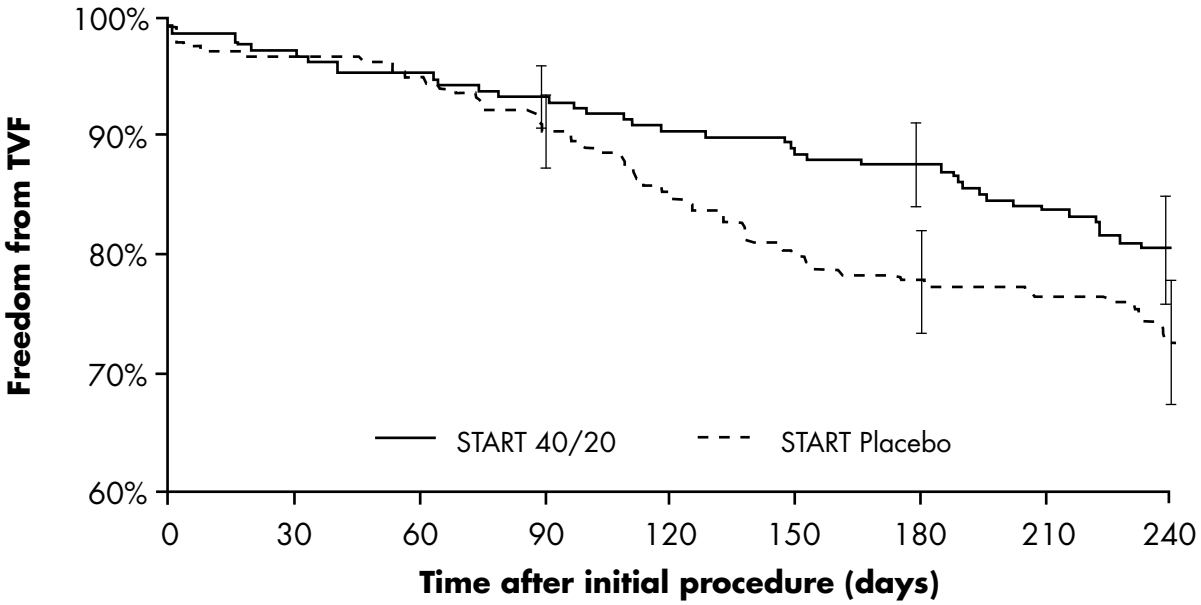
Site thrombosis was defined as myocardial infarction attributable to the target vessel with angiographic documentation (site-reported or by QCA) of thrombus or total occlusion at the target site >30 days after the index procedure in the absence of an intervening revascularization of the target vessel.

Aneurysm was defined as an expansion of the lumen by at least 20% compared with the normal lumen dimensions in the treatment region (analyzed segment) that extends with a wide or narrow mouth beyond the apparent normal contour.

†Baseline QCA for START Sr-90 patient 15/3 revealed the presence of an aneurysm. The Angiographic Core Laboratory reported the absolute size of the aneurysm changed very little from baseline to follow-up and that the larger appearance at follow-up was due to the smaller reference vessel dimension rather than an increase in aneurysm size.

Total Occlusion = An MLD of zero at follow-up as assessed by QCA.

Figure 2. Freedom from Target Vessel Failure (at 240 days)
Event-free Survival ± 1.5SE; All Patients Treated (N=439)
START 40/20 versus START Placebo



Time after initial procedure (days)

	0	30	60	90	120	150	180	210	240
START 40/20									
# Entered	207	206	199	193	189	183	179	174	162
# Lost to Follow-up	0	2	2	0	0	1	2	4	14
# Incomplete	0	0	0	0	0	0	0	0	0
# At risk	207.0	205.0	198.0	193.0	189.0	182.5	178.0	172.0	155.0
# Events	1	5	4	4	6	3	3	8	6
# Events/Month		5	4	4	6	3	3	8	6
% Survived	99.5%	97.1%	95.1%	93.2%	90.2%	88.7%	87.2%	83.2%	80.0%
% SE	0.5%	1.2%	1.5%	1.8%	2.1%	2.2%	2.4%	2.7%	3.0%
START Placebo									
# Entered	232	230	216	209	198	185	175	166	156
# Lost to Follow-up	0	8	2	2	0	0	4	7	31
# Incomplete	0	0	0	0	0	0	0	0	0
# At risk	232.0	226.0	215.0	208.0	198.0	185.0	173.0	162.5	140.5
# Events	2	6	5	9	13	10	5	3	7
# Events/Month		6	5	9	13	10	5	3	7
% Survived	99.1%	96.5%	94.3%	90.2%	84.3%	79.7%	77.4%	76.0%	72.2%
% SE	0.6%	1.2%	1.6%	2.0%	2.5%	2.7%	2.9%	3.0%	3.5%

Test Between Groups

Test	Chi-Square	Deg Frdm	P-Value
Wilcoxon	3.66	1	0.0559
Log-Rank	3.57	1	0.0590

RENO-Long Sub-Analysis

The European Surveillance **REgistry with the NOvoste Beta-Cath™ System (RENO)** Long Subgroup, a sub-analysis of 139 of the 1098 patients treated with the Beta-Cath™ (5F) System in the RENO Registry (a prospective commercial registry at 46 centers in Europe), began June 1, 1999. The RENO-Long subgroup focused on patients with diffuse in-stent restenotic lesions in single vessels treated by longer than 40 mm of radiation source train. Treatments with the Beta-Cath™ (5F) System included stepping (pullback)[1] procedures utilizing 30, 40 or 60 mm source trains or a single 60 mm source train. The acute and follow-up (6-month for RENO-Long and WRIST/Long WRIST and 8-month for START) clinical and angiographic results demonstrated that the procedural success rate, defined as the attainment of a residual stenosis <30% diameter stenosis at the time of intervention with successful delivery radiation therapy was 89.9% (124/138) as compared to 81.7% (76/93) in the WRIST/Long Wrist Control Group, 97.0% (225/232) in the START Placebo Group, and 97.1% (237/244) In the START Radiation Group. Freedom from MACE (6-month for RENO-Long and WRIST/Long WRIST and 8-month for START) was 82.1% (110/134) as compared to 35.1% (33/94) in the WRIST/Long Wrist Control Group (p<0.0001), 74.1% (172/232) in the START Placebo Group (p=0.0937), and 82.0% (200/244) In the START Radiation Group (p>0.9999). Freedom from TVR (6-month for RENO-Long and WRIST/Long WRIST and 8-month for START) was 85.1% (110/134) as compared to 39.4% (37/94) in the WRIST/Long Wrist Control Group (p<0.0001), 75.9% (176/232) in the START Placebo Group (p=0.0444), and 84.0% (205/244) in the START Radiation Group (p>0.8825).

Additionally, a comparison of the patients treated with stepping (pullback)[1] or a single 60 mm source train within the RENO-Long Subgroup demonstrated that the procedural success rate for the pullback group was 88.9% (96/109) as compared to 93.3% (28/30) in the 60 mm group. Freedom from MACE (6-month) was 81.0% (85/105) for the pullback group as compared to 86.2% (25/29) in the in the 60 mm group (p=0.5963). Freedom from TVR (6-month) was 83.8% (88/105) for the pullback group as compared to 89.7% (26/29) in the 60 mm group (p=0.5639).

A total of 139 patients of the 1098 enrolled in 46 centers in Europe were analyzed in the RENO-Long subgroup. Radiation was prescribed in the RENO registry according to the following schema:

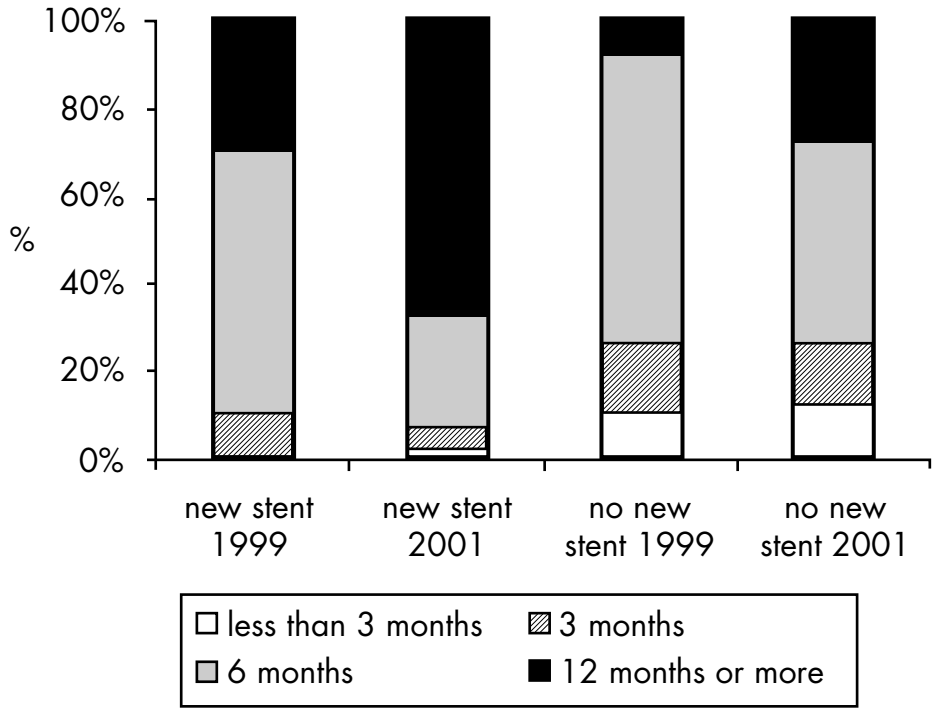
Without stent:
- 16.1 Gray at 2 mm if a maximum balloon diameter of ≥ 2.5 mm ≤ 3.5 mm was used; or
- 20.7 Gray at 2 mm if a maximum balloon diameter of > 3.5 mm < 4.0 mm was used; or
- 23.0 Gray at 2 mm if a maximum balloon diameter of ≥ 4.0 mm was used

With stent implantation (In-stent-restenosis or radiation after stent implantation):
- 18.4 Gray at 2 mm if a maximum balloon diameter of ≥ 2.5 mm ≤ 3.5 mm was used; or
- 23 Gray at 2 mm if a maximum balloon diameter of > 3.5 mm < 4.0 mm was used; or
- 25.3 Gray at 2 mm if a maximum balloon diameter of ≥ 4.0 mm was used

[1] The Beta-Cath™ System is not indicated for pullback (stepping).

The antiplatelet/anticoagulant regime administered for RENO was assessed with two questionnaires that were sent to investigators to define the prescribed duration of antiplatelet therapy. The first questionnaire was sent in July 1999 (3 months after patient recruitment had begun), and the second in April 2001 (at the time the last patients were followed-up for their 6-month visit). The survey demonstrated that most patients received greater than at least 6 months of antiplatelet therapy. The results of the survey are as follows:

Duration of combined antiplatelet regimen following VBT in the RENO Registry



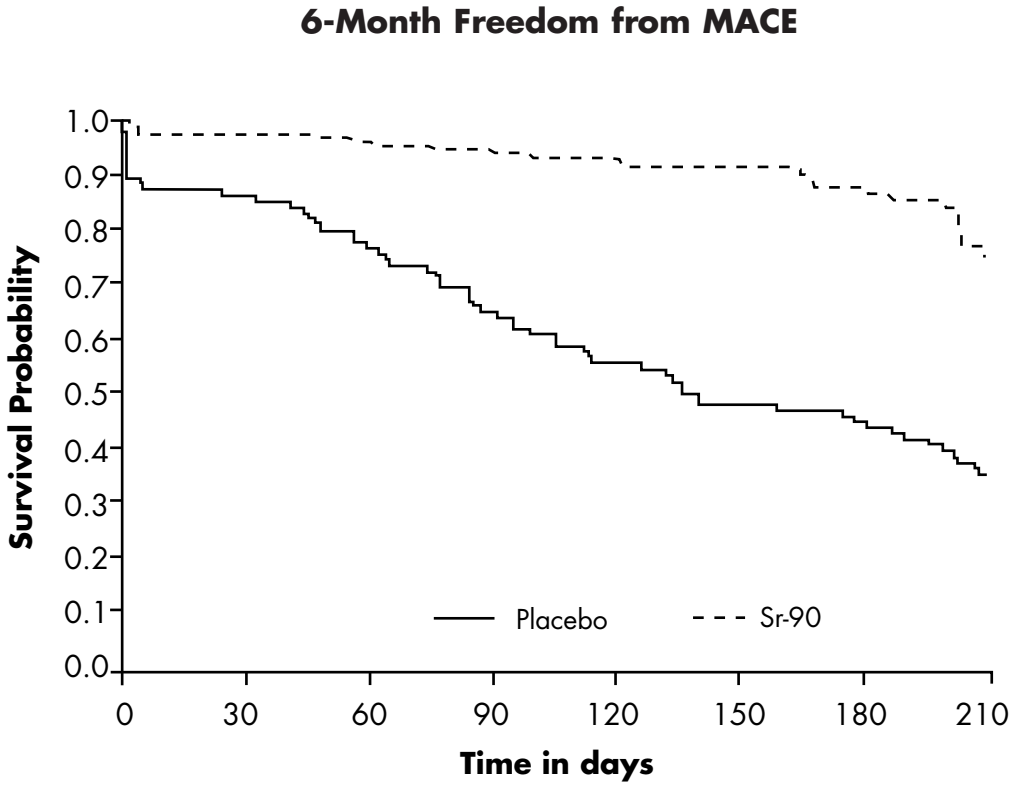
As reported in article submitted by Philip Urban, M.D., FACC, for publication in JACC, entitled: *A multicenter European Registry of Intraluminal Coronary Beta Brachytherapy.*

Table 4. Principal Effectiveness and Safety Results
RENO Long versus WRIST/Long WRIST Control
All Patients Treated (N=233)

Efficacy Measure	RENO-Long (N=139)	Wrist/Long Wrist Control (N=94)	Combined (N=233)	Relative Risk [95% C.I.]	Difference [95% C.I.]	p Value
Follow- up Done	**96.4%** (134/139)	**100.0%** (94/94)	**97.9%** (228/233)	**0.96** [0.93, 1.00]	**-3.60%** [-7.60, 0.40]	**0.0834**
Procedure Success	**89.9%** (124/138)	**81.7%** (76/93)	**86.6%** (200/231)	**1.10** [0.98, 1.23]	**8.13%** [-2.14, 18.41]	**0.0805**
Brachytherapy Success	**99.3%** (138/139)	**89.2%** (83/93)	**95.3%** (221/232)	**1.11** [1.04, 1.20]	**10.03%** [2.65, 17.42]	**0.0006**
MACE –Free at 6 months	**82.1%** (110/134)	**35.1%** (33/94)	**62.7%** (143/228)	**2.34** [1.76, 3.11]	**46.98%** [34.39, 59.57]	**<.0001**
TVR Free at 6 month	**85.1%** (114/134)	**39.4%** (37/94)	**66.2%** (151/228)	**2.16** [1.67, 2.81]	**45.71%** [33.18, 58.25]	**<.0001**
MACE at 6-months	**17.9%** (24/134)	**64.9%** (61/94)	**37.3%** (85/228)	**0.28** [0.19, 0.41]	**-46.98%** [-59.57, -34.39]	**<.0001**
TVR at 6-months	**14.9%** (20/134)	**60.6%** (57/94)	**33.8%** (77/228)	**0.25** [0.16, 0.38]	**-45.71%** [-58.25, -33.18]	**<.0001**
In-Hospital MACE	**2.3%** (3/131)	**11.7%** (11/94)	**6.2%** (14/225)	**0.20** [0.06, 0.68]	**-9.41%** [-17.35, -1.48]	**0.0050**
Out of Hospital MACE to 6 months	**16.4%** (22/134)	**61.7%** (58/94)	**35.1%** (80/228)	**0.27** [0.18, 0.40]	**-45.28** [-57.90, -32.66]	**<.0001**
CORE LAB SUBSET ANALYSIS						
In-Analysis Segment Late Loss at 6 months	**0.15 ± 0.71** (49)	**0.85 ± 0.57** (81)	**0.59 ± 0.71** (130)	**N/A**	**-0.70** [-0.92, -0.48]	**<.0001**
Stent Segment Late Loss at 6 months	**0.11 ± 0.90** (49)	**1.00 ± 0.66** (80)	**0.67 ± 0.87** (129)	**N/A**	**-0.89** [-1.16, -0.61]	**<.0001**
In-Analyisis Segment Late Loss Index at 6 Months	**-1.34± 7.32** (49)	**1.37 ± 4.78** (80)	**0.34 ± 6.00** (129)	**N/A**	**-2.71** [-4.82, -0.60]	**0.0240**
Stent Segment Late Loss Index at 6 Months	**0.01 ± 0.60** (49)	**0.86 ± 0.61** (79)	**0.54 ± 0.73** (128)	**N/A**	**-0.85** [-1.07, -0.63]	**<.0001**
In-Analysis Segment Binary Restenosis Rate at 6 Months	**28.6%** (14/49)	**76.5%** (62/81)	**58.5%** (76/130)	**0.37** [0.24, 0.59]	**-47.97%** [-65.41,- 30.54]	**<.0001**
Stent Segment Binary Restenosis Rate at 6 Months	**20.4%** (10/49)	**70.0%** (56/80)	**51.2%** (66/129)	**0.29** [0.16, 0.52]	**-49.59%** [-66.47, -32.71]	**<.0001**

Numbers are % (counts/n) or Mean ± SD (n)
CI= Confidence Interval
Relative Risk = p_1/p_2 SE = sqrt {((1-p_1)/n_1 p_1, + ((1-p_2/n_2p_2)} CI = RR* exp (±1.96* SE)
Difference = p_/p_ SE + sqrt {(p_1* (1-p_1)/(n_1 - 1) + p_2* (1 - p_2)/(n_2 - 1)} CI = diff. ± (1.96* SE + 0.5* (1/n_1 + 1/n_2))
NA = Not applicable
Procedure Success = Attainment of a <50% residual diameter stenosis using any percutaneous method and no in-hospital MACE.
Brachytherapy Success = Attainment of a <50% residual stenosis and successful delivery of the radiation device.
Restenosis was defined at ≥50% in-stent diameter stenosis at the follow-up angiogram. If an in-stent measurement was not available, the In-lesion diameter was used. In-Analysis Segment = Stent + Probe + Edges areas.
*Survival Estimates from Kaplan-Meier estimate. Standard Error estimate by Peto formula.
Mace-Free = No Death, Q Wave of Non-Q Wave MI, CABG, or Target Vessel Revascularization.

Figure 3. Principal Effectiveness and Safety Results
RENO Long versus WRIST/Long WRIST Control



Summary Statistics

	Total	Events	Censored	Event Free %
RENO	134	24	110	82.09%
Control	94	61	33	35.11%

Tests Between Groups

	Chi-Square	d.o.f.	P Value
Log-Rank	49.6	1	< .0001
Wilcoxon	55.2	1	< .0001

Table 5. Principal Effectiveness and Safety Results RENO-Long versus START Placebo All Patients Treated (N=371)

Efficacy Measure	RENO-Long (N=139)	START Placebo (N=232)	Combined (N=371)	Relative Risk [95% C.I]	Difference [95% C.I.]	p Value
Follow- up Done	**96.4%** (134/139)	**100.0%** (244/244)	**98.7%** (378/383)	**0.96** [0.93, 1.00]	**-3.60%** [-7.27, 0.07]	**0.0060**
Procedure Success	**89.9%** (124/138)	**97.0%** (225/232)	**94.3%** (349/370)	**0.93** [0.87, 0.98]	**-7.13%** [-13.22, -1.03]	**0.0088**
Brachytherapy Success	**99.3%** (138/139)	**N/A**	**99.3%** (138/139)	**N/A**	**N/A**	**N/A**
MACE –Free	**82.1%** (110/134)	**74.1%** (172/232)	**77.0%** (282/366)	**1.11** [0.99, 1.24]	**7.95%** [-1.26, 17.16]	**0.0937**
TVR Free	**85.1%** (114/134)	**75.9%** (176/232)	**79.2%** (290/366)	**1.12** [1.01, 1.24]	**9.21%** [0.43, 17.99]	**0.0444**
MACE	**17.9%** (24/134)	**25.9%** (60/232)	**23.0%** (84/336)	**0.69** [0.45, 1.06]	**-7.95%** [-17.16, 1.26]	**0.0937**
TVR	**14.9%** (20/134)	**24.1%** (56/232)	**20.8%** (76/366)	**0.62** [0.39, 0.98]	**-9.21%** [-17.99, -0.43]	**0.0444**
In-Hospital MACE	**2.2%** (3/139)	**2.2%** (5/232)	**2.2%** (8/371)	**1.00** [0.24, 4.13]	**0.00%** [-3.64, 3.64]	**>0.9999**
Out of Hospital MACE	**16.4%** (22/134)	**24.1%** (56/232)	**21.3%** (78/366)	**0.68** [0.44, 1.06]	**-7.72%** [-16.68, 1.24]	**0.0867**
CORE LAB SUBSET ANALYSIS						
In-Analysis Segment Late Loss	**0.15+/- 0.71** (49)	**0.55+/-0.59** (188)	**N/A**	**N/A**	**-0.40** [-0.59, -0.21]	**0.0006**
Stent Segment Late Loss	**0.11+/-0.90** (49)	**0.67+/-0.61** (187)	**N/A**	**N/A**	**-0.56** [-0.77, -0.35]	**0.0001**
In-Analysis Segment Late Loss Index	**-1.34+/-7.32** (49)	**0.84+/-3.41** (187)	**N/A**	**N/A**	**-2.18** [-3.60, -0.76]	**0.0476**
Stent Segment Late Loss Index	**0.01+/-0.60** (49)	**0.57+/-0.60** (186)	**N/A**	**N/A**	**-0.56** [-0.75, -0.37]	**<.0001**
In-Analysis Segment Binary Restenosis Rate	**28.6%** (14/49)	**45.2%** (85/188)	**41.8%** (99/237)	**0.63** [0.40, 1.01]	**-16.64%** [-32.56, -0.72]	**0.0502**
Stent Segment Binary Restenosis Rate	**20.4%** (10/49)	**41.2%** (77/187)	**36.9%** (87/236)	**0.50** [0.28, 0.88]	**-20.77%** [-35.47, -6.06]	**0.0077**

Numbers are % (counts/n) or Mean ± SD (n)
Relative Risk = p_1/p_2 SE = sqrt {$((1-p_1)/n_1\ p_1, + ((1-p_2)/n_2p_2)$}
Difference = p_1/p_2 SE + sqrt {$(p_1* (1-p_1)/(n_1 - 1) + p_2* (1 - p_2)/(n_2 - 1)$}
CI= Confidence Interval
CI = RR* exp (±1.96* SE)
CI = diff. ± (1.96* SE + 0.5* $(1/n_1 + 1/n_2)$)
NA = Not applicable
Procedure Success = Attainment of a <50% residual diameter stenosis using any percutaneous method and no in-hospital MACE.
Brachytherapy Success = Attainment of a <50% residual stenosis and successful delivery of the radiation device.
Restenosis was defined at ≥50% in-stent diameter stenosis at the follow-up angiogram. If an in-stent measurement was not available, the In-lesion diameter was used. In-Analysis Segment = Stent + Probe + Edges areas.
*Survival Estimates from Kaplan-Meier estimate. Standard Error estimate by Peto formula.
Mace-Free = No Death, Q Wave of Non-Q Wave MI, CABG, or Target Vessel Revascularization.

Table 6. Principal Effectiveness and Safety Results
RENO-Long versus START Radiation
All Patients Treated (N=383)

Efficacy Measure	RENO-Long (N=139)	START Radiation (N=244)	Combined (N=383)	Relative Risk [95% C.I]	Difference [95% C.I.]	p Value
Follow- up Done	**96.4%** (134/139)	**100.00%** (244/244)	**98.6%** (378/383)	N/A	N/A	N/A
Procedure Success	**89.9%** (124/138)	**97.1%** (237/244)	**94.5%** (361/382)	**0.93** [0.87, 0.98]	**-7.28%** [-13.32, -1.23]	**0.0042**
Brachytherapy Success	**99.3%** (138/139)	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**
MACE–Free	**82.1%** (110/134)	**82.0%** (200/244)	**82.0%** (310/378)	**1.00** [0.91, 1.11]	**0.12%** [-8.57, 8.81]	**>0.9999**
TVR-Free	**85.1%** (114/134)	**84.0%** (205/244)	**84.4%** (319/378)	**1.01** [0.93, 1.11]	**1.06%** [-7.13, 9.25]	**0.8825**
MACE	**17.9%** (24/134)	**18.0%** (44/244)	**18.0%** (68/378)	**0.99** [0.63, 1.56]	**-0.12%** [-8.81, 8.57]	**>0.9999**
TVR	**14.9%** (20/134)	**16.0%** (39/244)	**15.6%** (59/378)	**0.93** [0.57, 1.53]	**-1.06%** [-9.25, 7.13]	**0.8825**
In-Hospital MACE	**2.3%** (3/131)	**2.5%** (6/244)	**2.4%** (9/375)	**0.93** [0.24, 3.66]	**-0.17%** [-3.98, 3.64]	**>.0.9999**
Out of Hospital MACE	**16.4%** (22/134)	**16.0%** (39/244)	**16.1%** (61/378)	**1.03** [0.64, 1.66]	**0.43%** [-7.95, 8.81]	**>0.9999**
CORE LAB SUBSET ANALYSIS						
In-Analysis Segment Late Loss	**0.15+/-0.71** (49)	**0.28+/-0.56** (198)	**N/A**	**N/A**	**-0.13** [-0.32, 0.06]	**0.2373**
Stent Segment Late Loss	**0.11+/-0.90** (49)	**0.21+/-0.61** (197)	**N/A**	**N/A**	**-0.10** [-0.31, 0.11]	**0.4641**
In-Analyisis Segment Late Loss Index	**-1.34+/-7.32** (49)	**0.35+/-1.06** (198)	**N/A**	**N/A**	**-1.69** [-2.75, -0.63]	**0.1135**
Stent Segment Late Loss Index	**0.01+/-0.60** (49)	**0.09+/-1.28** (197)	**N/A**	**N/A**	**-0.08** [-0.45, 0.29]	**0.5236**
In-Analysis Segment Binary Restenosis Rate	**28.6%** (14/49)	**28.8%** (57/198)	**28.7%** (71/247)	**0.99** [0.61, 1.63]	**-0.22%** [-15.75, 15.32]	**>0.9999**
Stent Segment Binary Restenosis Rate	**20.4%** (10/49)	**14.2%** (28/197)	**15.4%** (38/246)	**1.44** [0.75, 2.75]	**6.19%** [-7.48, 19.87]	**0.2767**

Numbers are % (counts/n) or Mean ± SD (n) CI= Confidence Interval

Relative Risk = p_1/p_2 SE = sqrt $\{((1-p_1)/n_1\ p_1, + ((1-p_2)/n_2p_2)\}$ CI = RR* exp (±1.96* SE)

Difference = p_1/p_2 SE + sqrt $\{(p_1*\ (1-p_1)/(n_1 - 1) + p_2*\ (1 - p_2)/(n_2 - 1)\}$ CI = diff. ± (1.96* SE + 0.5* $(1/n_1 + 1/n_2)$)

NA = Not applicable

Procedure Success = Attainment of a <50% residual diameter stenosis using any percutaneous method and no in-hospital MACE.

Brachytherapy Success = Attainment of a <50% residual stenosis and successful delivery of the radiation device.

Restenosis was defined at ≥50% in-stent diameter stenosis at the follow-up angiogram. If an in-stent measurement was not available, the In-lesion diameter was used. In-Analysis Segment = Stent + Probe + Edges areas.

*Survival Estimates from Kaplan-Meier estimate. Standard Error estimate by Peto formula.

Tlr-Free= No Target Lesion Revascularization, Mace-Free = No Death, Q Wave of Non-Q Wave MI, CABG, or Target Vessel Revascularization.

Table 7. Principal Effectiveness and Safety Results
Pullback[1] versus Non-Pullback (60 mm)
All Patients Treated (N=139)

Efficacy Measure	Pullback[1] (N=109)	Non-pullback (N=30)	Combined (N=139)	Relative Risk	Difference	P Value
Follow- up Done	**96.3%** (105/109)	**96.7%** (29/30)	**96.4%** (134/139)	**1.00** [0.92, 1.08]	**-0.34%** [-9.90, 9.22]	**>0.9999**
Procedure Success	**88.9%** (96/109)	**93.3%** (28/30)	**89.9%** (124/138)	**0.95** [0.85, 1.07]	**-4.44%** [-17.43, 8.54]	**0.7342**
Brachytherapy Success	**100.0%** (109/109)	**96.7%** (29/30)	**99.3%** (138/139)	**1.03** [0.97, 1.11]	**3.33%** [-5.33, 11.99]	**0.2158**
MACE –Free at 6 months	**81.0%** (85/105)	**86.2%** (25/29)	**82.1%** (110/134)	**0.94** [0.79, 1.12]	**-5.25%** [-22.29, 11.78]	**0.5963**
TVR Free at 6 month	**83.8%** (88/105)	**89.7%** (26/29)	**85.1%** (114/134)	**0.93** [0.80, 1.09]	**-5.85%** [-21.36, 9.67]	**0.5639**
MACE at 6-months	**19.0%** (20/105)	**13.8%** (4/29)	**17.9%** (24/134)	**1.38** [0.51, 3.72]	**5.25%** [-11.78, 22.29]	**0.5963**
TVR at 6-months	**16.2%** (17/105)	**10.3%** (3/29)	**14.9%** (20/134)	**1.57** [0.49, 4.97]	**5.85%** [-9.67, 21.36]	**0.5639**
In-Hospital MACE	**0.9%** (1/109)	**6.7%** (2/30)	**2.2%** (3/139)	**0.14** [0.01, 1.47]	**-5.75%** [-17.13, 5.63]	**0.1175**
Out of Hospital MACE to 6 months	**18.1%** (19/105)	**10.3%** (3/29)	**16.4%** (22/134)	**1.75** [0.56, 5.50]	**7.75%** [-7.94, 23.44]	**0.4057**
CORE LAB SUBSET ANALYSIS						
In-Analysis Segment Late Loss at 6 months	**0.21 ± 0.74** (37)	**-0.02 ± 0.59** (12)	**0.15 ± 0.71** (49)	**N/A**	**0.22** [-0.25, 0.70]	**0.3446**
Stent Segment Late Loss at 6 months	**0.28 ± 0.95** (37)	**-0.38 ± 0.46** (12)	**0.11 ± 0.90** (49)	**N/A**	**0.66** [0.08, 1.23]	**0.0028**
In-Analyisis Segment Late Loss Index at 6 Months	**-1.68± 8.41** (37)	**-0.28 ± 0.95** (12)	**-1.34 ± 7.32** (49)	**N/A**	**1.40** [-6.33, 3.52]	**0.3256**
Stent Segment Late Loss Index at 6 Months	**0.12 ± 0.61** (37)	**-0.31 ± 0.44** (12)	**0.01 ± 0.60** (49)	**N/A**	**0.43** [0.05, 0.82]	**0.0289**
In-Analysis Segment Binary Restenosis Rate at 6 Months	**35.1%** (13/37)	**8.3%** (1/12)	**28.6%** (14/49)	**4.22** [0.61, 28.96]	**26.80%** [-1.30, 54.90]	**0.1391**
Stent Segment Binary Restenosis Rate at 6 Months	**27.0%** (10/37)	**0.0%** (0/12)	**20.4%** (10/49)	**7.18** [0.45, 114.22]	**27.03** [7.00, 47.05]	**0.0926**

Numbers are % (counts/n) or Mean ± SD (n) CI= Confidence Interval

Relative Risk = p_1/p_2 SE = sqrt $\{((1-p_1)/n_1\ p_1, + ((1-p_2)/n_2p_2)\}$ CI = RR* exp (±1.96* SE)

Difference = p_1/p_2 SE + sqrt $\{(p_1* (1-p_1)/(n_1 - 1) + p_2* (1 - p_2)/(n_2 - 1)\}$ CI = diff. ± (1.96* SE + 0.5* $(1/n_1 + 1/n_2)$)

NA = Not applicable

Procedure Success = Attainment of a <50% residual diameter stenosis using any percutaneous method and no in-hospital MACE.

Brachytherapy Success = Attainment of a <50% residual stenosis and successful delivery of the radiation device.

Restenosis was defined at ≥50% in-stent diameter stenosis at the follow-up angiogram. If an in-stent measurement was not available, the In-lesion diameter was used. In-Analysis Segment = Stent + Probe + Edges areas.

*Survival Estimates from Kaplan-Meier estimate. Standard Error estimate by Peto formula.

Tlr-Free= No Target Lesion Revascularization, Mace-Free = No Death, Q Wave of Non-Q Wave Mi, Cabg, or Target Vessel Revascularization.

[1] The Beta-Cath™ System is not indicated for pullback (stepping).

IV. Instructions For Use

The following section provides instructions for using the Beta-Cath™ 3.5F System from Novoste Corporation. The Beta-Cath™ 3.5F System is designed to be used by a team of appropriately trained personnel. At a minimum, this team should include a Cardiologist, Radiation Oncologist, and Medical Physicist.

Detailed Device Description

The Beta-Cath™ 3.5F System is designed to provide protection to health care workers and to minimize patient exposure to ionizing radiation. The unique design of the Transfer Device allows the beta sources to be contained and shielded during transport and storage without substantially modifying the safety procedures and protocols currently used in Cardiac Catheterization Labs. The Beta-Cath™ 3.5F System consists of four components; the two major components are described below:

1) The **Transfer Device** is a multiple-use, hand-held device used to store the Source Train and to deliver the sources to and from the vessel by means of the Delivery Catheter. The Transfer Device is designed to shield health care workers from beta radiation. The single-use Delivery Catheter does not allow the Sources to come in contact with the patient's blood or tissue. The Transfer Device will contain either an ACTIVE or NON-ACTIVE Source Train. The 3.5F System compatible Transfer Device is color-coded gray.

   The Transfer Device is available in <u>two</u> Models: the <u>Standard Model</u>, which has "Novoste Beta-Cath™ 3.5F System" stamped on the bottom of the front of the device, and a procedure counter on the bottom of the back of the device, and the <u>Exchangeable Battery Model</u>, which has "Novoste" stamped on the bottom of the front of the device, and an exchangeable battery compartment on the back of the device. Please refer to page 2 of this User's Manual for an illustration of the two Transfer Device Models.

   Note: Because the two Transfer Device Models have different service cycles, it is important to identify which Model you are using. Specific instructions for the different Models may be found in Sections *IV. Transfer Device Controls & Indicators*, and *VI. System Specifications*. The operation of and treatment with both Transfer Device Models is identical; they only differ as noted in the Transfer Device Controls & Indicators section and System Specifications.

   Note: Unless otherwise indicated, references to "Transfer Device" in this User's Manual apply to <u>both</u> Transfer Device Models.

   The ACTIVE Source Train will contain a wire jacketed "train" of 12 (30 mm Source Train), 16 (40 mm Source Train) or 24 (60 mm Source Train) miniature cylindrical radioactive sealed sources containing ^{90}Strontium/^{90}Yttrium (^{90}Sr/^{90}Y), pure beta emitters, and two (one distal and one proximal) radiopaque markers. The principal radiation emission is beta particles with energies up to 2.27 MeV. ^{90}Sr/^{90}Y has a radioactive half-life of 28.8 years. The long half-life simplifies treatment planning due to the slow rate of radioactive decay.

   The presence of the black and yellow Radioactive Warning Symbol will identify the ACTIVE Transfer Device.

   An optional NON-ACTIVE Transfer Device will contain a NON-ACTIVE Source Train consisting of 16 (40 mm Source Train) miniature cylindrical NON-ACTIVE sources, and two (one distal and one proximal) radiopaque markers. This Transfer Device is **NOT RADIOACTIVE** and will be labeled NON-ACTIVE.

2) The Novoste™ β-Rail™ 3.5F **Delivery Catheter** is a single-use, closed-end catheter, with a 1 cm distal rail segment. The Source Train is transported to the treatment site and back into the Transfer Device through the Delivery Catheter. The Delivery Catheter is compatible with the 30 mm, 40 mm and 60 mm versions of the Beta-Cath™ 3.5F System compatible Transfer Device.

   The Delivery Catheter is supplied sterile and includes an Indicator of Source Train (IST) pre-loaded into the Delivery Catheter, and a Flushing Cannula. The IST aids in the measurement and positioning of the Delivery Catheter to ensure placement of the radioactive Source Train across the entire interventional injury. The Proprietary Connector connects the Delivery Catheter exclusively to the Novoste™ Beta-Cath™ 3.5F System compatible Transfer Device.

How Supplied

The initial Beta-Cath™ 3.5F System shipment will include the following items:

- ACTIVE Transfer Device and White Lead-Lined Container in a Type A shipping container
- Start-Up Kit which contains the following items:
  - One Transport Case, which includes:
    - One Response Kit
  - One Temporary Storage Container
  - One 5-pack box of Medical Physicist's Kits

The β-Rail™ 3.5F Delivery Catheter which includes the Procedure Accessory Pack (supplied sterile) is sold separately.

All items are also sold individually.

Reusable Items

ACTIVE Transfer Device:

The Transfer Device containing the ACTIVE Source Train will be shipped to the hospital inside a White Lead-Lined Storage Container in a Type A (for shipping radioactive material) shipping container. The Transfer Device should be received by radiation personnel of the institution according to local regulations and institutional radiation procedures. After the radiation safety personnel perform the incoming Device Receipt Procedure, the White Lead-Lined Storage Container containing the ACTIVE Transfer Device with the ACTIVE Source Train should be placed in the Transport Case for movement within your institution and secured from unauthorized access.

The Transport Case is a plastic (non-sterile) storage case. It will be shipped to the hospital without radioactive material and functions only as a storage case (i.e. not a Type A container) for the following items:

Single Transport Case

- Combination Lock to help secure from unauthorized access.
- A Response Kit (shipped inside Transport Case):
  - Battery-operated flashlight
  - Tweezers
  - Source Recovery Probe
  - Source Container with a screw-on top (intended for single use)
  - Magnifying Glass
- Compartment to store the White Lead-Lined Storage Container containing the ACTIVE Transfer Device.
- An empty storage compartment.

The Transport Case with an ACTIVE Transfer Device should only be stored in a secure area designated for radioactive material storage.

The Twin Transport case is provided to those hospitals which possess two ACTIVE Transfer Devices. It contains the same items as the single Transport Case, but has an additional compartment to store a second White-Lead Lined Storage Container containing the second ACTIVE Transfer Device.

Twin Transport Case

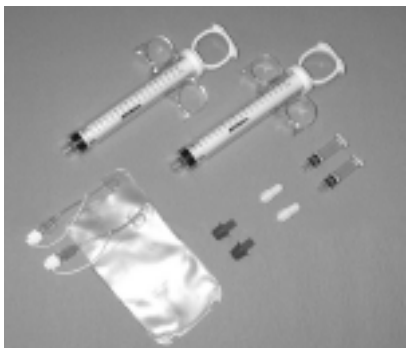
Temporary Storage Container:

The Temporary Storage Container is a clear plastic (non-sterile) container. This Container is designed to shield beta radiation and is used to temporarily store the Beta-Cath™ 3.5F System in the event that the ACTIVE Source Train is unable to be returned to the Source Chamber of the ACTIVE Transfer Device.

Medical Physicist's Kit:

The Medical Physicist's Kit contains the disposable accessories required to perform the initial Device Receipt Procedure and to purge fluid from the Transfer Device. The Kit contains:

- two (2) 3.5F Flushing Adapters
- two (2) 20 ml Three Ring Syringes
- two (2) Fluid Collection Bags
- two (2) 3.5F Quartz Caps
- two (2) Syringe Luer Caps



Single-Use Items

β-Rail™ 3.5F Delivery Catheter (Figure 4):

The β-Rail™ 3.5F Delivery Catheter is a distal rail-style catheter that allows the Source Train to be hydraulically delivered to and from the targeted site in the coronary vasculature. The Delivery Catheter is provided sterile and is packaged with the Procedure Accessory Pack, which includes the sterile accessories required to perform the procedure.

β-Rail™ 3.5F Delivery Catheter:

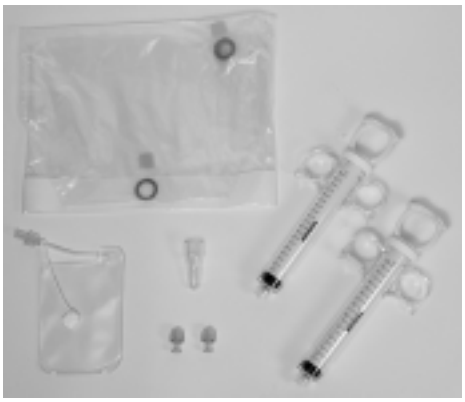
- ≥ 6F (1.7 mm/0.067" ID) guide catheter compatible.
- ≤ 0.014" (0.36 mm) steerable guidewire compatible.
- An open lumen allowing the guidewire to travel over the distal segment of the Delivery Catheter with the wire exiting 1 cm from the distal tip.
- A second lumen contains a preloaded Indicator of Source Train (IST) with radiopaque markers for 30 mm, 40 mm and 60 mm radiation source train positioning while in the catheter.
- Internal radiopaque marker (stop) at most distal source train position.
- A proximal depth marker positioned approximately 100 cm from the distal tip that facilitates placement of the Delivery Catheter through the Guiding Catheter.
- A proximal end that consists of a Proprietary Connector which utilizes squeeze tabs to ensure a secure connection between the Delivery Catheter and the Transfer Device.
- Working length of 135 cm.
- Overall length of:
  - 180 cm β-Rail 3.5F Delivery Catheter
  - 267 cm β-Rail 3.5F XL Delivery Catheter
- Sterile package includes one β-Rail™ 3.5F Delivery Catheter, pre-loaded IST and a Flushing Cannula.

Procedure Accessory Pack:

(included inside the β-Rail™ 3.5F Delivery Catheter Box)

The Procedure Accessory Pack contains the disposable, single use sterile accessories required to perform the procedure. The pack contains:

- minimum of (1) Fluid Collection Bag
- two (2) 20 ml Three Ring Syringes
- two (2) Extension Connectors
- minimum of (1) Sterile Bag
- minimum of (1) Proprietary Connector Cover



Transfer Device Controls & Indicators

The Transfer Device serves the following functions:

1) Stores the Source Train.

2) Aligns and connects the Delivery Catheter with the Transfer Device.

3) Controls the direction of fluid flow (allowing delivery and return of the Source Train).

4) Shields beta radiation.

Note: The color, lights or graphics associated with the Transfer Device are designed to convey the following:

Blue = Informational features of the Transfer Device.

Green = Features associated with the secured position in the Transfer Device (green arrow light on) or the successful return of the Source Train into the Transfer Device.

Amber = Features associated with sending the Source Train from the Transfer Device into the Delivery Catheter and maintaining the Source Train in the Treatment Zone or when the Source Train has been moved out of the proper position within the Source Chamber.

Red = Features associated with excessive or unsafe pressure being used with the Transfer Device.

For Use of Standard Model Only:
The Transfer Device can be turned ON or OFF by depressing the Blue ON/OFF button for 3-5 seconds. The system will automatically power off if the operator has not pressed the ON/OFF button within 5 minutes (except when the Source Train is out). When the Source Train is out, the system will automatically power off if there is 15 minutes of inactivity. When the ON/OFF button is initially depressed, the electronics will perform an LED light test indicated when all of the indicator lights alternately blink.

For Use of Exchangeable Battery Model Only:
The Transfer Device can be turned ON or OFF by depressing the Blue ON/OFF button for 3-5 seconds. When the ON/OFF button is initially depressed, the electronics will perform an LED light test indicated when all of the indicator lights alternately blink. The system will automatically power off after 50 minutes when the gate is closed, the ON/OFF button has not been pressed and the Source Train has not been sent/received. If the system powers OFF during a procedure, simply press the blue ON/OFF button again to turn the device back ON.

The Transfer Device incorporates an electronic source sensing system that independently verifies the position of the Source Train. Once the LED light test is completed, either the Green or Amber Arrow Indicator light will remain illuminated depending on the position of the Source Train in the Source Chamber. When the Source Train is properly positioned in the Transfer Device, the Green Arrow Indicator light is illuminated. When the Source Train has been moved out of the proper position within Source Chamber of the Transfer Device, the Amber Arrow Indicator light is illuminated.

The Fluid Control Lever allows for the sending and return of the Source Train from the Transfer Device. This action can only take place when the Transfer Device is properly connected to the Delivery Catheter, the Proprietary Connector is fully locked and the blue line is visible on the Proprietary Connector Lock Latch.

For Use of Exchangeable Battery Model Only:

Exchange of Battery Power Source

Novoste™ Transfer Devices are designed to allow for easy exchange of the product's power supply. A 6 Volt Lithium ion battery powers the Transfer Device. Included in the Transfer Device packaging is a 6 Volt Lithium ion battery. To insert or replace the battery, open the battery door and insert the battery. To open the battery door, simply use a screwdriver or other appropriate hand tool to turn the battery door screw located on the back of the Transfer Device. As the screw releases, the battery door will open on its hinge, exposing the battery compartment. Place the new battery inside the compartment with its contacts facing downward. Once inserted, close the battery door and tighten the screw by turning it to the right until it is firmly set. Test the Transfer Device power supply by pressing the ON/OFF button, as it is now ready for use. For **battery disposal**, follow battery manufacturer's instructions. For further assistance, see your Novoste representative.

PRECAUTION: Do not recharge, disassemble, expose to high temperatures or incinerate the provided Transfer Device battery. Keep in package until ready to use. Dispose of used battery properly.

Figure 4. Beta-Cath™ 3.5F System

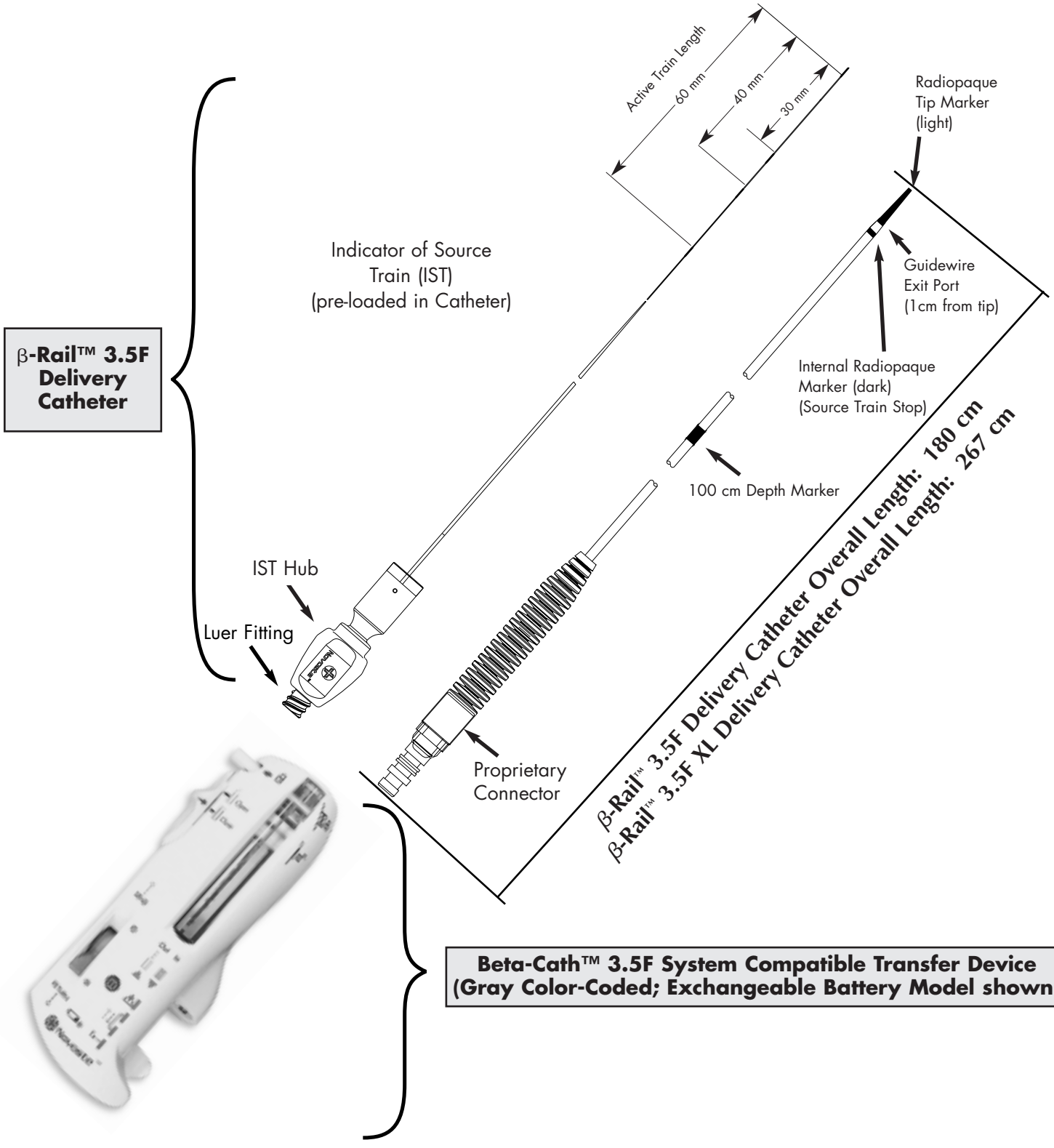


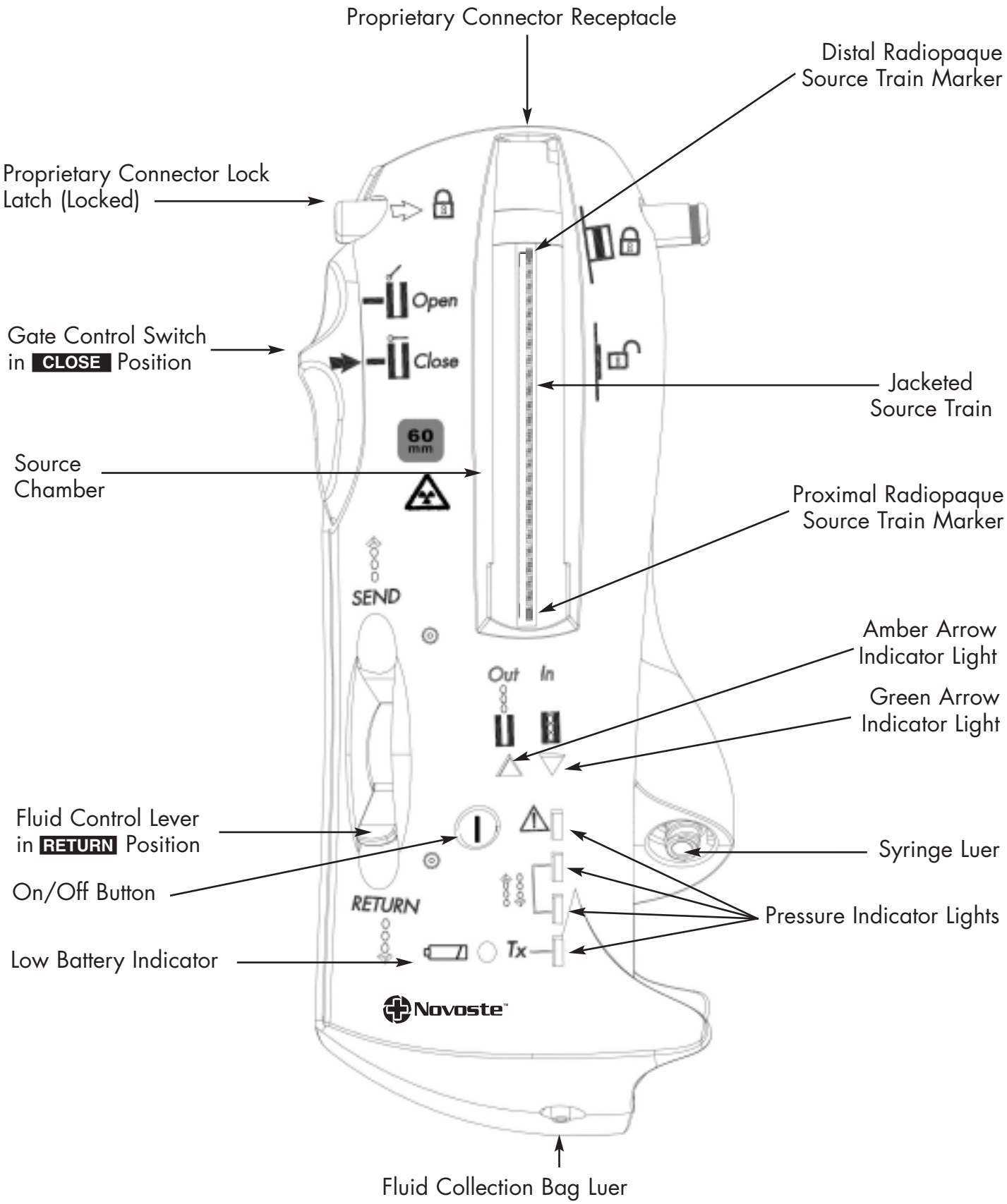
Table 8: Transfer Device Controls and Indicators (Figure 5)

ON/OFF BUTTON (Blue)	**For Standard Model Only:** The ON/OFF button activates the electronic circuitry for approximately 5 minutes. The first time the ON/OFF button is depressed, the electronics will perform a self-diagnostic test with all indicator lights alternately blinking on and off for approximately 5 seconds, then returning to their "normal" power state. The Transfer Device can be turned OFF by depressing the ON/OFF button for 3-5 seconds. **For Exchangeable Battery Model Only:** The ON/OFF button activates the electronic circuitry for approximately 50 minutes. When first switched "ON", the electronics will perform a self-diagnostic test with all indicator lights alternately blinking on and off for approximately 5 seconds, then returning to their "normal" power state. The Transfer Device can be turned OFF by depressing the ON/OFF button for 3-5 seconds. **PRECAUTION:** If the self-diagnostic test is not observed, do not use the device and call your Novoste Representative for service.
Low Battery Indicator (Amber Light)	Under normal power conditions, once the ON/OFF button has been activated, the Low Battery Indicator will blink for approximately 5 seconds and then go off. When battery power is low, the Low Battery Indicator light will continue to blink. **PRECAUTION:** Do not begin a procedure if the Low Battery light is blinking. If the Low Battery Indicator starts blinking during a procedure, there will be enough battery power to complete the procedure. Should this occur when using the Standard Model only, call your Novoste Representative for service after the procedure. For the Exchangeable Battery Model only, replace the battery per instructions found on page 31 of this User's Manual.
Proprietary Connector Lock Latch (Blue Line)	When the Latch locks the Proprietary Connector into the Transfer Device, the lock prevents disengagement of the Delivery Catheter from the Transfer Device. The Proprietary Connector is locked by fully depressing the white Proprietary Connector Lock Latch. The Latch is fully extended when a Blue line is visible on the Proprietary Connector Lock Latch. To unlock, depress the Lock Latch in the opposite direction so the blue line is no longer visible. The Proprietary Connector can only be disengaged from the Transfer Device when the Proprietary Connector is unlocked AND the Source Train is located in the Source Chamber with the Green Arrow Indicator light on.
Source Train Arrow Indicator Lights (Green and Amber)	There are two arrow indicator lights (Green and Amber) adjacent to the Source Chamber viewing window. After the LED light test is completed, either the Green or Amber Arrow Indicator light will remain illuminated depending on the position of the Source Train. When the Source Train is correctly positioned in the Transfer Device, a Green Arrow Indicator light will illuminate. After the Source Train has been moved out of proper position in the Transfer Device, an Amber Arrow Indicator light will illuminate.
Gate Control Switch	The Gate Control Switch is a sliding switch, which opens or closes the Gate to the Source Chamber allowing the Source Train to enter or exit the Source Chamber. To engage the Gate, slide the switch completely forward until the Blue Arrow aligns with **OPEN**.
Source Chamber Viewing Window	The clear window allows for magnified visual inspection of the Source Train.

Table 8: Transfer Device Controls and Indicators (Continued)

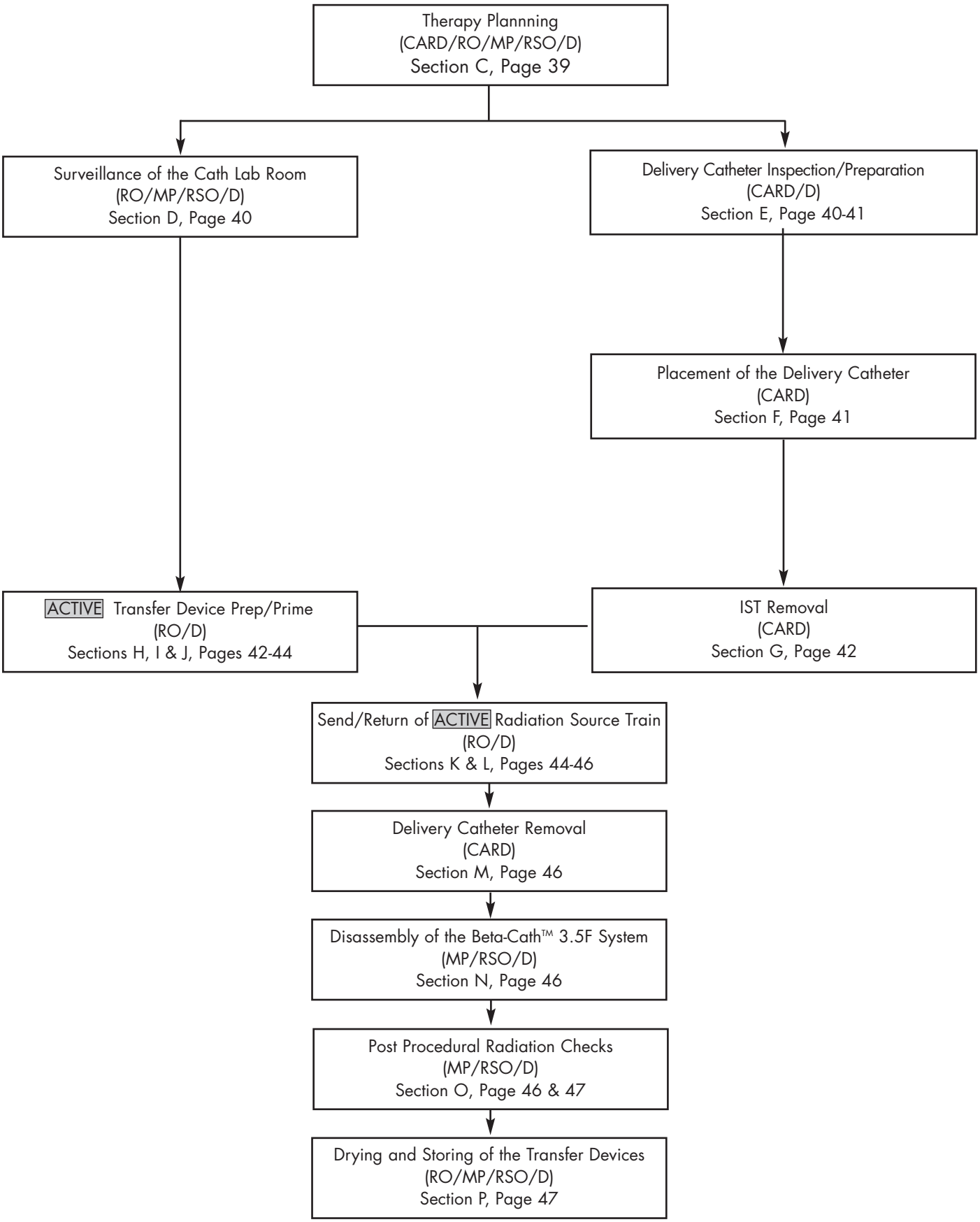
Fluid Control Lever	This two position lever controls the fluid flow and direction of Source Train movement. SEND will allow fluid to hydraulically transport the Source Train into the Delivery Catheter. RETURN will allow fluid to hydraulically transport the Source Train back into the Transfer Device. The Fluid Control Lever should always be maintained in the RETURN position, except when sending the Sources to the treatment area.
Fluid Pressure Indicator Lights (below)	The electronic sensing circuitry and Pressure Indicator lights sense the pressure delivered by the operator when depressing the syringe to SEND, Hold or RETURN the Source Train.
First (TX) Amber Pressure Indicator Lights	The first Amber Pressure Indicator light (identified by **TX**) illuminates when adequate pressure is applied to maintain Source Train positioning during treatment.
Second (↓↑) Amber Pressure Indicator Lights	The second Amber Pressure Indicator light (identified by ↓↑) will illuminate when additional pressure is applied. Illumination of this light without the Third Amber Pressure Indicator Light during the Send and Return indicates adequate pressure is being applied to move the Source Train.
Third (↓↑) Amber Pressure Indicator Lights	The third Amber Pressure Indicator light (identified by ↓↑) will illuminate when more pressure is applied. To send or return the Source Train, enough pressure must be applied to keep in the range (identified by the arrows next to the second and third Pressure Indicator lights, see Fig 5) where both the second and third Amber indicator lights are illuminated.
Fourth (⚠) Red Pressure Indicator Light	The fourth Pressure Indicator light, which is red (identified by a ⚠ caution symbol) will illuminate when too much pressure is applied. Pressure should be reduced to the 2nd or 3rd Amber Pressure Indicator light areas when sending and retrieving the Sources. If excessive pressure continues, there may not be adequate fluid volume remaining in the syringe to complete the procedure.
Treatment Counter/ Use Period	**PRECAUTION:** Do not use the Transfer Device if the controls and indicators are not functioning correctly. Please contact your Novoste Representative for service. **For Use of Standard Model Only:** The counter display keeps track of the number of times the Source Train is cycled in and out of the Transfer Device. The counter is located on the under side of the Transfer Device. It increments the count by one each time the Source Train leaves the quartz sleeve position within the Transfer Device. **PRECAUTION:** The Standard Model Transfer Device requires scheduled maintenance every 125 procedures or every six months, whichever event occurs first. Please contact your Novoste Representative to arrange for service. **For Use of Exchangeable Battery Model Only:** **PRECAUTION:** The Exchangeable Battery Model Transfer Device requires scheduled maintenance by Novoste Corporation within a period not to exceed twelve months. Refer to each Transfer Device's Calibration Certificate for its specified use period. Please contact your Novoste representative to arrange for service.

Figure 5: ACTIVE Beta-Cath ™ 3.5F System Compatible Transfer Device (60 mm Exchangeable Battery Model Version Shown)



Novoste™

Procedure Flow



A. Active Device Receipt RO/MP/RSO/D

Note: The following section describes procedures recommended by Novoste, which, unless superseded by local regulation or institutional policy or procedure, should be followed by the user. The Radiation Safety Personnel are responsible for ensuring the safe handling of radioactive materials at all times. It is incumbent upon these individuals to be thoroughly familiar with all handling procedures described herein and to augment them to comply with local regulations and institutional procedures if necessary. It is beyond the scope of this manual to provide a comprehensive review or adequate dissertation on health physics. This manual should be used as a guide to the health professional in the procedures for the safe handling of materials specific to the Beta-Cath™ 3.5F System. It is the user's responsibility to keep accurate records of the number of treatments administered with each ACTIVE *Transfer Device.*

The ACTIVE Transfer Device will be shipped in a White Lead-Lined Storage Container placed inside a Type A shipping container conspicuously marked with a Yellow II radiation label. Upon receipt of the ACTIVE Transfer Device, carefully inspect all components, perform an initial inspection, wipe test and leak test (if required) in an area designated for radioactive materials handling before placing the ACTIVE Transfer Device in the White Lead-Lined Storage Container and into the Transport Case.

Note: The Exchangeable Battery Transfer Device requires insertion of the 6 Volt Lithium ion battery that is located in the foam insert placed over the Transfer Device (as described on page 31).

PRECAUTION: The individual performing the wipe tests for leaking radioactive material should use good contamination control techniques.

1. Using a portable Radiation Survey Meter which is capable of detecting beta radiation and measuring radiation levels from background to 1 rad/hour, determine the highest levels of radiation at contact and at one meter from the shipping container. Record results on your Institution's Radiation Procedural Records.

2. Wipe discrete locations on the outside of the shipping container (totaling at least 300 cm^2), labeling each wipe for the area assessed.

3. Count the wipes with a method capable of detecting $^{90}Sr/^{90}Y$ contamination on the wipes.

4. Note results of the wipe readings along with their respective locations on objects in your Institution's Radiation Protection Records and in accordance with your institution's policies and/or local regulations.

5. Remove the tamper-proof seal. Remove the ring and the lid.

6. Remove the White Lead-Lined Storage Container and wipe at least 100 cm^2 of the outside of the container, labeling the wipes accordingly.

WARNING: Radiation is emitted from the ACTIVE Transfer Device when the Radiation Sources are in the Source Chamber. To minimize hand dose, the Transfer Device is designed to be held on the underside and may also be set down when appropriate.

7. Open the White Lead-Lined Storage Container and remove the ACTIVE Transfer Device, wiping at least 100 cm^2 of the outside of the Transfer Device.

PRECAUTION: If the transferable contamination exceeds 200 dpm/100 cm^2 (or the level determined by local regulation or institutional policy) on any wipe — place the contaminated object(s) in a plastic bag and label "Caution-Radioactive Material." Immediately inform institutional Radiation Safety personnel, implement containment control procedures and call your Novoste Representative. Should this occur, do not continue with this procedure.

8. Place the shipping container, packaging, White Lead-Lined Storage Container, and Transfer Device in a secure location until the wipes have been evaluated.

9. Count the wipes with a method capable of detecting $^{90}Sr/^{90}Y$ contamination on the wipes.

10. Note results of the wipe readings along with their respective locations on objects in your Institution's Radiation Protection Records and in accordance with your institution's policies and/or local regulations.

11. If the results of all the wipe tests are <200 dpm/ 100 cm^2 or within locally determined level, if desired, perform a Device Leak Test (see Section B below). **Insert the 6 Volt Lithium ion battery packaged in the foam insert placed over the Transfer Device (as described on page 31 for the Exchangeable Battery Model only)**. After successfully completing the Leak Test, place the ACTIVE Transfer Device in the White Lead-Lined Storage Container and confirm that the black and yellow Radiation Warning symbol is on the White Lead-Lined Storage Container.

12. Place the White Lead-Lined Storage Container in the appropriate slot in the Transport Case and LOCK. Only trained, authorized persons should have access to the Transport Case and the key to the lock.

A. ACTIVE Device Receipt
Continued RO/MP/RSO/D

13. Apply the "Caution Radioactive Material Label" or equivalent in accordance with local regulations or institutional policies and procedures on the Transport Case.

14. Store the Transport Case in a secure area designated for storage of radioactive materials in accordance with the institution's requirements.

B. Radioactive Sealed Source/ Device Leak Test Procedure
RO/MP/RSO/D

Required Materials:

- ACTIVE Transfer Device
- Flushing Adapter
- Fluid Collection Bag
- Syringe
- **Sterile Water for Irrigation**

PRECAUTION: Use only **Sterile Water for Irrigation**, which may also be referred to as sterile distilled non-pyrogenic water, in the Transfer Device. Do not use saline as a hydraulic fluid in the Transfer Device; corrosion may occur.

Only trained, authorized personnel should perform this procedure. After performing the Device Receipt Procedure to assess transferable contamination, if desired, perform the following procedure for the ACTIVE Transfer Device. Refer to the Transfer Device Controls and Indicators on Page 33, and the ACTIVE Transfer Device diagram on Page 35 to become familiar with the components.

1. Remove caps from Transfer Device and place in White Lead-Lined Storage Container.
2. Insert the 3.5F compatible Flushing Adapter (3.5F compatible Flushing Adapter supplied in the Medical Physicist's Kit) and secure into the Proprietary Connector receptacle of the ACTIVE Transfer Device by depressing the white Proprietary Connector Lock Latch until it is fully extended and a blue line is visible on the Latch.

3.5F compatible Flushing Adapter

PRECAUTION: Use only the 3.5F compatible Flushing Adapter provided with the Beta-Cath™ 3.5F System. Use of any other Beta-Cath™ Flushing Adapter will result in an improper fit and an inability to properly perform the Leak Test Procedure.

PRECAUTION: Do not force the connector lock latch into position. If resistance is felt, reposition the 3.5F compatible Flushing Adapter to ensure proper engagement with the Transfer Device.

3. Connect a Fluid Collection Bag to the Fluid Collection Bag Luer Port of the ACTIVE Transfer Device.
4. Connect a 20 ml syringe filled with approximately 5 ml of water to the Syringe Luer of the ACTIVE Transfer Device.
5. Ensure that the Fluid Control Lever of the ACTIVE Transfer Device is in **RETURN**.
6. Flush 5 ml of water through the ACTIVE Transfer Device.
7. Disconnect the syringe, fill with 5 ml of air and reconnect to Transfer Device and flush 5 ml of air through the ACTIVE Transfer Device.
8. Disconnect the syringe and the Flushing Adapter from the ACTIVE Transfer Device.
9. Disconnect the Fluid Collection Bag from the ACTIVE Transfer Device and cap the Fluid Collection Bag.
10. There are two acceptable methods for counting the fluid to determine the radioactive content:
    a. If a liquid scintillation counter is used, add the scintillation cocktail to the scintillation vial and add the water from the Fluid Collection Bag. Use a documented technique of known efficiency to assess the radioactive contents of the vial.
    b. If a planchet counter is used, apply the fluid from the Fluid Collection Bag onto a planchet. Allow the fluid in the planchet to evaporate. Use a planchet counter with known counting efficiency for $^{90}Sr/^{90}Y$ beta radiation to evaluate the planchet.
11. Record results of the count on your Institution's Radiation Procedure Record. If results exceed 11,100 dpm, notify your Radiation Safety Personnel.

PRECAUTION: If the Leak test results exceed 11,100 dpm (or the level determined by local regulation or institutional policy) on any sample, place the device in a plastic bag and label "Caution-Radioactive Material." Immediately inform institutional Radiation Safety personnel, implement containment control procedures and call your Novoste Representative. Should this occur, do not continue with this procedure.

12. Insert Quartz Cap into Proprietary Connector receptacle. Place the Syringe Luer Cap over the Syringe Luer of the Transfer Device and store in accordance with institutional policy.

C. Therapy Planning CARD/RO/MP/RSO/D

With the Beta-Cath™ 3.5F System, recommended prescription doses are as follows:

Reference Vessel Diameter	Recommended Prescription Dose for In-Stent Restenosis
≥ 2.7 ≤ 3.35 mm	18.4 Gy*
> 3.35 ≤ 4.0 mm	23.0 Gy*

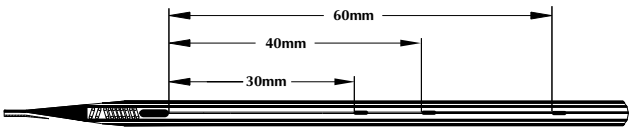
*18.4 and 23 Gray reflect the NIST-recommended adjustments to the documented doses as described in Technical Report DSGN-0311-A and are equivalent to the 16 and 20 Gray documented doses described in the START trial.

Each Source Train is shipped with a Calibration Certificate. Each Calibration Certificate provides the calibrated dose rate for the Source Train at 2 mm from the centerline in water and the recommended dose and treatment times (dwell times) for reference vessel diameter ranges. The recommended dose and treatment times provided have accounted for typical stent attenuation, as was studied in the clinical trial. The Calibration Certificate should be followed for dose and associated treatment times.

Note: For Exchangeable Battery Transfer Devices that have a use period exceeding 6 months, two separate tables of dose and treatment times are provided on the Transfer Device Calibration Certificate. The first table provides the recommended dose and treatment times for the first 6 months of use. The second table provides the recommended dose and treatment times for the remainder of the Transfer Device's use period. Please ensure the proper table of dose and treatment times is followed.

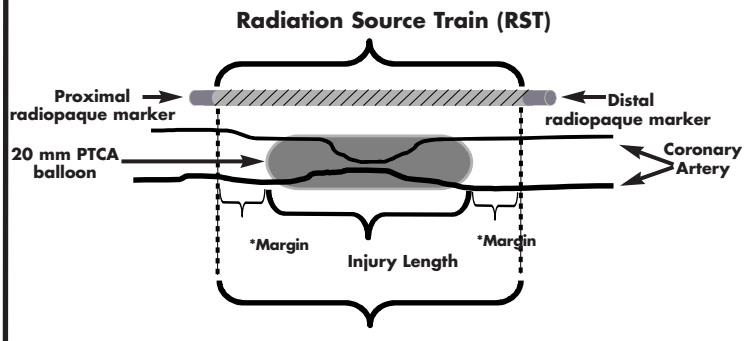
The appropriate ACTIVE Source Train length (30 mm, 40 mm or 60 mm) is selected by determining the entire injury length and desired margin. The Interventional Cardiologist will determine the size and length of the entire injury site. Entire injury site is defined as the entire vessel segment that is injured by balloon inflations, stent deployment or debulking devices. Filming with contrast medium the deflated balloon positions and the start and end positions of debulking devices will help define the injury length. The dose and treatment time is then determined by matching the artery reference vessel diameter with the reference vessel diameter ranges provided on the Calibration Certificate.

Figure 6. IST Marker Positions



The radiopaque markers of the Indicator of Source Train (IST) define the radioactive segment for each respective ACTIVE Source Train. Selection of a 30 mm Transfer Device will provide for 5 mm margins and selection of a 40 mm or a 60 mm Transfer Device will provide for 10 mm margins.

Figure 7. Appropriate Radiation Coverage



Recommended Radiation Coverage

*5 mm margins for 30 mm RST
*10 mm margins for 40 mm RST
*10 mm margins for 60 mm RST

D. Surveillance of the Cath Lab Room RO/MP/RSO/D

The following Radiation Surveillance Procedure is suggested for use with the Beta-Cath™ 3.5F System in the Cath Lab. Institutional procedures or local requirements may require alternative procedures.

The following materials are required to complete the procedure:

- Transport Case which contains an ACTIVE Transfer Device and Response Kit
- Delivery Catheter and Procedure Accessory Pack
- **Sterile Water for Irrigation**
- Temporary Storage Container
- Portable Survey Meter for beta and bremsstrahlung
- Sterile Probe Cover (for Survey Meter)
- Institutional Radiation Procedural Record

1. Obtain the ACTIVE Transfer Device stored in the locked Transport Case.

2. Conduct a Radiation Survey of the ACTIVE Transfer Device and note results for future reference as ACTIVE Transfer Device baseline reading. If, at any time, a Survey Meter reading of the ACTIVE Transfer Device is significantly different from the initial baseline reading, stop all activity and re-survey the ACTIVE Transfer Device making sure the fluoroscopy is off. If the reading is not within the acceptable baseline range, then refer to Section Q, Emergency Source Recovery Procedure.

3. Inventory the Source Train and radiopaque markers within the Transfer Device and record results.

4. Return the Transfer Device to the White Lead-Lined Storage Container until trained, authorized personnel request the device for the procedure.

5. Survey the procedure room and note results. Fluoroscopy MUST be off during the radiation surveys.

6. Survey the Delivery Catheter before opening the packaging and note results as initial Delivery Catheter background reading. If, at any time, a Survey Meter reading of the Delivery Catheter is significantly different from the initial background reading, stop all activity and re-survey the Delivery Catheter making sure the fluoroscopy is off. If the reading is not within the acceptable background range, then refer to Section Q, Emergency Source Recovery Procedure.

7. When requested, remove the ACTIVE Transfer Device from the White Lead-Lined Storage Container. Remove Caps from the Transfer Device. Inventory and record that all components of the Source Train are present prior to giving the ACTIVE Transfer Device to the Radiation Oncologist (RO).

Note: When conducting the room survey during the patient treatment, the operator's hand holding the Survey Meter should be covered with a Sterile Probe Cover to maintain a sterile field. The Sterile Probe Cover should be extended to its full length and secured at the operator's elbow. Additionally, this person should observe all procedures relating to sterile technique and avoid any contact with the sterile field.

E. Delivery Catheter Inspection/Preparation CARD/D

PRECAUTION: The Delivery Catheter and Procedure Accessory Pack items are intended for single use. Do not re-sterilize and/or reuse these items. Do not use if sterile package is damaged.

1. Open the Delivery Catheter and the Procedure Accessory Pack onto the sterile field.

PRECAUTION: Use only **Sterile Water for Irrigation,** which may also be referred to as sterile distilled non-pyrogenic water, in the Transfer Device. Do not use saline as a hydraulic fluid in the Transfer Device; corrosion may occur.

Note: To use the optional Fluid Management System, open a Merit Medical® 3-Way Stopcock (200 psi minimum) and Merit Medical® High Pressure (200 psi minimum) Injection Line (Merit Medical Systems, Inc.) onto sterile field. (Figure 10)*

**Or Novoste™ qualified equivalent*

2. Fill two 20 ml syringes with **Sterile Water for Irrigation**. Attach an Extension Connector to each of the 20 ml Syringes. Place the syringes on the prep table.

3. Flush the Delivery Catheter guidewire lumen by inserting the blunt Flushing Cannula into distal tip of catheter and flush with 1 ml heparinized saline.

4. Examine the Delivery Catheter prior to use for bends, kinks, or other signs of damage.

PRECAUTION: Do not use the Delivery Catheter if there is evidence of damage. Damaged catheters may cause vessel trauma or unpredictable results during use.

5. Visually confirm that the Indicator of Source Train (IST) is inserted into and seated against the internal distal marker/stop at the end of the Delivery Catheter.
6. Attach one of the two 20 ml syringes, filled with **Sterile Water for Irrigation**, to the IST hub and flush the inner lumen of the Delivery Catheter with 2-3 ml of **Sterile Water for Irrigation** while observing the tip of the Delivery Catheter for any evidence of fluid leakage.

PRECAUTION: Do not use the Delivery Catheter if there is evidence of fluid leakage other than at the IST hub vent position.

7. Withdraw the IST hub from the tip of the Delivery Catheter Proprietary Connector sufficiently to expose the two o-rings of the Proprietary Connector. Wet the o-rings of the Delivery Catheter Proprietary Connector with **Sterile Water for Irrigation** and reattach the IST hub onto the tip of the Delivery Catheter Proprietary Connector.

8. Visually confirm that the IST is fully reinserted into the Delivery Catheter and seated against its internal distal marker/stop.

F. Placement of Delivery Catheter CARD

WARNING: Use of an Internal Mammary (IM) Artery Guide Catheter may impede the path of the ACTIVE Source Train and may cause unintentional exposure of radiation and/or unintended results.

1. After completing the intervention to the target lesion, remove interventional devices, leaving the guidewire and guiding catheter in place.

2. Wipe the guidewire remaining outside the patient with a sterile gauze pad soaked in saline to remove any blood or contrast media that may be on the surface.

3. Review films of the contrast medium injections noting the positions of all interventional devices used to define the entire interventional injury site.

4. Advance the Delivery Catheter over the 0.014" guidewire, through the guiding catheter to the interventional injury site. A depth marker band has been provided approximately 100 cm from the distal tip of the Delivery Catheter as a position reference.

PRECAUTION: Always advance the Delivery Catheter with the IST in position within the Delivery Catheter.

PRECAUTION: Always advance or withdraw the Delivery Catheter slowly and observe under fluoroscopy.

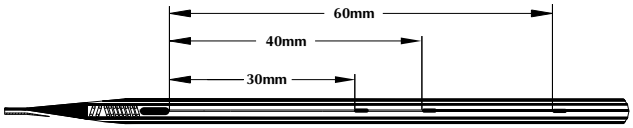
WARNING: Never advance or withdraw the Delivery Catheter against resistance. If any resistance is felt, stop immediately and determine the cause of resistance before proceeding. Catheter damage and/or patient injury could occur.

PRECAUTION: Do not advance the Delivery Catheter over the floppy portion of the guidewire as the guidewire may prolapse when the Delivery Catheter is withdrawn. If this occurs, attempt to resolve the prolapse by gently pulling back on the guidewire while simultaneously advancing the catheter. If the prolapse persists, disengage the Delivery Catheter from the guidewire by continuing to advance the Delivery Catheter while gently pulling back on the guidewire.

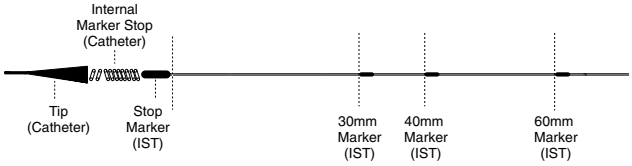
5. Under fluoroscopy, use the IST to position the Delivery Catheter across the interventional injury site. Confirm the appropriate Transfer Device/Source Train Length by referencing the IST marker (30 mm, 40 mm or 60 mm) that provides complete injuy length and desired margin coverage (see Figure 8).

Figure 8. Delivery Catheter Positioning Using the IST

Active Train Length



Fluoroscopic View of Delivery Catheter and IST



6. Provide the interventional injury site measurement (length and diameter) and desired margin coverage to the Radiation Oncologist/Therapist for selection of the appropriate Transfer Device/Source Train and determination of treatment time.

G. IST Removal CARD

1. Once the Delivery Catheter has been positioned with the Indicator of Source Train (IST) across the interventional injury site, close the hemostatic valve.
2. Grasp the proximal end of the IST and gently withdraw the IST far enough into the guiding catheter (to approximately the projection of the aortic arch) and readvance it (at least twice) to find any potential obstacle for the ACTIVE Source Train.

PRECAUTION: If resistance is felt and believed to be due to patient anatomy, withdraw the entire Delivery Catheter (including IST) and optimize guiding catheter selection and/or perform a re-intervention at the target lesion. Reposition the Delivery Catheter (including IST) per Section F - Placement of Delivery Catheter. If resistance is felt and believed to be due to the Delivery Catheter, remove the entire Delivery Catheter (including IST) from the patient and return the Delivery Catheter to Novoste Corporation. Prepare another Delivery Catheter for use begining with Section E - Delivery Catheter Inspection/Preparation.

3. Gently remove the IST from the Delivery Catheter while maintaining the position of the Delivery Catheter under fluoroscopy.
4. Coil wire portion of IST into 2-3 loops and fold ends inside loops for temporary use.

H. ACTIVE Transfer Device Preparation with the β-Rail™ 3.5F Delivery Catheter RO/D

*Note: Follow the instructions in this section when using the Transfer Device **inside** the sterile field with the β-Rail™ 3.5F or β-Rail™ 3.5F XL Delivery Catheter. If using the Transfer Device **outside** the sterile field with the β-Rail™ 3.5F XL Delivery Catheter, see Section I.*

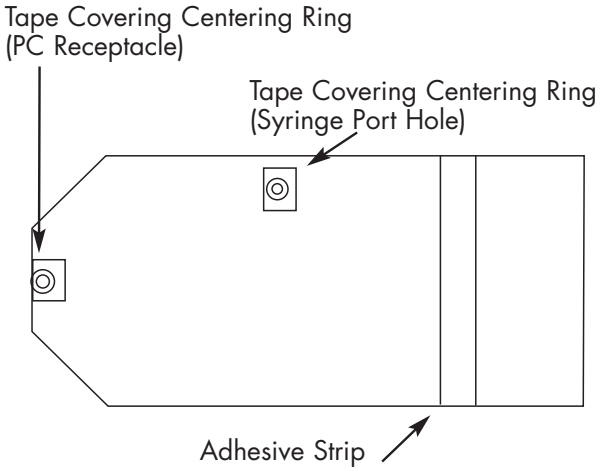
WARNING: Radiation is emitted from the ACTIVE Transfer Device when the Radiation Sources are in the Source Chamber. To minimize hand dose, the Transfer Device is designed to be held on the underside and may also be set down when appropriate.

1. Once the appropriate Beta-Cath™ 3.5F System compatible Transfer Device/Source Train is selected (based upon the interventional injury length and desired margin coverage), confirm the following ACTIVE Transfer Device conditions:
   - The radioactive warning symbols are on the device.
   - The Gate Control Switch is in the CLOSE position.
   - The distal radiopaque marker of the ACTIVE Source Train is away from the Gate.
   - The Fluid Control Lever is set to RETURN .
   - The power is turned ON.
2. Connect the Fluid Collection Bag to the Fluid Collection Bag Luer Port of the ACTIVE Transfer Device and cup the Fluid Collection Bag around the bottom of the device.

PRECAUTION: The Transfer Device is not sterile. A Sterile Bag is provided to maintain a sterile field during the procedure. Handle the Transfer Device carefully. If the Transfer Device is dropped, do not use. Contact your Novoste Representative.

3. Using aseptic technique, place gloved hands inside the cuffs of the Sterile Bag. Carefully place the non-sterile ACTIVE Transfer Device with the attached Fluid Collection Bag into the Sterile Bag. Orient the Transfer Device Syringe Luer toward the Syringe Port Hole of the Sterile Bag. Refer to Figure 9. Unfold cuffs of the Sterile Bag and secure the ACTIVE Transfer Device by folding the proximal end of the Sterile Bag two (2) times and secure with adhesive strip.

Figure 9. Sterile Bag



4. Align the centering ring of Syringe Port Hole of the Sterile Bag over the Syringe Luer of the ACTIVE Transfer Device. Remove the proximal tape covering the Port Hole of the Sterile Bag and secure in place.

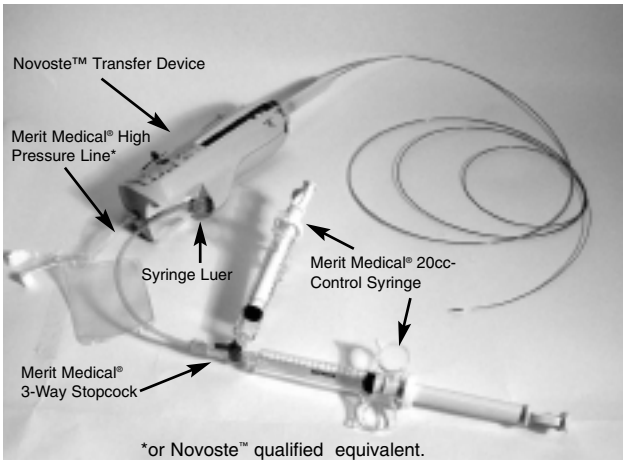
PRECAUTION: The inside portion of the tape covering the Syringe Port Hole is not sterile; remove from the sterile field.

5. Insert the Syringe with Extension Connector into the Syringe Port Hole and tighten to Syringe Luer.

   Note: To use Fluid Management System: Connect a Merit Medical® High Pressure (200 psi minimum) Injection Line or Novoste™ qualified equivalent to Syringe Luer, connect Merit Medical® 3-way Stopcock (200 psi minimum) to High Pressure line and connect a syringe to each port on the stopcock. Turn stopcock ON to the primary syringe and proceed with prepping procedure below. The User may elect to not use the stopcock and connect the syringe directly onto the high-pressure extension tubing. See Figure 10.

PRECAUTION: When attaching the syringe (or extension tubing) to the Transfer Device, use care to ensure that the syringe hub does not pinch the Sterile Bag during the process. Do not over-tighten the syringe when connecting the Extension Connector to the Syringe Luer.

Figure 10. Fluid Management System



6. Align the distal Centering Ring over the Proprietary Connector Receptacle of the ACTIVE Transfer Device. Remove the tape covering the distal hole of the Sterile Bag.
7. Bring prepared ACTIVE Transfer Device to pre-positioned Delivery Catheter.

PRECAUTION: The inside portion of the tape covering the Proprietary Connector Port Hole is not sterile; remove from the sterile field to avoid compromise of sterile field.

8. Wet tip of the Delivery Catheter Proprietary Connector with **Sterile Water for Irrigation**, to ease insertion and insert the Proprietary Connector of the Delivery Catheter through the distal hole of the Sterile Bag into the Proprietary Connector Receptacle of the ACTIVE Transfer Device. Rotate Proprietary Connector to ensure a secure connection.

PRECAUTION: When attaching the Proprietary Connector to the Transfer Device, use care to ensure that the Proprietary Connector does not catch the Sterile Bag during insertion.

9. Lock the Proprietary Connector to the ACTIVE Transfer Device by fully depressing the Proprietary Connector Lock Latch until a blue line is visible.

PRECAUTION: Do not force the connector lock latch into position. If resistance is felt, reposition the proprietary connector to ensure proper engagement with the Transfer Device

Note: Continue to Section J.

I. ACTIVE Transfer Device Preparation with the β-Rail™ 3.5F XL Delivery Catheter RO/D

*Note: This section is intended for using the Transfer Device **outside** the sterile field with the β-Rail™ 3.5F XL Delivery Catheter only. When using the Transfer Device **inside** the sterile field, follow Section H.*

WARNING: Radiation is emitted from the ACTIVE Transfer Device when the Radiation Sources are in the Source Chamber. To minimize hand dose, the Transfer Device is designed to be held on the underside and may also be set down when appropriate.

1. Once the appropriate Beta-Cath™ 3.5F System compatible Transfer Device/Source Train is selected (based upon the interventional injury length and desired margin coverage), confirm the following ACTIVE Transfer Device conditions:
   - The radioactive warning symbols are on the device.
   - The Gate Control Switch is in the CLOSE position.
   - The distal radiopaque marker of the ACTIVE Source Train is away from the Gate.
   - The Fluid Control Lever is set to RETURN .
   - The power is turned ON.
2. Connect the Fluid Collection Bag to the Fluid Collection Bag Luer Port of the ACTIVE Transfer Device.

PRECAUTION: Handle the Transfer Device carefully. If the Transfer Device is dropped, do not use. Contact your Novoste Representative for service.

3. Insert the Syringe into the Syringe Port Hole and tighten to Syringe Luer.

   Note: To use Fluid Management System: Connect a Merit Medical® high pressure (200 psi minimum) injection line or Novoste™ qualified equivalent to syringe luer, connect Merit Medical® 3-way stopcock (200 psi minimum) to high pressure line and connect a syringe to each port on the stopcock. Turn stopcock ON to the primary syringe and proceed with prepping procedure below. The User may elect to not use the stopcock and connect the syringe directly onto the high-pressure extension tubing. See Figure 10.

4. Wet tip of the Delivery Catheter Proprietary Connector with **Sterile Water for Irrigation**, to ease insertion and insert the Proprietary Connector of the Delivery Catheter into the Proprietary Connector Receptacle of the ACTIVE Transfer Device. Rotate Proprietary Connector to ensure a secure connection.
5. Lock the Proprietary Connector to the ACTIVE Transfer Device by fully depressing the Proprietary Connector Lock Latch until a blue line is visible.

PRECAUTION: Do not force the connector lock latch into position. If resistance is felt, reposition the proprietary connector to ensure proper engagement with the Transfer Device

J. ACTIVE Transfer Device Priming RO/D

1. Ensure that the Gate Control Switch is in the CLOSE position.

2. Ensure that the Fluid Control Lever is on RETURN.

3. Flush Transfer Device and Delivery Catheter System with 6 ml of **Sterile Water for Irrigation** Confirm the device is primed properly by observing the absence of air bubbles and the entry of water into the Fluid Collection Bag.

K. Delivery of the ACTIVE Source Train RO/D

1. Check for adequate (14 ml minimum) fluid volume in the syringe.

   Note: If using Fluid Management System, turn stopcock to secondary syringe if additional fluid is required, or replace with a filled syringe prior to sending the ACTIVE Source Train.

PRECAUTION: Ensure a sufficient number of water-filled syringes are available before beginning treatment. Always reserve at least 10 ml of water for the return of the ACTIVE Source Train to prevent unintentional radiation exposure.

2. Ensure that hemostatic valve is in the OPEN position.

WARNING: Failure to open the hemostatic valve may prevent the radiation source train from returning to the device and may result in unnecessary radiation exposure to the patient or personnel.

3. Ensure that power is ON; depress the ON/OFF button if power has turned OFF.

4. Slide the Gate Control Switch forward until the Blue Arrow aligns with the OPEN position.

Note: If the Gate Control Switch cannot be moved to the open position, and the green SOURCES IN LED is illuminated, then move the Gate Control Switch back to the fully closed position and power down the Transfer Device. Restart the Transfer Device and proceed as normal.

5. Move the Fluid Control Lever to SEND.

6. While observing with fluoroscopy, depress the syringe plunger to transport the ACTIVE Source Train to the Interventional Injury Site of the Delivery Catheter. All three Amber ↓↑ Pressure Indicator lights should be illuminated while SENDING the ACTIVE Source Train. An audible click will be heard as the ACTIVE Source Train leaves the Source Chamber.

PRECAUTION: Illumination of the Red Pressure Indicator ⚠ light during a procedure indicates excessive pressure is being used; reduce applied pressure to return to the Amber ↓↑ Pressure Indicator area.

7. Use fluoroscopy to confirm proper placement of the entire ACTIVE Source Train at the interventional injury site.
   a. In the event that the ACTIVE Source Train cannot be confirmed to have reached the injury site, immediately perform the following maneuver to reposition the ACTIVE Source Train:
      - Confirm the hemostatic valve is open.
      - Confirm the Fluid Control Lever is in SEND position.
      - Pull to withdraw approximately 1 ml **Sterile Water for Irrigation** and push to apply forward pressure to the syringe plunger to reposition the ACTIVE Source Train.

   b. In the event that the ACTIVE Source Train still cannot be confirmed to have reached the injury site, immediately perform the following maneuver to return the ACTIVE Source Train to the ACTIVE Transfer Device:
      - Move the Fluid Control Lever to RETURN.
      - Depress syringe and apply continuous, positive pressure so that all three Amber Pressure Indicator lights are illuminated during the return of the ACTIVE Source Train. An audible "click" will be heard as the ACTIVE Source Train returns to the Source Chamber.
      - Maintain Pressure on the syringe while visually confirming that the entire ACTIVE Source Train is located within the Source Chamber and that the Green Arrow Indicator light is "ON".

   Note: Once the ACTIVE Source Train is located within the Source Chamber of the ACTIVE Transfer Device, the Delivery Catheter can be removed and the procedure restarted with a new Delivery Catheter, following standard Test and Placement procedures.

   c. In the event the ACTIVE Source Train has not reached the treatment site or been returned to the Source Chamber of the ACTIVE Transfer Device after 15 seconds has elapsed since initiating the send of the Source Train, immediately perform the following maneuver to withdraw the entire Beta-Cath™ 3.5F System:
      - Loosen the hemostatic valve with left hand.
      - Use four or more saline-soaked gauze sponges to grasp and remove the Delivery Catheter and guidewire from patient.
      - Place Delivery Catheter and ACTIVE Transfer Device (still attached) into Temporary Storage Container. Refer to Section Q - Emergency Source Train Recovery Procedure for further instructions.

WARNING: Avoid direct contact with unshielded radiation sources in the Delivery Catheter as unintended radiation exposure will occur.

WARNING: Do not grasp catheter directly with hands or cut the catheter, as unintended radiation exposure may result.

8. Cine with contrast medium to document placement of the ACTIVE Source Train

WARNING: Failure to correctly position the ACTIVE Source Train at the interventional injury site may underexpose the targeted treatment area and expose tissue not targeted for treatment to unintentional radiation; unpredictable results may occur.

9. Maintain placement of the ACTIVE Source Train at the Treatment Zone for the prescribed period of time by applying continuous, positive pressure. Adequate pressure is indicated by the illumination of the first Amber **TX** Pressure Indication Light.

WARNING: Migration of the ACTIVE Source Train or improper location of the ACTIVE Source Train may cause unintentional radiation exposure to occur and may decrease treatment efficacy.

10. Start Treatment time once Cardiologist confirms that the ACTIVE Source Train is across the entire interventional injury site.
11. Consult the Medical Physicist to confirm the treatment time for the prescribed dose.

WARNING: Exceeding the prescribed radiation treatment time will result in a higher than intended dose.

12. Monitor patient status during radiation treatment.
13. Monitor the amount of **Sterile Water for Irrigation** in the Syringe and the Fluid Collection Bag.

    Note: If using Fluid Management System, turn stopcock to secondary syringe if additional fluid is required or replace with a filled syringe prior to returning the ACTIVE Source Train.
14. Ensure that sufficient pressure is applied such that the first (**TX**) Amber Pressure Indicator light remains on during treatment.
15. Use fluoroscopy approximately every 15-30 seconds and cine with contrast media at least once during the radiation treatment to confirm and record the proper position of the ACTIVE Source Train across the interventional injury site.

L. ACTIVE Source Train Return RO/D

1. Check for adequate (10 ml minimum) fluid volume in the syringe.

   Note: If using Fluid Management System, turn stopcock to secondary syringe if additional fluid is required or replace with a filled syringe prior to returning the ACTIVE Source Train.
2. Ensure that the hemostatic valve is open.

WARNING: Failure to open the hemostatic valve may prevent the radiation source train from returning to the device and may result in unintended radiation exposure to the patient or personnel.

3. Move the Fluid Control Lever to RETURN.
4. Depress syringe and apply continuous pressure so that all three Amber ↓↑ Pressure Indicator lights are illuminated during the return of the ACTIVE Source Train. An audible click will be heard as the ACTIVE Source Train returns to the Source Chamber.
5. Maintain pressure on the syringe while visually confirming that the ACTIVE Source Train is located within the Source Chamber and that the Green Arrow Indicator light is ON.
6. Visually confirm that the ACTIVE Source Train is located in the Source Chamber and the distal radiopaque marker of the jacketed Source Train is clearly present.
   a. In the event that the entire ACTIVE Source Train cannot be confirmed to have returned to the ACTIVE Transfer Device after the treatment, immediately:
      - Confirm the hemostatic valve is open.
      - Confirm the Fluid Control Lever is in RETURN position.
      - Pull to withdraw approximately 1 ml **Sterile Water for Irrigation** and push to apply forward pressure to the syringe plunger to return the ACTIVE Source Train to the Source Chamber of the ACTIVE Transfer Device.

b. In the event the ACTIVE Source Train has not returned to the Source Chamber of the ACTIVE Transfer Device after 15 seconds has elapsed since initiating the return of the Source Train, immediately perform the following maneuver to withdraw the entire Beta-Cath™ 3.5F System:

- Loosen the hemostatic valve with left hand.
- Use four or more saline-soaked gauze sponges to grasp and remove the Delivery Catheter and guidewire from patient.
- Place the Delivery Catheter and ACTIVE Transfer Device (still attached) into Temporary Storage Container. Refer to Section Q - Emergency Source Train Recovery Procedure for further instructions.

WARNING: Avoid direct contact with unshielded radiation sources in the Delivery Catheter as unintended radiation exposure will occur.

WARNING: Do not grasp catheter directly with hands or cut the catheter, as unintended radiation exposure may result.

7. While continuing to apply pressure on syringe, slide the Gate Control Switch to the CLOSE position.

PRECAUTION: Ensure that the Gate Control Switch is completely closed, as incomplete closure may render the Gate inoperable

8. Perform a Survey of the patient's chest and groin area and note results.

M. Delivery Catheter Removal CARD

1. Remove the entire Beta-Cath™ 3.5F System under fluoroscopy, as a single unit, while maintaining guide wire placement.

WARNING: Never withdraw the Delivery Catheter against resistance. If any resistance is felt, stop immediately and determine the cause of resistance before proceeding. Catheter damage and/or patient injury could occur.

PRECAUTION: Exercise care when withdrawing the Delivery Catheter through any area of increased restriction, such as a stent, guide catheter tip, or hemostatic valve. Always withdraw the Delivery Catheter slowly and observe under fluoroscopy, whenever possible.

PRECAUTION: If the guidewire prolapses during Delivery Catheter withdrawal, attempt to resolve the prolapse by gently pulling back on the guidewire while simultaneously advancing the catheter. If the prolapse persists and cannot be resolved, withdraw the Delivery Catheter and guidewire together as one unit.

N. Disassembly of the System MP/RSO/D

1. When the complete system has been removed from the patient, visually confirm that the ACTIVE Source Train is contained in the Source Chamber of the ACTIVE Transfer Device and the distal radiopaque marker of the jacketed Source Train is clearly present.
2. Unlock the ACTIVE Transfer Device from the Delivery Catheter by depressing the Proprietary Connector Lock Latch such that the blue line is no longer visible.
3. Disconnect the Delivery Catheter from the ACTIVE Transfer Device by depressing both squeeze tabs located on the Proprietary Connector while withdrawing the Proprietary Connector from the ACTIVE Transfer Device. If the Delivery Catheter will not disconnect from the ACTIVE Transfer Device, place the entire system into the Temporary Storage Container and refer to Section Q - Emergency Source Train Recovery for further instructions.

PRECAUTION: The Proprietary Connector of the Delivery Catheter is no longer sterile once handled outside the sterile field or disconnected from the ACTIVE Transfer Device. Care should be taken not to contaminate the sterile field. If contamination is believed to have occurred, take appropriate steps to re-establish a sterile field.

4. Disconnect the Syringe and the Extension Connector from the ACTIVE Transfer Device.
5. Return the ACTIVE Transfer Device with attached Fluid Collection Bag and Delivery Catheter to MP/RSO for Safety Check and Drying.

O. Post-Procedural Radiation Checks MP/RSO/D

PRECAUTION: Failure to perform adequate visual and radiation surveys post-procedure to verify source accountability may subject patients and/or personnel to unintended radiation exposure.

1. Confirm presence of the Source Train in the ACTIVE Transfer Device.
2. Survey the ACTIVE Transfer Device with the Fluid Collection Bag still connected and note results.
3. Remove the ACTIVE Transfer Device from the Sterile Bag; disconnect and cap the Fluid Collection Bag.
4. Survey the Delivery Catheter and capped Fluid Collection Bag and note results. These readings should be comparable to the initial background readings noted.

WARNING: If the fluid in the capped Fluid Collection Bag is found to be contaminated after scanning, then the Transfer Device and capped Fluid Collection Bag should be placed in the Temporary Storage Container and returned to the radiation vault to await inspection by the Radiation Personnel.

5. Survey the procedure room and note results.

WARNING: If Survey readings are significantly different from the initial background reading, cease all activity and refer to Section Q - Emergency Source Train Recovery.

6. After the post-procedural Radiation Survey, the ACTIVE Transfer Device must be dried (see Section P - Drying and Storing of the Transfer Device).

P. Drying and Storing of the Transfer Device RO/MP/RSO/D

The following is the recommended procedure for properly drying, cleaning and storing the ACTIVE Transfer Device following a procedure. Only trained, authorized personnel should perform this procedure.

The following materials are required to complete the procedure:

- ACTIVE Transfer Device containing the ACTIVE Source Train
- Medical Physicist's Kit
- Response Kit
- Survey meter
- Clean towels
- Non-sterile gloves

Preparation:

1. The Authorized Personnel responsible for cleaning the Transfer Device should put on gloves and then obtain the Transfer Device.
2. Survey the Transfer Device and note results.
3. Visually inspect and confirm that the jacketed Source Train is present in the Transfer Device and that the Gate Control Switch is in the CLOSE position.

Drying Procedure:

PRECAUTION: Do not turn the Transfer Device power ON or attempt to OPEN the Gate Control Switch during the Drying Procedure

PRECAUTION: Use only the 3.5F compatible Flushing Adapter provided with the Beta-Cath™ 3.5F System. Use of any other Beta-Cath™ Flushing Adapter will result in an improper fit and an inability to properly perform the Drying Procedure.

1. Insert the Flushing Adapter (3.5F compatible) into the Transfer Device.
2. Secure by depressing the Proprietary Connector Lock Latch.

PRECAUTION: Do not force the connector lock latch into position. If resistance is felt, reposition the 3.5F compatible Flushing Adapter to ensure proper engagement with the Transfer Device.

3. Connect a Fluid Collection Bag.
4. Connect a 20 ml syringe filled with air to the Syringe Luer.
5. Ensure that the Fluid Control Lever is in RETURN.
6. Rapidly flush the Transfer Device with air, pausing at the end to allow all air flush to be expelled.
7. Remove the Syringe, refill with air and repeat air flush 3-5 times until all noticeable fluid is removed.
8. Remove the Fluid Collection Bag and Flushing Adapter.

Cleaning and Storing Procedure:

1. Insert the Quartz Cap into the Proprietary Connector receptacle of the Transfer Device.
2. Place the Syringe Luer Cap onto Syringe Luer of the Transfer Device.
3. Remove any visible debris from the surface by wiping the outside of the Transfer Device with a cloth dampened with water.
4. Place the Transfer Device in the appropriate storage container and store in accordance with institutional policy.

Q. Emergency Source Train Recovery RO/MP/RSO/D

This procedure provides guidance for recovering an ACTIVE Source Train when it cannot be confirmed to have reached the injury site, will not return to the Transfer Device or has escaped the containment of the System. This document provides direction for the user to safely return the ACTIVE Source Train to a controlled location.

REQUIRED MATERIALS:

- Gloves, non-sterile
- Response Kit
- Water
- Four or more saline-soaked gauze sponges (pads)
- Survey Meter
- Whole body and extremity personnel dosimeters for the individual performing the recovery
- Temporary Storage Container

WARNING: Should Breach of ACTIVE Source Train containment occur:

- Notify personnel present of missing Source Train
- No personnel should be allowed to enter or leave the room until the Source Train is contained.
- Individuals involved in Source Train recovery should wear disposable gloves, an extremity dosimeter on the hand expected to receive the highest dose and a whole body dosimeter on the front of the body between the neck and the waist.

UNDER NO CIRCUMSTANCES should an individual pick up the ACTIVE Source Train with his/her fingers, because unintended radiation exposure and injury may result. Required equipment is provided for this purpose in the Response Kit.

1. If the ACTIVE Source Train does not return to the ACTIVE Transfer Device and if the Delivery Catheter has not been disconnected from the ACTIVE Transfer Device, the ACTIVE Source Train is considered to be lodged in the Catheter. If the Catheter has not been withdrawn from the patient, the Cardiologist should immediately perform the following maneuver to withdraw the entire Beta-Cath™ 3.5F System.
   - Loosen the hemostatic valve with left hand.
   - Use four or more saline-soaked gauze sponges to grasp and remove the Delivery Catheter and guidewire from patient.
   - Place the Delivery Catheter and ACTIVE Transfer Device (still attached) into the Temporary Storage Container.
   - Close the Temporary Storage Container.

WARNING: Avoid direct contact with unshielded radiation sources in the Delivery Catheter as unintended radiation exposure will occur.

WARNING: Do not grasp catheter directly with hands or cut the catheter, as unintended radiation exposure may result.

2. After the entire system has been placed into the Temporary Storage Container obtain the Radiation Survey Meter. If the Survey Meter has a sliding beta shield on the detector, open the shield to increase the sensitivity to beta radiation. Survey the patient and surrounding area. If the background radiation coming from the Temporary Storage Container prevents a good Survey, move the Temporary Storage Container to a secure location. If increased room levels of radiation are found that were not measured in the background Survey made before the procedure, Source(s) may be out of the Temporary Storage Container.

3. Without raising the lid on the Container, look through the transparent sides of the Container to attempt to locate the missing jacketed Source Train. If the jacketed Source Train can be located in the Catheter or ACTIVE Transfer Device in the Temporary Storage Container, place the Temporary Storage Container in a shielded, secure location and call your Novoste Representative to assist with transferring the jacketed Source Train back to the Transfer Device. If any portion of the jacketed Source Train cannot be located in the Temporary Storage Container, proceed with the next step to locate the missing Source(s).

PRECAUTION: Under undefined handling conditions outside the System, the ACTIVE Source Train jacket may be damaged, allowing individual ACTIVE Sources to be released. Use care when locating and handling the Radioactive Source Train to ensure that all individual ACTIVE Sources remain intact (jacketed) and are recovered and returned to safe, shielded storage.

WARNING: Never cut the Delivery Catheter. Cutting the Delivery Catheter may result in damage to the ACTIVE Source Train, compromise containment of the sealed radioactive material and may result in unnecessary contamination and radiation exposure of the patient, workers, equipment, facilities and/or the public environment.

4. If the jacketed ACTIVE Source Train is damaged, allowing individual ACTIVE Sources to be released, a thorough Radiation Survey (using a Radiation Survey Meter) should be performed. Survey the room carefully until a radiation increase is detected. Keep in mind other possible sources of radiation such as fluoroscope, other sealed sources, or even sources in adjoining rooms. Compare the levels of radiation from other sources to those noted in the Survey performed before the procedure.

5. When increased radiation is located using the Radiation Survey Meter, use the Response Kit, which contains a magnifying glass and flashlight, to assist in locating the ACTIVE Source(s). The ACTIVE Source(s) can be shielded by placing objects (such as a piece of plastic or book) over the ACTIVE Source(s). Ensure that the object does not come in direct contact with the ACTIVE Source(s), but is only used to shield the ACTIVE Source(s).

6. Fill the Source Container found in the Response Kit approximately two thirds full of water to provide shielding for the ACTIVE Source(s).

PRECAUTION: The Response Kit contains two Source Recovery Tools for picking up and transferring a Source(s) to a safe location: a) the Source Recovery Probe and b) the spring-loaded Tweezers. The Source Recovery Probe is the preferred method as it minimizes potential damage to the Source(s) and permits the operators hand to be placed further from the Source(s).

7a. The magnetic Source Recovery Probe will pick up a source when the narrow end of the magnetic Probe is placed near the source. The Source(s) can be released into the water in the Source Container when the Source(s) are within the Source Container and the release lever on the other end of the probe is raised.

PRECAUTION: The magnetic Source Recovery Probe should be held and operated near its release lever in order to avoid unnecessary radiation exposure.

7b. Alternatively, the spring-loaded Tweezers may be used to pick up the Source(s) and place it in the Source Container.

8. When all missing ACTIVE Sources have been located and placed in the water in the Source Container, screw the lid back on the container and move the container to a safe, secure location.

9. Mark the Source Container with a Radioactive Materials sticker. Lock the container in a secure location to prevent unauthorized handling of the Source(s).

10. Call your Novoste Representative immediately to assist with returning the recovered ACTIVE Source Train and ACTIVE Transfer Device to Novoste Corporation.

Temporary Storage Container Cleaning:

If the Temporary Storage Container is used to store a contaminated system during the return of an ACTIVE Source Train into the ACTIVE Transfer Device, the Temporary Storage Container should be cleaned. Please refer to institutional Hospital Infection Control Procedures for cleaning biohazardous materials.

R. Optional Instructions CARD/D

1. IST Reinsertion

The following is the recommended procedure for maintaining field sterility when reinserting the IST into the Delivery Catheter for re-advancement of the Delivery Catheter (e.g., repositioning).

IST reinsertion should be performed only due to the inadvertent movement or misplacement of the delivery catheter and not for additional radiation treatments.

PRECAUTION: After the Delivery Catheter is attached to and primed with a Transfer Device, the fluid within the Delivery Catheter and the tip of the Delivery Catheter Proprietary Connector (portion inserted into the Transfer Device) are no longer sterile. Use care when handling the Delivery Catheter to avoid contamination of field sterility.

PRECAUTION: After performing the IST Reinsertion procedure do not attempt to reinsert the IST a second time into the Delivery Catheter, since the IST will no longer be sterile.

The following materials are recommended in order to complete the IST reinsertion procedure:

- Sterile gauze pad, non-absorbent backed
- Sterile gauze sponges, 4 in.x 4 in. (10.2 cm. x 10.2 cm.)

Delivery Catheter Preparation:

1. Remove the Delivery Catheter from the patient.

2. Carefully place a sterile Proprietary Connector Cover over the tip of the Proprietary Connector to prevent contamination of the sterile field and place the Delivery Catheter onto the sterile prep table.

3. Place a non-absorbent backed sterile gauze pad under the Delivery Catheter Proprietary Connector, to collect displaced non-sterile water.

4. Place several sterile gauze sponges around the Delivery Catheter Proprietary Connector and hold firmly.

5. Have a non-sterile assistant put on sterile gloves and perform the following:

   - Carefully uncoil the sterile IST.
   - Remove the Proprietary Connector Cover and discard.
   - Carefully insert the IST fully into the Delivery Catheter Proprietary Connector, until the IST hub is fully seated against the hub of the Delivery Catheter Proprietary Connector.

PRECAUTION: Displaced water is non-sterile. Discard contaminated gloves.

6. Once the IST is reinserted into the Delivery Catheter, discard the gauze pad and sponges.

7. Move the Delivery Catheter with loaded IST to the patient, and place the Delivery Catheter across the interventional injury site, per Section F- Placement of the Delivery Catheter.

IST Removal:

1. Once the Delivery Catheter has been positioned with the IST across the interventional injury site, close the hemostatic valve.

2. Grasp the proximal end of the IST and gently withdraw the IST far enough into the guiding catheter (to approximately the projection of the aortic arch) and readvance it (at least twice) to find any potential obstacle for the ACTIVE Source Train.

PRECAUTION: If resistance is felt and believed to be due to patient anatomy, withdraw the entire Delivery Catheter (including IST) and optimize guiding catheter selection and/or perform a re-intervention at the target lesion. Reposition the Delivery Catheter (including IST) per Section F - Placement of Delivery Catheter.

PRECAUTION: If resistance is felt and believed to be due to the Delivery Catheter, remove the entire Delivery Catheter (including IST) from the patient and prepare another Delivery Catheter for use begining with Section E - Delivery Catheter Inspection/ Preparation.

3. Prior to IST removal, have a non-sterile assistant put on sterile gloves and perform the following:

PRECAUTION: Upon removal from the Delivery Catheter, **the IST is non-sterile**. Carefully handle the **non-sterile IST** to ensure no contamination of field sterility.

- Grasp the **non-sterile IST** and carefully remove the **non-sterile IST** from the Delivery Catheter, while the position of the Delivery Catheter is maintained under fluoroscopy.
- Discard the **non-sterile IST** and gloves.

Delivery Catheter – Transfer Device Reattachment:

1. Bring the prepared ACTIVE Transfer Device to the positioned Delivery Catheter.
2. Insert the Proprietary Connector of the Delivery Catheter through the distal hole of the Sterile Bag into the Proprietary Connector Receptacle of the ACTIVE Transfer Device. Rotate the Proprietary Connector to ensure a secure connection.
3. Lock the Proprietary Connector to the ACTIVE Transfer Device by fully depressing the Proprietary Connector Lock Latch until a blue line is visible.

PRECAUTION: Do not force the connector lock latch into position. If resistance is felt, reposition the proprietary connector to ensure proper engagement with the Transfer Device.

4. Continue procedure, per Section J - ACTIVE Transfer Device Priming.

2. In-Vivo Transport of a NON-ACTIVE Source Train RO/D

The following is the procedure for performing in-vivo transport of a NON-ACTIVE Source Train (e.g., as a test of in-vivo Delivery Catheter source train lumen patency). This optional procedure is only intended to be performed when required by institutional procedures and when:

- The Delivery Catheter has been properly prepared (per Section E- Delivery Catheter Inspection/ Preparation);
- The Delivery Catheter has been placed at the interventional injury site (per Section F- Placement of the Delivery Catheter);
- The Delivery Catheter's pre-loaded IST has been removed (per Section G- IST Removal); and
- Delivery Catheter positioning across the interventional injury site has been maintained (as confirmed by fluoroscopy).

Note: Use only a Novoste™ NON-ACTIVE 3.5F System compatible Transfer Device (Catalog Number TDN-6040) when performing this procedure.

NON-ACTIVE Transfer Device Preparation:

1. Follow the same Transfer Device preparation steps as outlined in Section H or I - ACTIVE Transfer Device Preparation.

NON-ACTIVE Transfer Device Priming:

1. Follow the same instructions as found in Section J - ACTIVE Transfer Device Priming.

Delivery of the NON-ACTIVE Source Train:

1. Ensure that the hemostatic valve is open.
2. Ensure that Power is ON.
3. Slide the Gate Control Switch forward until the Blue Arrow aligns with OPEN.

Note: If the Gate Control Switch cannot be moved to the open position, and the green SOURCES IN LED is illuminated, then move the Gate Control Switch back to the fully closed position and power down the Transfer Device. Restart the Transfer Device and proceed as normal.

4. Move the Fluid Control Lever to SEND.
5. While observing with fluoroscopy, depress the syringe plunger to transport the NON-ACTIVE Source Train to the interventional injury site of the Delivery Catheter. All three Amber ↓↑ Pressure Indicator lights should be illuminated while SENDING the NON-ACTIVE Source

R. Optional Instructions *continued*

Train. An audible click will be heard as the NON-ACTIVE Source Train leaves the Source Chamber.

6. Use fluoroscopy to confirm proper placement of the entire NON-ACTIVE Source Train at the interventional injury site.

   a. In the event that the NON-ACTIVE Source Train can not be confirmed to have reached the injury site, immediately perform the following maneuver to reposition the NON-ACTIVE Source Train:

      - Confirm the hemostatic valve is open.
      - Confirm the Fluid Control Lever is in SEND position.
      - Pull to withdraw approximately 1 ml **Sterile Water for Irrigation** and push to apply forward pressure to the syringe plunger to reposition the NON-ACTIVE Source Train.

   b. In the event that the NON-ACTIVE Source Train still cannot be confirmed to have reached the injury site, immediately perform the following maneuver to return the NON-ACTIVE Source Train to the NON-ACTIVE Transfer Device:

      - Move the Fluid Control Lever to RETURN.
      - Depress syringe and apply continuous, positive pressure so that all three Amber Pressure Indicator lights are illuminated during the return of the NON-ACTIVE Source Train. An audible "click"will be heard as the NON-ACTIVE Source Train returns to the Source Chamber.
      - Maintain Pressure on the syringe while visually confirming that the entire NON-ACTIVE Source Train is located within the Source Chamber and that the Green Arrow Indicator light is "ON".

      Note: Once the NON-ACTIVE Source Train is located within the Source Chamber of the NON-ACTIVE Transfer Device, the Delivery Catheter can be removed and the procedure restarted with a new Delivery Catheter, following standard Test and Placement procedures.

   c. In the event the NON-ACTIVE Source Train has not reached the injury site or been returned to the Device, perform the following:

      - Loosen the hemostatic valve with left hand.
      - Remove the Delivery Catheter from the patient (leaving the guiding catheter and guidewire in place), return the NON-ACTIVE Source Train to the NON-ACTIVE Transfer Device and reattempt the procedure with a new Delivery Catheter, following standard Test and Placement procedures.

NON-ACTIVE Source Train Return:

1. Ensure that the hemostatic valve is open.
2. Move the Fluid Control Lever to RETURN.
3. Depress the syringe plunger so that all three Amber Pressure Indicator lights are illuminated during the return of the NON-ACTIVE Source Train. An audible click will be heard as the NON-ACTIVE Source Train returns to the Source Chamber.
4. Maintain pressure on the syringe while visually confirming that the NON-ACTIVE Source Train is located within the Source Chamber and that the Green Arrow Indicator Light is ON.
5. Visually confirm that the NON-ACTIVE Source Train is located in the Source Chamber and the distal radiopaque marker of the jacketed Source Train is clearly present.

   a. In the event that the entire NON-ACTIVE Source Train cannot be confirmed to have returned to the NON-ACTIVE Transfer Device, perform the following:

      - Confirm the hemostatic valve is open.
      - Confirm the Fluid Control Lever is in RETURN position.
      - Pull to withdraw approximately 1 ml **Sterile Water for Irrigation** and push to apply forward pressure to the syringe plunger to return the NON-ACTIVE Source Train to the Source Chamber of the NON-ACTIVE Transfer Device.

   b. In the event the NON-ACTIVE Source Train has not returned to the Source Chamber of the NON-ACTIVE Transfer Device, perform the following:

      - Loosen the hemostatic valve with left hand.
      - Remove the Delivery Catheter from the patient (leaving the guiding catheter and guidewire in place), return the NON-ACTIVE Source Train to the NON-ACTIVE Transfer Device and reattempt the procedure with a new Delivery Catheter, following standard Test and Placement procedures.

6. While continuing to apply pressure on syringe, slide the Gate Control Switch to the CLOSE position.
7. Unlock the NON-ACTIVE Transfer Device from the Delivery Catheter by depressing the Proprietary Connector Lock Latch such that the blue line is no longer visible.
8. Disconnect the Delivery Catheter from the NON-ACTIVE Transfer Device while maintaining Delivery Catheter

positioning at the targeted interventional injury site. Disconnect the Delivery Catheter by depressing both squeeze tabs located on the Proprietary Connector while withdrawing the Proprietary Connector from the NON-ACTIVE Transfer Device.

9. Carefully place a sterile Proprietary Connector Cover over the tip of the Proprietary Connector to prevent contamination of the sterile field.

10. Carefully return the NON-ACTIVE Transfer Device to the sterile prep table.

11. Proceed with Section H or I - ACTIVE Transfer Device Preparation.

Note: Before performing step H.8 or I.4 (to insert the Delivery Catheter Proprietary Connector into the ACTIVE Transfer Device), conduct the following actions:

- Confirm appropriate position of the Delivery Catheter, using fluoroscopy.
- Remove and discard the Proprietary Connector Cover from the tip of the Proprietary Connector.

V. Customer Service Information

To reorder supplies, call for repair service or to report an adverse event, device failure or complaint, contact:

Novoste Corporation
4350 International Blvd.
Norcross, Georgia 30093 USA

Tel: +1-800-Novoste
Fax: +1-770-717-1283

VI. Beta-Cath™ 3.5F System Specifications

β-Rail™ 3.5F DELIVERY CATHETER:

Single use

Sterile (by ethylene oxide) and Non-pyrogenic.

β-Rail™ 3.5F Delivery Catheter overall length: 180 cm
β-Rail™ 3.5F XL Delivery Catheter overall length: 267 cm

Outer Diameter:	3.5F (1.17 mm/0.046")
Catheter Markings:	
External Proximal Depth Marker:	100 cm from distal tip
Internal Radiopaque Marker (dark):	At Most Distal Point (Stop) of Source Train
Internal Radiopaque Tip Marker (light):	At Catheter Tip
Indicator of Source Train:	Radiopaque 30 mm, 40 mm and 60 mm Radiation Train Length Markings
Guidewire Exit Port:	1 cm from distal tip of the Delivery Catheter
Maximum Guidewire:	0.014" (0.36 mm)
Minimum Guiding Catheter:	6F (1.7 mm/0.067") ID

TRANSFER DEVICE:

Size: (length x width x height)	22.2 cm x 8.9 cm x 7.0 cm
Weight:	0.68 kg
Operating Environmental Conditions:	
Temperature	18°C to 27°C
Relative Humidity	45 % - 85 %
Pressure	550 mmHg to 795 mmHg

For Use of Exchangeable Battery Model Only:

Battery Power Source:	6.0 Volt Lithium Ion*

*Commercially available camera battery e.g., Duracell DL223A, Sanyo CRP2 or compatible.

SEALED SOURCES:

Isotope:	^{90}Strontium
Sealed Source Size :	2.5 mm x 0.38 mm (length x diameter)
Source Train Jacket:	Stainless Steel 304 0.42 mm ID 0.47 mm OD
30 mm Source Train:	2 Radiopaque markers 12 Radioactive Sources
40 mm Source Train:	2 Radiopaque markers 16 Radioactive Sources
60 mm Source Train:	2 Radiopaque markers 24 Radioactive Sources
^{90}Strontium Half-life:	28.8 years

Dose Rate and Activity: Activity and absorbed dose rate to water at 2mm from the Source Train is determined with a NIST traceable Source Train by Novoste and provided on the Novoste Calibration Certificate.

Note: Do not ship the Transfer Device unless a Leak Test has been performed within the previous 6 months. Follow the radiation safety and handling instructions in this User's Manual. Test the Transfer Device for leakage at intervals not to exceed 6 months. Use a Leak Test method capable of detecting 185 Bq (0.005 μCi) of Sr/Y-90. Immediately withdraw a leaking device from use and store it for disposal and/or return to Novoste Corporation. File a report of any leaking device with the authority and notify Novoste Corporation. Retain Leak Test records.

VII. STORAGE AND TRANSPORT:

Store Delivery Catheters, Procedure Accessory Packs, Transfer Devices and Transport Case in a cool, dry place and protect from sunlight. Store the ACTIVE Transfer Device and Transport Case in an area designed by your institutional policies and/or procedures for radioactive materials.

Attachment A: Symbols and Graphics Used with the Beta-Cath™ 3.5F System (in the manual or on the products)

Attention! See Accompanying Documents

Type CF Equipment. Equipment or Parts of Equipment Intended for Direct Cardiac Contact

Radioactive (Radiation) Warning Symbol

Equipment Protected Against Dripping Water

IPX1

Use Before Date

Date of Manufacture

Single Use Only, Do Not Reuse

Storage/Shipping Temperatures

Protect from Direct Sunlight

Store in a Dry Place

Sterile Product, Sterilized by Ethylene Oxide Gas

STERILE | EO

Non-Sterile Product

NON-STERILE

beta

β

Lot Number

LOT

Catalog Number or Reorder Number

REF

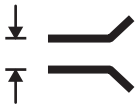
Serial Number

SN

Part Number

PN

Minimum Required Guiding Catheter Inner Diameter



Radioactive Source Train

ACTIVE

Non-Active Source Train

NON-ACTIVE

Locked

Unlocked

Gate Switch Lock Position Indicator

Fluid Lever ON

Power ON/OFF Button

Low Battery Indicator

SEND

SEND

RETURN

RETURN

Adequate Pressure to Hold Sources at Treatment Area (Amber light illuminated)

TX

Adequate Pressure to Send/Return Sources Amber light illuminated)

Excessive Pressure (Red light illuminated)

Source Train OUT of the CHAMBER

Source Train IN the CHAMBER

Gate OPEN

Gate CLOSE

Attachment B: Additional Dosimetry Information for the Beta-Cath™ 3.5F System

Estimated Doses to Patient (Non Target Tissues) and Clinicians in a Typical Procedure

The following are the estimated doses to the Cardiologist, Radiation Oncologist, Cath Lab Staff and Patient from fluoroscopy during PTCA and from the Beta-Cath™ 3.5F System:

Clinician Hand Dose during Pre- and Post-Treatment Activities with the β-Rail™ 3.5F Delivery Catheter

(Assumes 2 minutes for device preparation & 2 minutes for post-treatment activities)

30 mm Beta-Cath™ 3.5F System Hand Dose = 4 mrem (0.04 mSv)[1]
30 mm Beta-Cath™ 3.5F System Skin Dose Equivalent*= 18 mrem (0.18 mSv)[1]
40 mm Beta-Cath™ 3.5F System Hand Dose = 5 mrem (0.05 mSv)[1]
40 mm Beta-Cath™ 3.5F System Skin Dose Equivalent*= 24 mrem (0.24 mSv)[1]
60 mm Beta-Cath™ 3.5F System Hand Dose = 8 mrem (0.08 mSv)[1]
60 mm Beta-Cath™ 3.5F System Skin Dose Equivalent*= 36 mrem (0.36 mSv)[1]

Annual Hand and Skin Dose Limit for Occupational Workers = 50,000 mrem (500 mSv)

The estimated dose from the 30 mm Beta-Cath™ 3.5F System is 0.04% of the annual dose limit, the estimated dose from the 40 mm Beta-Cath™ 3.5F System is 0.05% of the annual dose limit, and the estimated dose from the 60 mm Beta-Cath™ 3.5F System is 0.07% of the annual dose limit.

*Skin dose is defined here as the dose received to the unprotected hand only, not the whole body dose.

Clinician Hand Dose during Pre- and Post-Treatment Activities with β-Cath™ 3.5F XL Delivery Catheter

(Assumes 2 minutes for device preparation & 2 minutes for post-treatment activities)

30 mm Beta-Cath™ System Hand Dose = 4 mrem (0.04 mSv)[1]
30 mm Beta-Cath™ System Skin Dose Equivalent* = 50 mrem (0.50 mSv)[1]
40 mm Beta-Cath™ System Hand Dose = 5 mrem (0.05 mSv)[1]
40 mm Beta-Cath™ System Skin Dose Equivalent* = 67 mrem (0.67 mSv)[1]
60 mm Beta-Cath™ System Hand Dose = 8 mrem (0.08 mSv)[1]
60 mm Beta-Cath™ System Skin Dose Equivalent* = 100 mrem (1.0 mSv)[1]

The estimated dose from the 30 mm Beta-Cath™ System is 0.1% of the annual dose limit, the estimated dose from the 40 mm Beta-Cath™ System is 0.13% of the annual dose limit, and the estimated dose from the 60 mm Beta-Cath™ 3.5F System is 0.2% of the annual dose limit.

*Skin dose is defined here as the dose received to the unprotected hand only, not the whole body dose.

Clinician Whole Body Dose per Treatment

Fluoroscopy during PTCA = 4 to 16 mrem (0.04 to 0.16 mSv)[2]
30 mm Beta-Cath™ 3.5F System = 0.2 mrem (0.002 mSv)[1]
40 mm Beta-Cath™ 3.5F System = 0.3 mrem (0.003 mSv)[1]
60 mm Beta-Cath™ 3.5F System = 0.4 mrem (0.004 mSv)[1]
(No dose reduction applied for a lead apron)
Annual Whole Body Dose Limit for Occupational Workers = 5,000 mrem (50 mSv)

The estimated dose from the 30 mm Beta-Cath™ 3.5F System is 0.004% of the annual dose limit, the estimated dose from the 40 mm Beta-Cath™ 3.5F System is 0.006% of the annual dose limit, and the estimated dose from the 60 mm Beta-Cath™ 3.5F System is 0.008% of the annual dose limit.

Cath Lab Staff Whole Body Dose per Treatment

30 mm Beta-Cath™ 3.5F System = 0.03 mrem (0.0003 mSv)[1]
40 mm Beta-Cath™ 3.5F System = 0.04 mrem (0.0004 mSv)[1]
60 mm Beta-Cath™ 3.5F System = 0.06 mrem (0.0006 mSv)[1]
(No dose reduction applied for a lead apron)
Annual Whole Body Dose Limit for Occupational Workers = 5,000 mrem (50 mSv)

The estimated dose per procedure from the 30 mm Beta-Cath™ 3.5F System is 0.0006% of the annual dose limit, the estimated dose per procedure from the 40 mm Beta-Cath™ 3.5F System is 0.0008% of the annual dose limit, and the estimated dose per procedure from the 60 mm Beta-Cath™ 3.5F System is 0.0012% of the annual dose limit.

Patient Whole Body Dose Per Treatment

Fluoroscopy during PTCA = 340 mrem (3.4 mSv)[3]
30 mm Beta-Cath™ 3.5F System = 0.19 mrem during treatment and 0.08 mrem during transit for a total of 0.27 mrem (0.0027 mSv)[1] per treatment.
40 mm Beta-Cath™ 3.5F System = 0.25 mrem during treatment and 0.11 mrem during transit for a total of 0.36 mrem (0.0036 mSv)[1] per treatment.
60 mm Beta-Cath™ 3.5F System = 0.38 mrem during treatment and 0.16 mrem during transit for a total of 0.54 mrem (0.0054 mSv)[1] per treatment.

The estimated patient whole body dose from the 30 mm Beta-Cath™ 3.5F System is approximately 0.08% of the whole body dose from fluoroscopy during a PTCA, the estimated patient whole body dose from the 40 mm Beta-Cath™ 3.5F System is approximately 0.11% of the whole body dose from fluoroscopy during a PTCA, and the estimated patient whole body dose from the 60 mm

Attachment B: Additional Dosimetry Information for the Beta-Cath™ 3.5F System *continued*

Beta-Cath™ 3.5F System is approximately 0.16% of the whole body dose from fluoroscopy during a PTCA.

1 Data on file, Novoste Corporation.
2 Limacher, MD MC, et al. Radiation Safety in the Practice of Cardiology. JACC. March 15, 1998:892-913.
3 Harrison D, Ricciardello M, Collins L. Evaluation of radiation dose and risk to the patient from coronary angiography. Aust NZ J Med 1998; 597-603.

Dose Verification

Novoste calibrates each ACTIVE Source Train, with techniques and standards traceable to a National Institute of Standards and Technology (NIST) standard, at 2 mm from the centerline of the ACTIVE Source Train. Each ACTIVE Transfer Device is shipped with its own Calibration Certificate that provides the dose rate and associated treatment times.

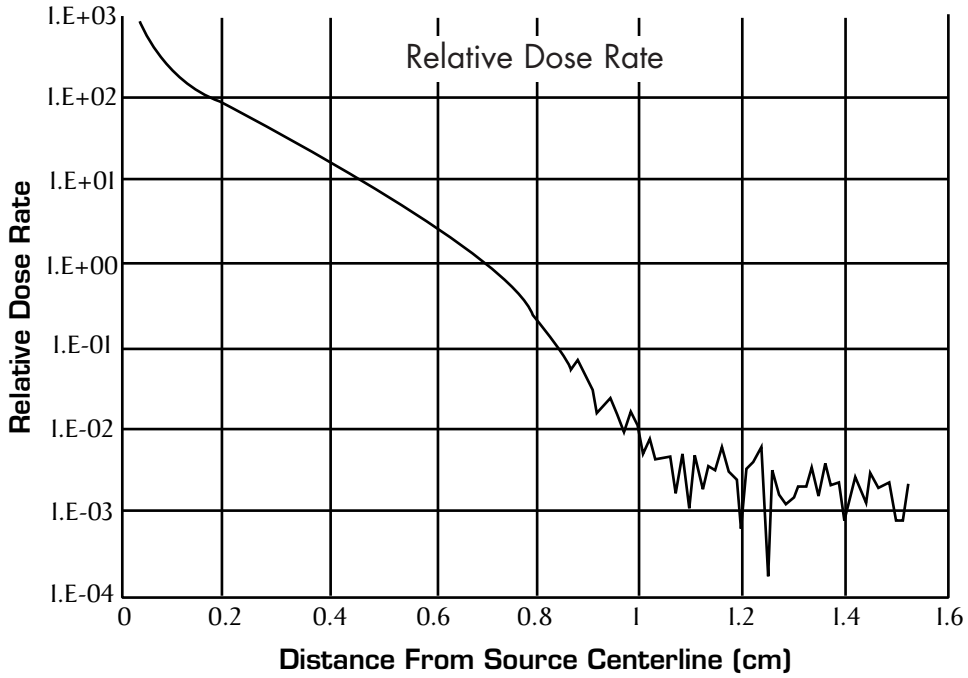
Any instrument or dosimeter used to directly measure the dose rate from the ACTIVE Source Train must be small enough to measure the dose rate at 2 mm from the centerline of the ACTIVE Source Train. Radiation Personnel can utilize Radiochromic Film or a scintillation system, which has the properties required for the measurement of absolute doses in very small volumes.

Dose Distribution

The dose rate from the ACTIVE Source Train is determined in water at 2 mm from the centerline of the ACTIVE Source Train. The dose rate diminishes significantly as the distance from the sources increases. Figure 9 describes the relative dose rate as a function of distance from the centerline of the Source Train. This data was obtained using Monte Carlo computer codes. The graph demonstrates the advantage of using beta radiation for the treatment of restenosis because tissues other than the injury site receive comparatively little dose.

Attachment B: Additional Dosimetry Information for the Beta-Cath™ 3.5F System

Figure 11. Relative Dose Rate from ACTIVE Source Train as a Function of Distance in Water.



Note: This graph represents a model of dose as a function of distance from the source in water. The graph is not intended for dose planning. Refer to the Calibration Certificate for the recommended dose prescription and treatment time calculation.

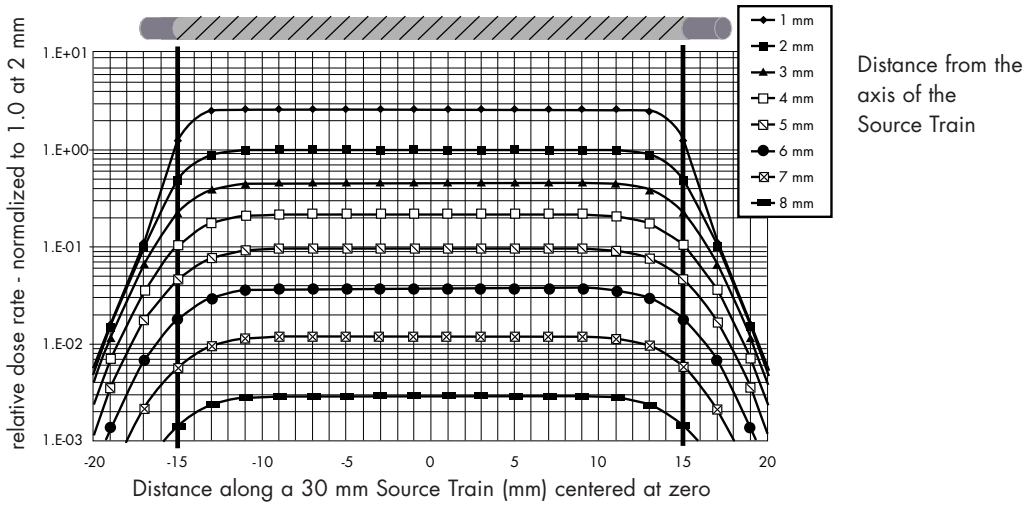
Additionally, tabular values of the depth dose, normalized to 100% at the reference point of 2mm from the centerline of the source train in water, are provided below. The data provides the dose rate at the distance of interest relative to the reference dose rate at 2mm from the centerline of the source train in water.

Distance from Source Centerline (mm)	% Relative Dose
0.75	370
1.00	261
1.25	196
1.50	155
1.75	121
2.00	100
2.25	81.3
2.50	67.1
2.75	53.8
3.00	45.6
3.25	38.5
3.50	31.6
3.75	25.8
4.00	20.9
4.25	17.4
4.50	14.2
4.75	11.3
5.00	9.2
5.25	7.22
5.50	5.83
5.75	4.42
6.00	3.54
6.25	2.77
6.50	2.07

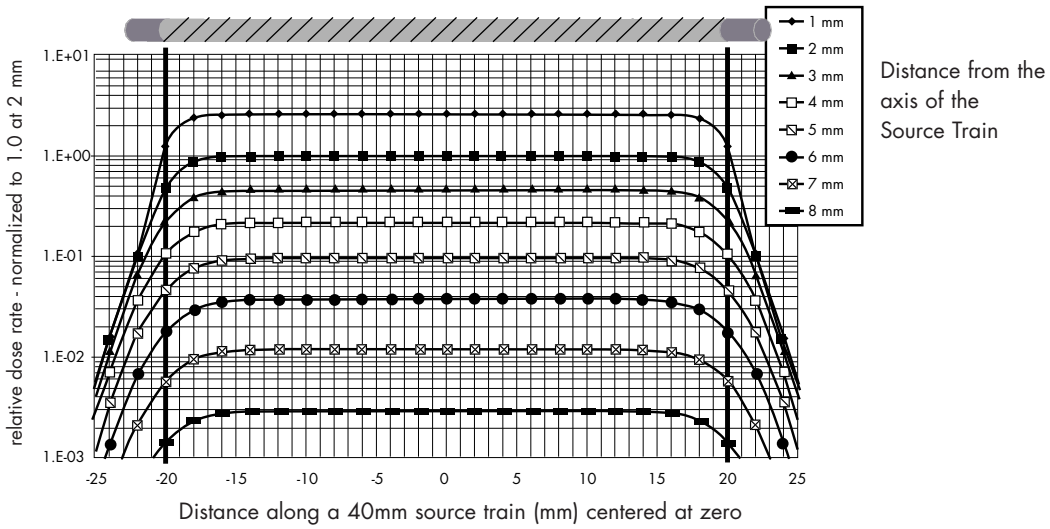
Attachment B: Additional Dosimetry Information for the Beta-Cath™ 3.5F System

The following graphs provide doses along the centerline of 30mm, 40mm and 60mm Source Trains at various radial distances in water.

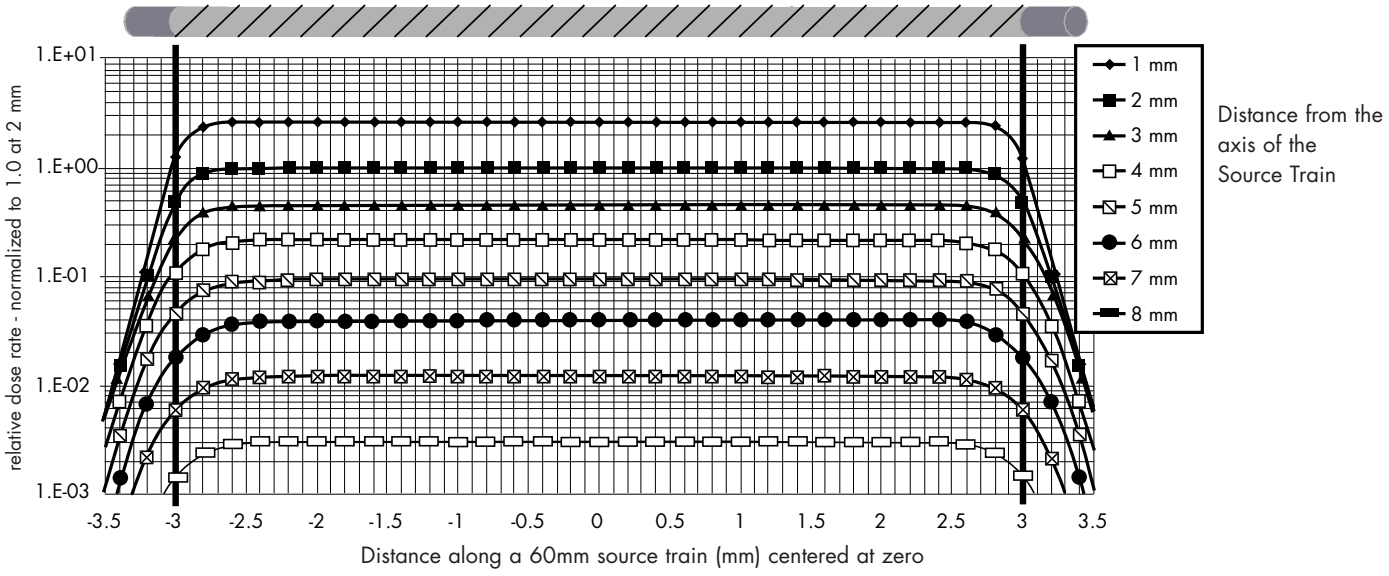
Dose Profiles Along the Axis of the 30 mm Source Train at Various Radial Distances in Water



Dose Profiles Along the Axis of the 40 mm Source Train at Various Radial Distances in Water



Dose Profiles Along the Axis of the 60 mm Source Train at Various Radial Distances in Water



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