BETA-CATH SYSTEM

User's Manual

Beta-Cath™ System

DRAFT

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

Novoste™

TABLE OF CONTENTS

I. Introduction....3
How To Use This Manual....3
II. System Description....4
III. Essential Prescribing Information....4
Indications....4
Contraindications....4
Warnings....4
Precautions....5
Special Considerations....7
Adverse Events....8
Antiplatelet Therapy....10
Novoste START Trial....10
Table 1. Principal Effectiveness and Safety Results....11
Figure 1. Freedom from Target Vessel Failure (at 12 months)....13
IV. Instructions for Use....14
Detailed Device Description....14
How Supplied....15
Figure 2. **Beta-Cath™** System....18
Transfer Device Controls and Indicators....18
Table 2. Transfer Device Controls and Indicators....20
Figure 3. 30 mm ACTIVE Transfer Device....23
A. ACTIVE Device Receipt....25
B. Radioactive Sealed Source/Device Leak Test Procedure....26
C. Therapy Planning....28
Figure 4. Recommended Radiation Coverage....28
D. Surveillance of the Cath Lab Room....29
E. β-Cath™ Delivery Catheter Inspection/Preparation....30
Figure 5. Fluid Management System....30
F. NON-ACTIVE Transfer Device Preparation....31
Figure 6. Sterile Bag....31
G. NON-ACTIVE Transfer Device Priming....32
H. β -Cath™ Delivery Catheter Integrity Test....33
I. NON-ACTIVE Source Train Return....33
J. ACTIVE Transfer Device Preparation....34
K. ACTIVE Transfer Device Priming....36
L. Placement of the β -Cath™ Delivery Catheter....36
M. Delivery of the ACTIVE Radiation Source Train....37
N. ACTIVE Source Train Return....39
O. β -Cath™ Delivery Catheter Removal....40
P. Disassembly of the **Beta-Cath™** System....40
Q. Post Procedural Radiation Checks....41
R. Drying and Storing of the Transfer Devices....42
S. Emergency Source Recovery Procedure....43
V. Customer Service Information....46
VI. Specifications....46
VII. Storage and Transport....47
Attachment A: Symbols and Graphics Used with the **Beta-Cath™** System....48
Attachment B: Additional Dosimetry Information....51
Estimated Dose to Patient (Non-Target Tissue) and Clinicians in aTypical Procedure....51
Dose Verification....52
Dose Distribution....52
Figure 7. Relative Dose Rate from ACTIVE Source Train as a Function of Distance....52

25

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™** 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 description of the disease or conditions 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 or permanent damage to body structure, or necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

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

PRECAUTION: 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	**CARD**
Performed by Radiation Oncologist or Designee	**RO/D**
Performed by Radiation Oncologist, Medical Physicist, Radiation	

II. System Description

The **Beta-Cath™** System is an integrated system comprised of four components: the **ß- Cath™** Delivery Catheter, the 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-Cath™** Delivery Catheter provides the path through which the Source Train is delivered to and retrieved from the site of interventional injury.

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 Source Train consists of a series of individual, cylindrical, sealed sources containing Sr90/Y90 and an inactive 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™** 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.

III. Essential Prescribing Information

Indications

The **Beta-Cath™** 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) 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.**

Delivery Catheter & Source Train Placement

- 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.
- Failure to correctly position the ACTIVE Source Train at the injury site may under expose the targeted treatment area and expose tissue not targeted for treatment to unintentional radiation. Exceeding the prescribed radiation treatment time will result in a higher than intended dose.

Migration or improper location of the ACTIVE Source Train may cause unintentional radiation exposure to occur. The effect of unintentional radiation exposures and higher than intended doses are unknown.

- 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.
- Upon return of the radiation source train, 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 comply with the specific use of the Transfer Device controls may result in injury or unintended radiation exposure. 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.

Intravascular Radiation Procedure

- 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 ACTIVE Transfer Device, Delivery Catheter, Fluid Collection Bag, or Procedure Room is significantly different from initial baseline readings, stop all activity and re-survey the ACTIVE 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 miss-placed source, refer to Section S, "Emergency Source Recovery Procedure."
- **UNDER NO CIRCUMSTANCES** should an individual attempt to remove the radiation source train from the **Beta-Cath™** System, grasp the catheter directly with hands, 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.
- 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™** 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 System Preparation

- Prior to any procedure, the equipment should be thoroughly examined to verify the proper function and integrity of the system.
- Use the Delivery Catheter and Procedure Accessory Pack before the expiration date noted on the package. Verify that the sterility of the devices have 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 the Delivery Catheter if there is evidence of damage. If the Delivery Catheter Integrity Test detects a breach of catheter integrity, or restricted movement of the Source Train, note the observation and return the Source Train to the Transfer Device. Return the Delivery Catheter to Novoste Corporation. Prepare another Delivery Catheter for use beginning with Section E, the -Cath™ Delivery Catheter Inspection/Preparation.
- 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.
- Do not use saline as a hydraulic fluid in the Transfer Device; corrosion may occur.
- 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.
- Use caution when connecting the Proprietary Connector to the ACTIVE Transfer Device. The Proprietary Connector of the Delivery Catheter is no longer sterile once disconnected from the NON-ACTIVE 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.
- Ensure that the Gate Control Switch is completely closed, as incomplete closure may render the Gate inoperable.

Intravascular Radiation Procedure

- Utilize a manual Blood Pressure Cuff to monitor patient status during the radiation treatment because arterial wave form pressure may be dampened while Delivery Catheter is in place.
- The ACTIVE 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.
- 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.
- 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.
- The Transfer Device requires scheduled maintenance by Novoste Corporation every 250 procedures or six months, whichever event occurs first.
- 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 the potential damage to a source.

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 (5Fr).
- 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-Cath™ Delivery Catheter.
- Patients presenting with:
    - thrombotic lesions;
    - multiple vessel lesions;,
    - vein graft segments;
    - overlapping stents;
    - myocardial infarction less than or equal to 72 hours of the procedure; and/or
    - ejection fractions less 30%.
- Patients who have received a heart transplant.
- Women of child bearing potential who are pregnant or suspect pregnancy.

Adverse Events

The **Beta-Cath™** System was evaluated in the STents And Radiation Therapy (START) Trial, a multicenter, randomized, placebo-controlled trial involving 476 patients. 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.

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™ 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)

The following adverse events were NOT observed during the clinical investigation, but are recognized as potential adverse events associated with the non-radioactive portion of vascular brachytherapy (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

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. If a new stent is not implanted in conjunction with the radiation therapy, antiplatelet therapy should be administered at the physicians discretion.

Novoste START Trial

The STents And Radiation Therapy (START) Trial, a multicenter, randomized, placebo-controlled trial began in September 1998. 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™** System (n=244) or placebo **Beta-Cath™** 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 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 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™** 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 regime 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 (75 mg/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 19mm.

Table 1. Principal Effectiveness and Safety Results
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)	22.8±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. CI = Confidence Interval

N/A = Not applicable.

Relative Risk = Sr-90/Placebo SE = $\text{sqrt}\{(1-p_1)/n_{11}+(1-p_2)/n_{21}\}$ CI = RR*exp(±1.96*SE)

Difference = Sr-90 – Placebo SE = $\text{sqrt}(p_1*q_1/n_1+p_2*q_2/n_2)$ CI = Diff±1.96*SE

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.

77

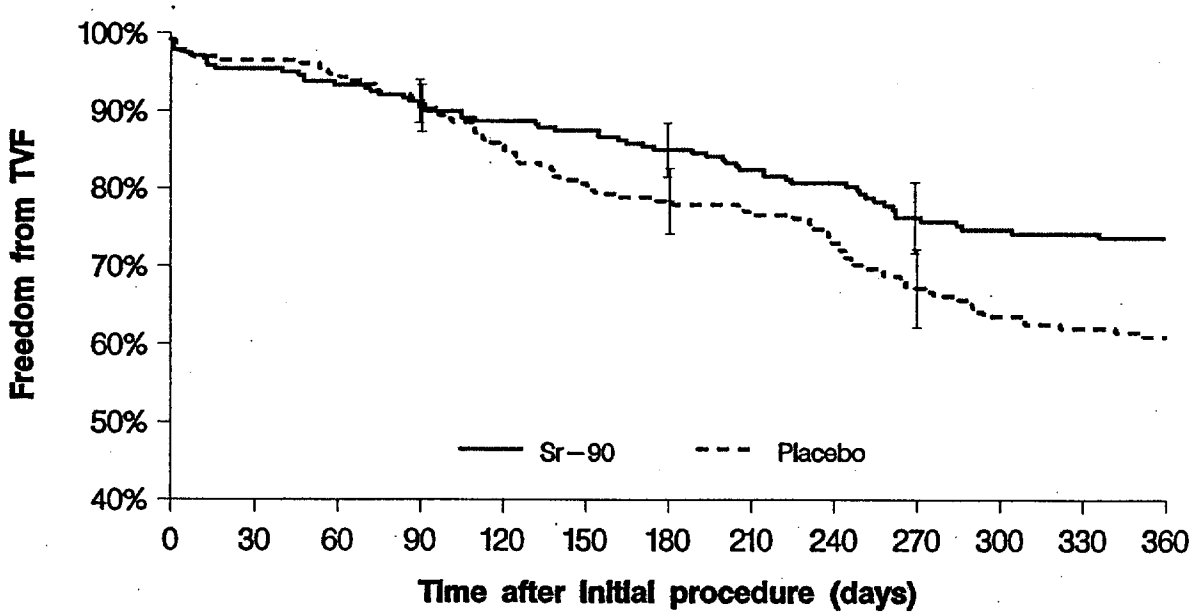
Procedure Success = Attainment of a final residual stenosis of <50% (by QCA) using any percutaneous method and no in-hospital major adverse cardiac events (MACE). If QCA was not available, the visual estimate of diameter stenosis was used.

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 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)



	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%

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

IV. Instructions For Use

The following section provides instructions for using the **Beta-Cath™** System from Novoste™ Corporation. The **Beta-Cath™** 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™** 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™** 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 the 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 ACTIVE Source Train will contain a "train" of 12 (30 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) gold-colored 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.

   The NON-ACTIVE Transfer Device will contain a NON-ACTIVE Source Train consisting of 12 (30 mm Source Train) miniature cylindrical NON-ACTIVE sources, and two (one distal and one proximal) gold-colored markers. This Transfer Device is **NOT RADIOACTIVE** and is used to test the Delivery Catheter.

   The NON-ACTIVE (**NOT RADIOACTIVE**) Transfer Device will be labeled with a NON-ACTIVE sticker.

2) The **β-Cath™** Delivery Catheter is a single use, closed end, over-the-wire catheter through which the Source Train is transported hydraulically to the Treatment Zone and back into the Transfer Device.

The β-Cath™ Delivery Catheter is supplied sterile and includes a Proprietary Connector that connects the Delivery Catheter exclusively to the Transfer Device.

How Supplied

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

- ACTIVE Transfer Device and White Lead-Lined Container in a Type A shipping container
- NON-ACTIVE Transfer Device
- 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

Additionally, the β-Cath™ Delivery Catheter with Procedure Accessory Pack (supplied sterile) are 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 personnel perform the in-coming 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.

Transport Case:

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 package) for the following items:

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

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

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™** 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) Flushing Adapters
- two (2) 20 ml Three Ring Syringes
- two (2) Fluid Collection Bags
- two (2) Quartz Caps

Single Use Items

β-Cath™ Delivery Catheter (Figure 2):

The **β-Cath™** Delivery Catheter is an over-the-wire catheter that allows the Source Train to be hydraulically delivered to and from the targeted site in the coronary vasculature. The **β-Cath™** Delivery Catheter features:

- $\geq$ 7F (2.3 mm) 0.078" guide catheter compatible.
- $\leq$ 0.014" 300 cm steerable guidewire compatible. Docking wires are not recommended.

- Two (2) radiopaque catheter markers measuring 35 mm apart (inside to inside) to designate the 30 mm Treatment Zones, respectively.

- A tapered tip from 5 F (1.67 mm/0.066") to 2 F (0.66 mm/0.026") distal to the distal radiopaque marker.

- An open guidewire lumen allows the catheter to travel over a 300 cm guidewire.

- A second, dedicated lumen contains the Source Train while in the catheter.

- A third lumen completes the fluid path.

- A proximal depth marker positioned approximately 90 cm from the distal tip that facilitates placement of the Delivery Catheter through the femoral 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.

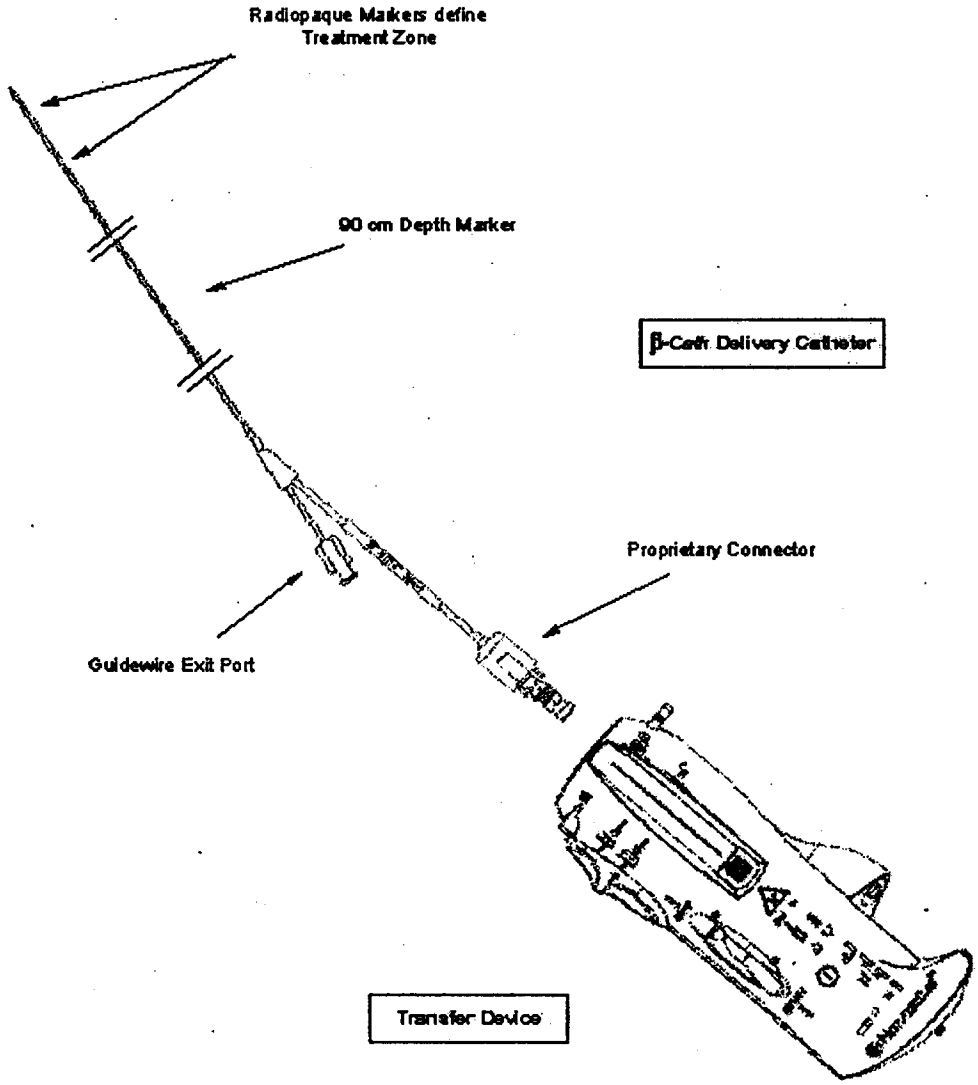
- Sterile package includes one β-Cath™ Delivery Catheter.

Procedure Accessory Pack:
(included inside the β-Cath™ Delivery Catheter Box)

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

- two (2) Fluid Collection Bags
- two (2) 20 ml Three Ring Syringes
- two (2) Extension Connectors
- two (2) Sterile Bags
- two (2) Proprietary Connector Covers

Figure 2. Beta-Cath™ System



Transfer Device Controls and 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.

The Transfer Device can be turned ON or OFF by depressing the Blue ON/OFF button for 3 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). Each time the power button is depressed, the 5-minute period countdown is restarted. 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 a LED light test indicated when all of the indicator lights alternately blink. A non-user serviceable battery powers the Transfer Device.

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.

Table 2: Transfer Device Controls and Indicators (Figure 3)

ON/OFF BUTTON (Blue)	ON/OFF button activates the electronic circuitry for 5 minutes. When first switched "ON", the electronics will perform a LED light 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 seconds.
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.
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.

Table 2: Transfer Device Controls and Indicators (Continued)

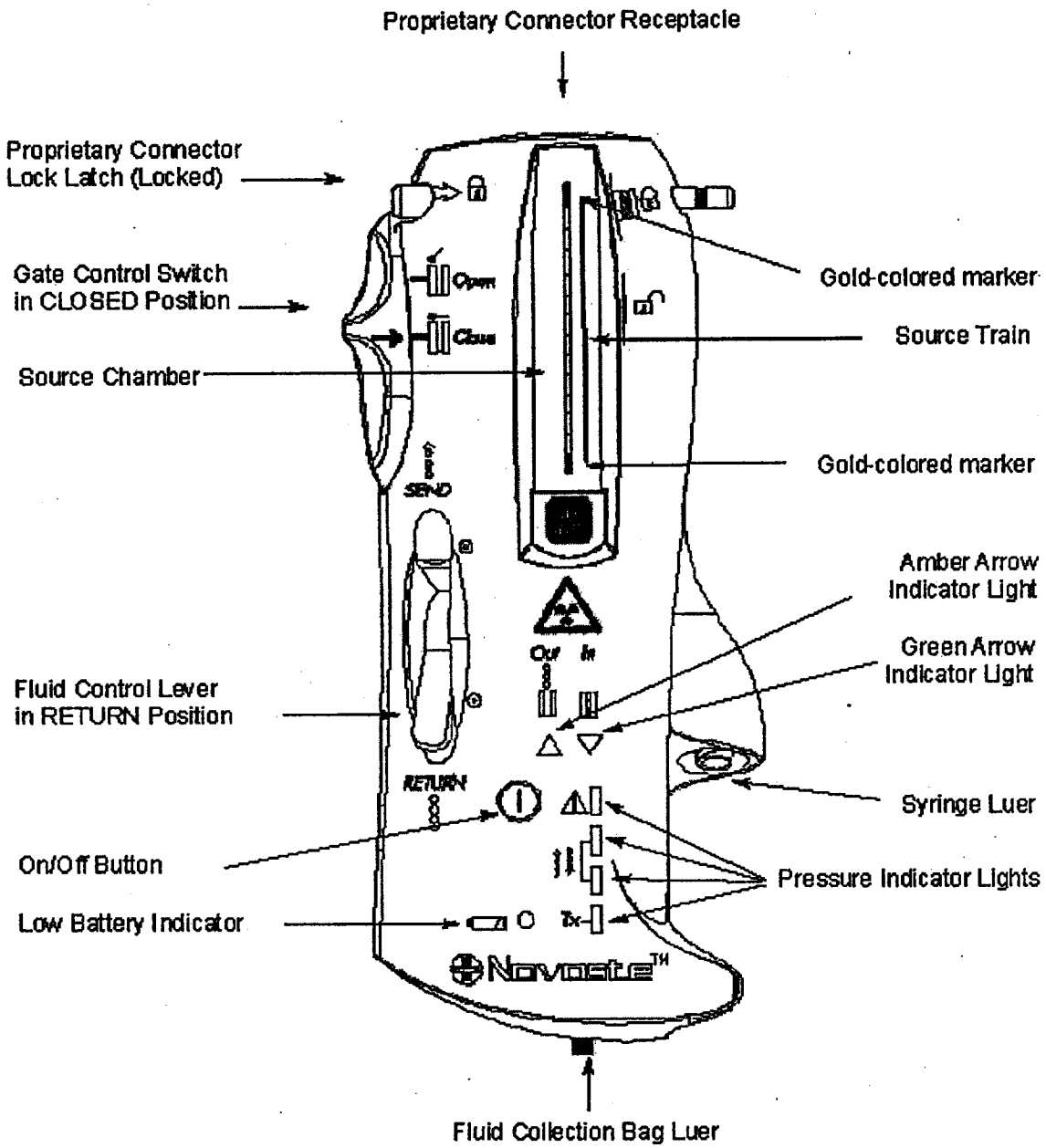
Source Chamber Viewing Window	The clear window allows for magnified visual inspection of the Source Train.
Fluid Control Lever	This two position lever controls the fluid flow and direction of Source Train movement. SEND will allow fluid to hydraulically transport the Source Train into the Delivery Catheter. RETURN will allow fluid to hydraulically transport the Source Train back into 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 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 see Fig 3) where the second and third Amber indicators 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.

Table 2: Transfer Device Controls and Indicators (Continued)

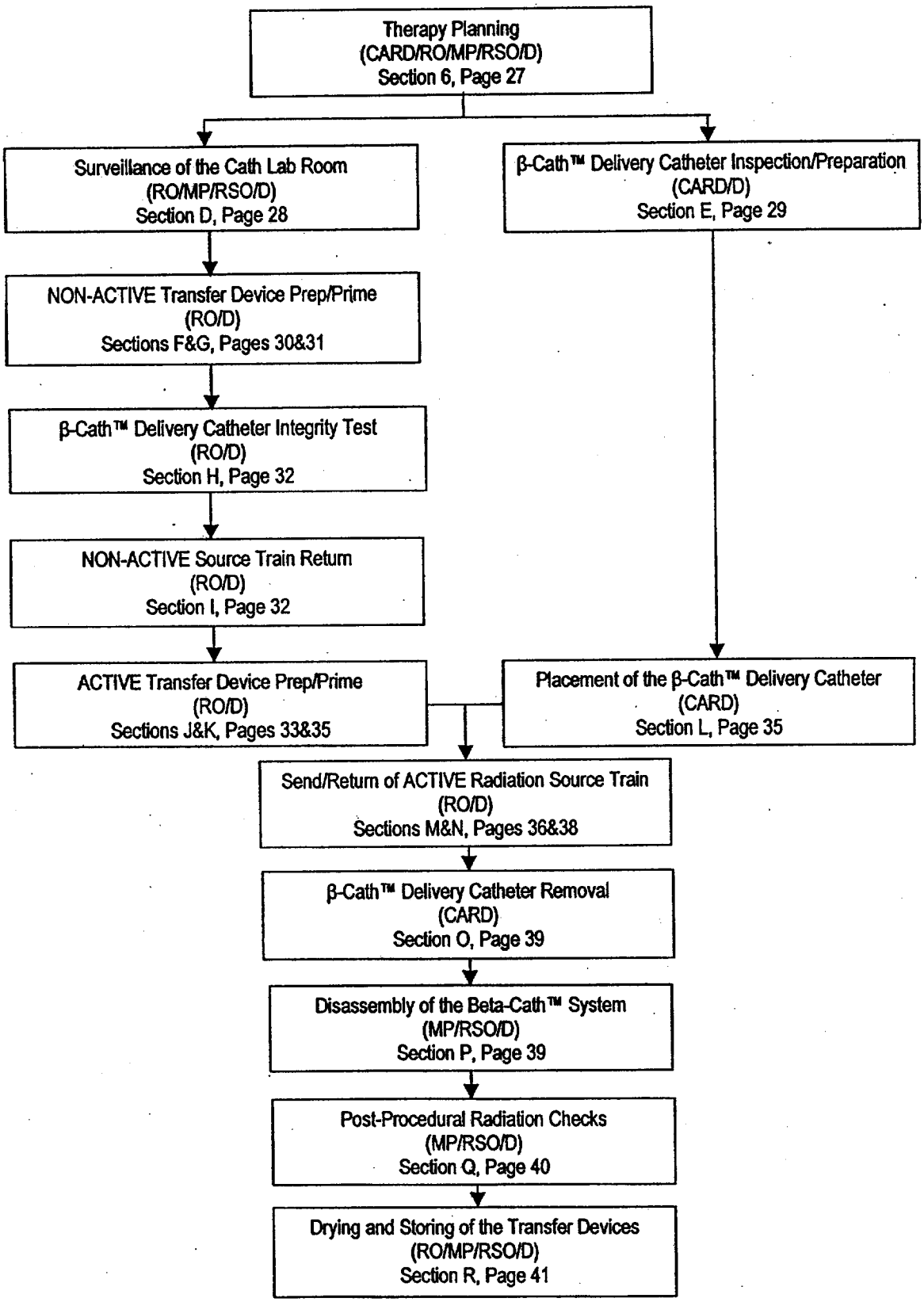
Treatment Counter	The counter display keeps track of the number of procedures the Transfer Device has performed. The counter is located on the under side of the Transfer Device. It increments the count by one each time a treatment procedure or a test run is performed.

PRECAUTION: Do not use the use the Transfer Device if the controls and indicators are not functioning correctly. Please contact your Novoste Representative for service.

Figure 3. 30 mm ACTIVE Transfer Device



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 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™** *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 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.

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

1) Using a portable 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) Using a wrench, loosen the nut on the ring around the lid and remove the ring and the lid.

6) Perform initial device Survey of White Lead-Lined Storage Container and ACTIVE Transfer Device and note as initial reading for future reference.

7) 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.

8) 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.

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

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

11) 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.

12) 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). 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.

13) 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.

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

15) 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
- Distilled or Sterile Water

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 Table 2 - Transfer Device Controls and Indicators and Figure 3 - Novoste 30 mm Transfer Device to become familiar with the components.

1) Remove Quartz Cap from the Proprietary Connector receptacle of the Transfer Device and place in White Lead-Lined Storage Container.

2) Insert the 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.

PRECAUTION: Do not use saline as a hydraulic fluid in the Transfer Device; corrosion may occur.

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 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 a results exceeds 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 of the Transfer Device and store in

accordance with institutional policy.

C. Therapy Planning

CARD/RO/MP/RSO/D

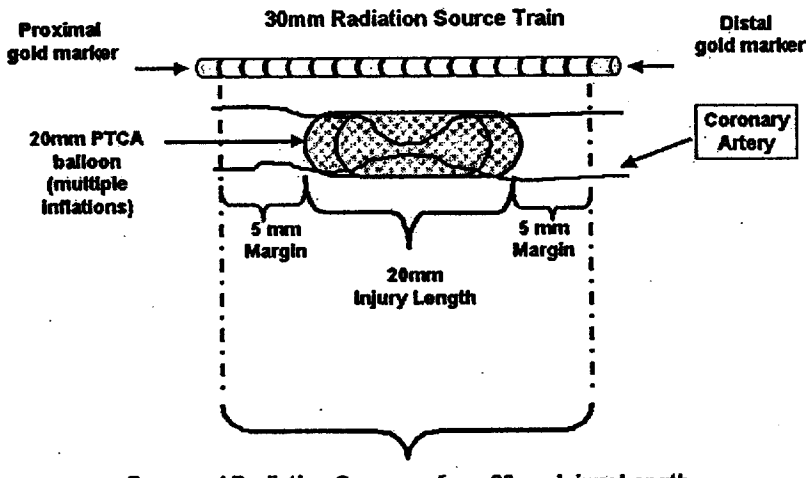
With the **Beta-Cath™** System, recommended prescription doses:

Reference Vessel Diameter	Recommended Prescription Dose for In-Stent Restenosis treatable with up to a 20 mm balloon
≥ 2.7 ≤ 3.35 mm	18.4 Gy*
> 3.35 ≤ 4.0 mm	23 Gy*

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. 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. The Delivery Catheter should be positioned with a minimum of a 5 mm margin on each side of the entire injury (Figure 4).

*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.

Figure 4. Recommended Radiation Coverage



Proposed Radiation Coverage for a 20mm Injury Length

56

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

The following Radiation Surveillance Procedure is suggested for use with the **Beta-Cath™** 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 ACTIVE and NON-ACTIVE Transfer Devices and Response Kit
- Delivery Catheter and Procedure Accessory Pack
- Sterile Water
- 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 readings, 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 S, "Emergency Source Recovery Procedure."

3) Inventory the Source Train and gold-colored 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 S, "Emergency Source Recovery Procedure."

7) When requested, remove the ACTIVE Transfer Device from the White Lead-Lined Storage Container, remove Quartz Cap from the Proprietary Connector receptacle of 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. β-Cath™ 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.

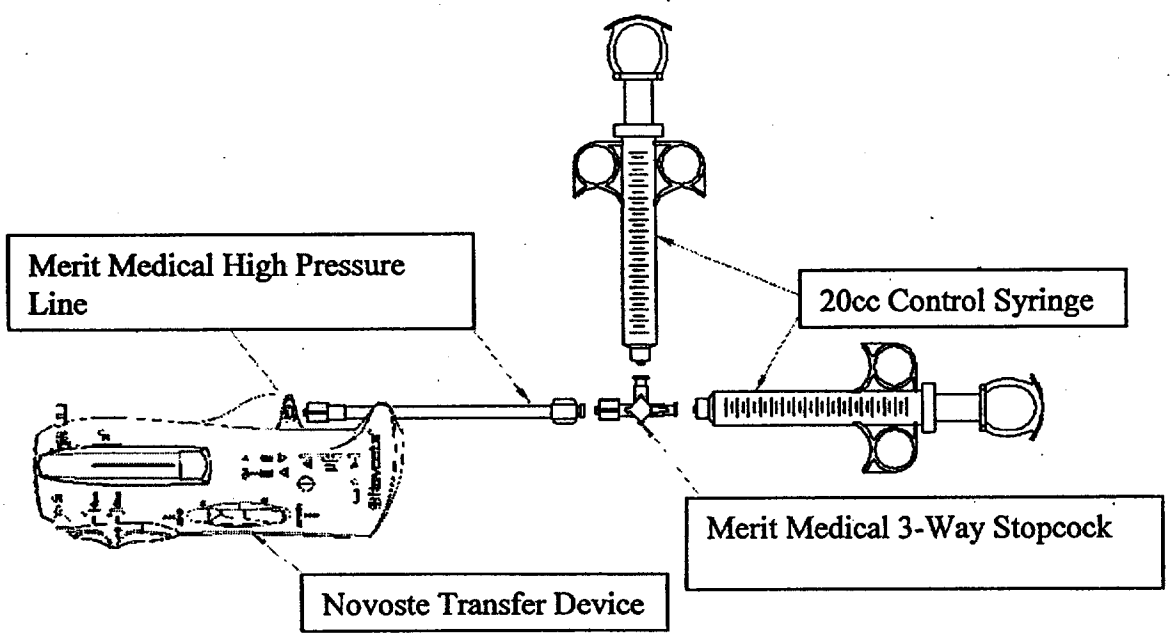
1) Open the Delivery Catheter and the Procedure Accessory Pack onto the sterile field.

PRECAUTION: Do not use saline as a hydraulic fluid in the Transfer Device, corrosion may occur.

2) Fill two 20 ml syringes with sterile water. Attach an Extension Connector to each of the 20cc Syringes. Place the syringes on the prep table.

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 5)

Figure 5. Fluid Management System



3) 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.

F. NON-ACTIVE Transfer Device Preparation RO/D

1) Confirm that the NON-ACTIVE Transfer Device has:

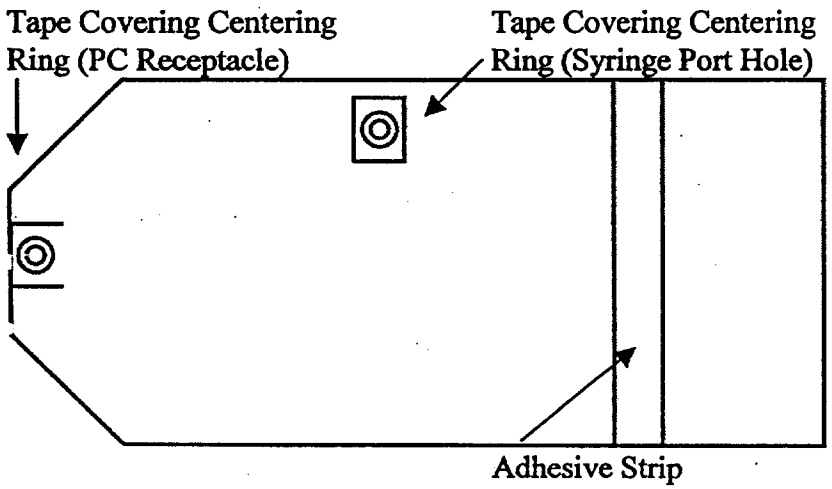
- A NON-ACTIVE sticker on the Transfer Device.
- The Gate Control Switch is CLOSED.
- The distal gold-colored marker of the NON-ACTIVE Source Train is away from the Gate.
- The Fluid Control Lever is set to RETURN.
- The power is turned ON.

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 for service.

2) Connect a Fluid Collection Bag to the Fluid Collection Bag Luer Port fitting on the back of the NON-ACTIVE Transfer Device and cup the Fluid Collection Bag around the bottom of the device.

3) Using aseptic technique, place gloved hands inside cuffs of the Sterile Bag. Carefully place the non-sterile NON-ACTIVE Transfer Device with attached Fluid Collection Bag inside the Sterile Bag. Orient the Transfer Device Syringe Luer toward the Syringe Port Hole on the Sterile Bag. (Figure 6) Unfold cuffs of Sterile Bag and secure the NON-ACTIVE Transfer Device by folding the proximal end of the Sterile Bag two (2) times and secure with adhesive strip.

Figure 6. Sterile Bag



4) Align the centering ring of Syringe Port Hole of the Sterile Bag over the Syringe Luer of the NON-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.

PRECAUTION: When attaching the syringe (or extension tubing), 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.

6) Align the distal Centering Ring over the Proprietary Connector Receptacle of the NON-ACTIVE Transfer Device. Remove the tape covering the distal hole of the Sterile Bag.

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

7) Wet tip of the Delivery Catheter Proprietary Connector with sterile water, to ease insertion and insert the Proprietary Connector through the distal hole of the Sterile Bag into the Proprietary Connector Receptacle of the NON-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.

8) Lock the Proprietary Connector to the NON-ACTIVE Transfer Device by fully depressing the white Proprietary Connector Lock Latch until a blue line is visible on the Latch.

G. NON-ACTIVE Transfer Device Priming RO/D

1) Ensure that the Gate is CLOSED.

2) Ensure that the Fluid Control Lever is in RETURN.

3) Flush System with 6 ml's of water. Confirm the device is primed properly by observing the absence of air bubbles and the entry of water into the Fluid Collection Bag.

H. β-Cath™ Delivery Catheter Integrity Test RO/D

1) Ensure that the Power is ON.

2) Slide the Gate Control Switch forward until the Blue Arrow aligns with OPEN.

3) Move the Fluid Control Lever to SEND.

4) Depress the syringe to transport the NON-ACTIVE Source Train to the distal end of the Delivery Catheter-all three Amber ↑↑ Pressure Indicator lights should be illuminated during the "SENDING" of the Source Train. An audible "click" will be heard as the NON-ACTIVE Source Train leaves the Source Chamber.

5) Once the entire NON-ACTIVE Source Train has reached the Treatment Zone of the Delivery Catheter, apply continuous, positive pressure to maintain the sources at the tip. Adequate pressure is indicated by the illumination of the first Amber **TX** Pressure Indication Light.

6) Confirm visually that the entire NON-ACTIVE Source Train has reached the Treatment Zone. Assure that there is at least 10 ml water remaining to return the NON-ACTIVE Source Train to the Source Chamber.

PRECAUTION: If the Delivery Catheter Integrity Test detects a breach of catheter integrity, or restricted movement of the Source Train, note the observation and return the Source Train to the Transfer Device. Return the Delivery Catheter to Novoste Corporation. Prepare another Delivery Catheter for use beginning with Section E, the **β-Cath™** Delivery Catheter Inspection/Preparation.

I. NON-ACTIVE Source Train Return RO/D

1) Move the Fluid Control Lever to RETURN.

2) Depress the 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.

3) Maintain pressure on the syringe while confirming visually that the entire NON-ACTIVE Source Train is located within the Source Chamber and that the Green Arrow Indicator light is ON. An audible "click" will be heard as the NON-ACTIVE Source Train returns to the Source Chamber.

4) Visually confirm that the entire NON-ACTIVE Source Train is located in the Source Chamber and all Sources are away from the Gate.

5) While continuing to apply pressure on syringe, slide the Gate Control Switch to CLOSED.

6) Carefully place the NON-ACTIVE Transfer Device and the attached Delivery Catheter on the sterile prep table.

7) Unlock the Delivery Catheter from the NON-ACTIVE Transfer Device by fully depressing the

Proprietary Connector Lock Latch.

8) Disconnect the Delivery Catheter Proprietary Connector from the NON-ACTIVE Transfer Device by fully depressing both squeeze tabs simultaneously 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.

PRECAUTION: The Proprietary Connector of the Delivery Catheter is no longer sterile once disconnected from the NON-ACTIVE Transfer Device. Use caution when connecting the Proprietary Connector to the ACTIVE Transfer Device.

J. ACTIVE Transfer Device Preparation RO/D

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.

WARNING: Do not remove the radiation source train from the **Beta-Cath™** System as unintended radiation exposure may occur. Do not attempt to clean or sterilize the radiation sources.

1) Confirm that the ACTIVE Transfer Device has:
- The Radioactive warning symbols on the device.
- The Gate Control Switch is CLOSED.
- The distal gold-colored marker of the Source Train is away from the Gate.
- The Fluid Control Lever is set to RETURN.
- The power is turned ON.

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

2) Connect the Fluid Collection Bag to the Fluid Collection Bag Luer Port on the back of the ACTIVE Transfer Device and cup the Fluid Collection Bag around the bottom of the device.

3) Using aseptic technique, place gloved hands inside cuffs of the Sterile Bag. Carefully place the non-sterile ACTIVE Transfer Device with the attached Fluid Collection Bag into a Sterile Bag. Orient the ACTIVE Transfer Device Syringe Luer toward the Syringe Port Hole on the Sterile Bag. Refer to Figure 6. Unfold cuffs of 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.

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 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. (Figure 5)

PRECAUTION: When attaching the syringe (or extension tubing), 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.

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.

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

7) Remove Proprietary Connector Cover from the proximal end of the Proprietary Connector.

8) 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.

10) Examine the catheter for kinks, bends, obstructions or other damage.

K. ACTIVE Transfer Device Priming RO/D

1) Ensure that the Gate is in the position marked "CLOSED."

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

3) Flush Transfer Device and Delivery Catheter System with 6 ml's of water. Confirm the device is primed properly by observing the absence of air bubbles and the entry of water into the Fluid Collection Bag.

L. Placement of the β-Cath™ Delivery Catheter CARD

1) Perform the intervention on the target lesion, until successful angiographic results are obtained.

2) Remove the interventional device, leaving the guidewire and guiding catheter in place.

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

4) Flush the guidewire lumen of the β-**Cath™** Delivery Catheter by connecting syringe into Guidewire Extension Luer Port and flush with 2 ml saline.

Note: The use of an Arrow® Super Arrow Flex® Percutaneous Sheath Introducer (Arrow International, Inc.) inserted over the β-Cath™ Delivery Catheter and into the hemostatic valve will allow catheter support and finger tightening of the hemostatic valve during the procedure.

5) While supporting the Transfer Device, carefully insert and advance the Delivery Catheter over the 0.014" (0.36 mm) guidewire and through the guiding catheter to the injury site. A depth marker band has been provided approximately 90 cm from the distal tip of the β-*Cath*™ Delivery Catheter to facilitate positioning of the system in the vasculature.

WARNING: Never advance or withdraw the Delivery Catheter against resistance.

6) Using fluoroscopy, place the Treatment Zone of the Delivery Catheter at the injury site. Allow a 5 mm margin on each side of the injury site to ensure coverage of the entire injury site.

WARNING: Do not 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.

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

7) Review films with contrast medium of the deflated balloon positions and the start and end positions of debulking devices to define the entire injury length.

M. Delivery of the ACTIVE Radiation Source Train RO/D

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

Note: If using Fluid Management System, turn stopcock to secondary syringe if additional fluid 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 open.

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.

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 Treatment Zone 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 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 Treatment Zone.

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 water and push to apply forward pressure to the syringe barrel 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 and it is determined that the ACTIVE Source Train was not delivered to the treatment site, the **Beta-Cath™** Delivery Catheter can be removed and the procedure restarted with a new **Beta-Cath™** 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™** System:

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

WARNING: Avoid direct contact with unshielded radiation sources in the **Beta-Cath™** 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 injury site may underexpose the targeted treatment area and expose tissue not targeted for treatment to unintentional radiation.

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.

10) Start Timer once Cardiologist confirms that the entire ACTIVE Source Train is across the entire injury site.

11) Consult the Medical Physicist to confirm the treatment time for prescribed dose per the Source Train Calibration Certificate.

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 water 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.

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

14) Use fluoroscopy, approximately every 15-30 seconds and cine with contrast once, during the radiation treatment to confirm the proper positioning of the ACTIVE Source Train across the interventional injury site.

15) Perform a Radiation Survey of the patient's chest and groin area and note results.

N. ACTIVE Source Train Return RO/D

1) Check for adequate (10 ml) 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, 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.

5) 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".

6) Visually confirm that the entire ACTIVE Source Train is located in the Source Chamber and all Sources are away from the Gate.

a) In the event that the entire ACTIVE Source Train has not returned to the ACTIVE Transfer Device after the treatment, immediately:

- Confirm the hemostatic valve is open.
- Confirm the Fluid Control Lever is in the RETURN position.
- Pull to withdraw approximately 1 ml water and push to apply forward pressure to the syringe barrel to return the ACTIVE Source Train to the 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™** System:

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

WARNING: Avoid direct contact with unshielded radiation sources in the **Beta-Cath™** 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 CLOSED.

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

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

O. β-Cath™ Delivery Catheter Removal CARD

1) Remove the entire system under fluoroscopy, as a single unit, while maintaining guidewire placement.

P. Disassembly of the Beta-Cath™ System MP/RSO/D

1) When the complete system has been removed from the patient, visually inspect the ACTIVE Source Train in the Source Chamber of the ACTIVE Transfer Device and confirm that it contains all components of the Radiation Source Train.

2) Unlock the ACTIVE Transfer Device from the Delivery Catheter.

3) Disconnect the Delivery Catheter Proprietary Connector 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.

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

4) Disconnect the Syringe and the attached Extension Connector from the ACTIVE Transfer Device.

5) Return the ACTIVE Transfer Device with attached Fluid Collection Bag and Delivery Catheter to RO/MP/RSO/D for Radiation Check and Drying.

Q. 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) Inventory the Source Train in the ACTIVE Transfer Device after disconnecting it from the Delivery Catheter.

2) Survey the ACTIVE Transfer Device with the Fluid Collection Bag still connected and note results. If Survey readings are significantly different from the initial reading, cease all activity and refer to Section S, "Emergency Source Recovery Procedure."

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. Immediately inform Institutional Radiation Safety personnel, implement contamination control procedures and call your Novoste Representative.

5) Survey the procedure room and note results. If survey readings are significantly different than initial background readings, cease all activity and refer to Section S, "Emergency Source Recovery Procedure."

6) After the post-procedure Survey, the ACTIVE and NON-ACTIVE Transfer Device must be dried (see "Drying and Storing of the Transfer Devices" below).

R. Drying and Storing of the Transfer Devices RO/MP/RSO/D

The following is the recommended procedure intended to instruct how to properly dry and store the ACTIVE and NON-ACTIVE Transfer Devices 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
- NON-ACTIVE Transfer Device containing the NON-ACTIVE Source Train
- Medical Physicist's Kit
- Response Kit
- Clean towels
- Survey meter
- Non-sterile gloves

Pre-Procedure:

1) The Authorized Personnel responsible for cleaning the Transfer Device should put on gloves and then obtain the Transfer Devices.

2) Survey both Transfer Devices and note results.

3) Visually inspect to confirm that the Source Trains are present in both Transfer Devices and that the Gate Control Switches are CLOSED . Report any unusual appearance or discoloration to your Novoste Representative.

4) To remove any visible debris from the surface, wipe the outside of both Transfer Devices with a cloth dampened with water.

Drying Procedure:

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

1) Insert the Flushing Adapter into the Transfer Device.

2) Secure by depressing the Proprietary Connector Lock Latch.

3) Connect a Fluid Collection Bag.

4) Connect a new 20 ml syringe filled with air to the Syringe Luer.

5) Ensure that the fluid control lever is in the RETURN position.

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.

9) Insert Quartz Cap into the Proprietary Connector receptacle of the Transfer Device.

10) Place the Transfer Device in the appropriate storage containers and store in accordance with institutional policy.

S. Emergency Source Recovery Procedure RO/MP/RSO/D

This procedure provides guidance for recovering a source 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 procedure should be augmented with any institutional policies and procedure on radiological emergencies involving source recovery. This document provides direction for the user to safely return a source to a controlled location.

REQUIRED MATERIALS:

- Gloves, non-sterile
- Response Kit
- Water
- 4 or more saline soaked gauze sponges
- Survey Meter/ thin walled GM tube
- 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(s).
- Follow institutional procedures regarding personnel allowed to enter or leave the room until the source is contained.
- 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.

UNDER NO CIRCUMSTANCES should an individual 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.

1) If a Source(s) 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(s) is considered to be lodged in the Delivery 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™** System:

   - Loosen the hemostatic valve with left hand.
   - Use four or more saline soaked gauze sponges to grasp and remove the **Beta-Cath™** System from patient.
   - Place **Beta-Cath™** 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 **β-Cath™** 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) 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 Source(s). If all the Sources and gold-colored markers 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 Sources back to the Transfer Device. If any of the Sources cannot be located in the Temporary Storage Container, proceed with the next step to locate the missing Source(s).

4) Missing Source(s) can best be found with the thin walled GM tube or acceptable alternative. 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 the increased radiation is located, 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 soft plastic) over the 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 sources. Use the Source Recovery Tools with extreme care in source recovery. Improper use can damage sources and potentially release radioactive material.

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 dropped into the water in the plastic container when the thumb tab on the other end of the probe is raised.

7b) Alternatively, the spring-loaded forceps may be used to pick up the source(s) and place it in the source container.

8) When all the 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.

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 internal Hospital Infection Control Procedures for cleaning biohazardous materials.

V. Customer Service Information

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

Novoste™ Corporation
3890 Steve Reynolds Blvd.
Norcross, Georgia 30093 USA

Tel: +1-770-717-0904
Fax: +1-770-717-1283

VI. Specifications

β-Cath™ Delivery Catheter:

Single use

Sterile (by ethylene oxide) and non-pyrogenic.

Total Length / Working Length:	155 cm / 135 cm
Proximal Shaft Outer Diameter to Distal Tip Outer Diameter:	5 F (0.066") to 2 F (0.026")
Available Radiation Treatment Length:	30 mm
Marker Bands Measure (inside to inside):	35 mm
Tip Taper Length:	10 mm
Maximum Guidewire:	0.014" (0.36 mm)
Minimum Guiding Catheter:	7 F (0.092") 0.078" ID

Transfer Device:

Size: (length x width x height)	22.2cm x 8.9cm x 7.0cm
Weight:	0.676kg
Operating Environmental Conditions:	
Temperature	18°C to 27°C
Relative Humidity	45 % - 85 %
Pressure	550 mmHg to 795 mmHg

Radioactive Sealed Sources in ACTIVE Transfer Device:

Source Model:	BEBIG Sr0.S03
Source Size: (length x diameter)	2.5 mm x 0.64 mm
Isotope:	^{90}Strontium
ISO 2919 Classification:	C63211
30 mm Radiation Source Train Components:	2 gold-colored markers 12 radioactive sources
90Sr Half-life:	28.8 years
Activity and Dose Rate:	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.

VII. Storage and Transport

Storage and Transport Environmental Conditions:

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.

77

Attachment A: Symbols and Graphics Used with the Beta-Cath™ 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

Non-Sterile Product

Beta

Lot Number

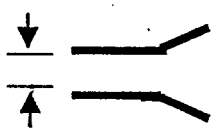
Catalog Number or Reorder Number

Serial Number

Part Number

Radiation Treatment Length

Minimum Required Guiding Catheter Inner Diameter



Radioactive Source Train

Non-Active Source Train

Locked

Unlocked 

2 Gate Switch Lock Position Indicator 

4 Fluid Lever ON 

6 Power ON/OFF Button 

8 Low Battery Indicator 

10 SEND 

12 RETURN 

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

16 Adequate Pressure to Send/Return Sources (Amber light illuminated) 

18 Excessive Pressure (Red light illuminated) 

Source Train OUT of the CHAMBER 
20

Source Train IN the CHAMBER 

22 Gate OPEN 

Gate CLOSED 
24

2

4

6

Attachment B: Additional Dosimetry Information

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™** System:

Clinician Hand Dose during Pre- and Post-Treatment Activities

(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* = 9 mrem (0.09 mSv)[1]
Annual Hand and Skin Dose Limit for Occupational Workers = 50,000 mrem (500 mSv)

The estimated dose from the **Beta-Cath™** System is 0.02% 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™** System = 0.2 mrem (0.002 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 **Beta-Cath™** System is 0.004% of the annual dose limit.

Cath Lab Staff Whole Body Dose per Treatment

30 mm **Beta-Cath™** System = 0.03 mrem (0.0003 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 **Beta-Cath™** System is 0.0006% of the annual dose limit.

Patient Whole Body Dose Per Treatment

Fluoroscopy during PTCA = 340 mrem (3.4 mSv)[3]
30 mm **Beta-Cath™** 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.
The estimated patient whole body dose from the **Beta-Cath™** System is approximately 1-2% 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

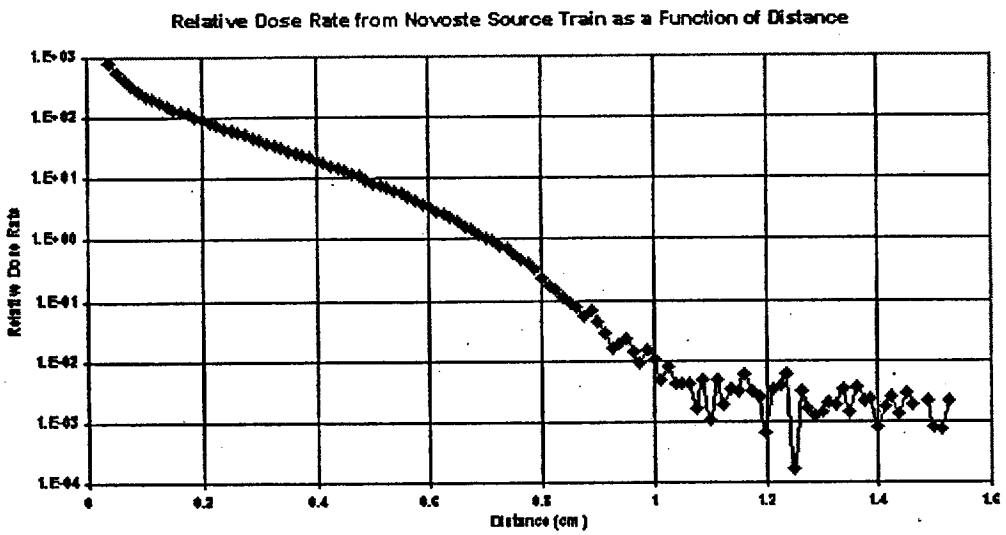
Novoste calibrates each ACTIVE Source Train, with techniques and standards traceable to a National Institute of Standards and Technology (NIST) standard, at 2 mm from the centerline of the ACTIVE Source Train. Each ACTIVE Transfer Device is shipped with its own Calibration Certificate that provides the 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 7 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.

Figure 7. Relative Dose Rate from ACTIVE Source Train as a Function of Distance



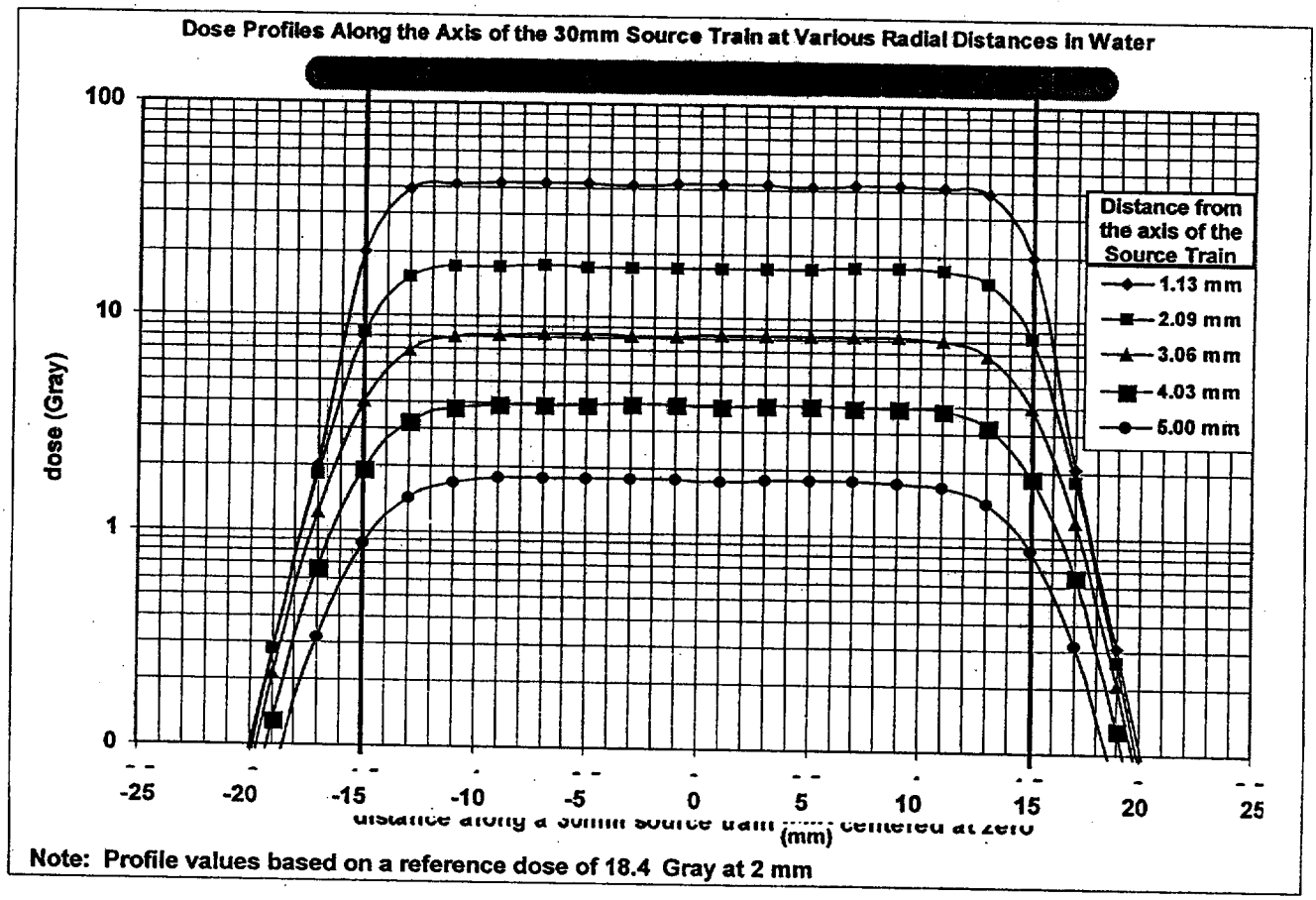
Note: This graph represents a model of dose as a function of distance from the source in water. The graph is not intended for dose planning. Refer to the calibration certificate for the recommended dose prescription and treatment time calculation.

84

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 (Gy)	Distance from Source Centerline (mm)	% Relative Dose (Gy)
0.50	631.62	5.25	7.77
0.75	379.31	5.50	6.11
1.00	263.73	5.75	4.72
1.25	197.14	6.00	3.62
1.50	152.87	6.25	2.78
1.75	122.35	6.50	2.10
2.00	100.00	6.75	1.56
2.25	82.28	7.00	1.14
2.50	67.54	7.25	0.83
2.75	55.36	7.50	0.59
3.00	45.89	7.75	0.42
3.25	38.46	8.00	0.28
3.50	31.86	8.25	0.18
3.75	26.06	8.50	0.12
4.00	21.39	8.75	0.07
4.25	17.65	9.00	0.05
4.50	14.52	9.25	0.03
4.75	11.74	9.50	0.02
5.00	9.50	10.00	0.01

The following graph provides doses along the centerline of a 30mm source train at various radial distances in water based on a reference dose of 18.4 Gray at 2 mm from the centerline of the source train.



Note: Profile values based on a reference dose of 18.4 Gray at 2 mm

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