RX Herculink Elite® Renal and Biliary Stent System
Instructions for Use

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

1.0 DEVICE DESCRIPTION

The **RX Herculink Elite Renal Stent System** includes:

- A balloon expandable L605 cobalt chromium alloy stent pre-mounted on the balloon of a rapid exchange (RX) stent delivery system
- Two radiopaque markers located underneath the balloon which identify the stent position and fluoroscopically mark the working length of the balloon
- Proximal shaft markers to aid with delivery catheter position, relative to a renal guiding catheter tip
- A third marker located approximately 30 cm from the center of the balloon that aids in locating the guide wire exit lumen and facilitating catheter removal and exchange

The delivery system can be utilized to optimize the stent wall apposition post stent deployment.

Table 1. *In Vitro Device Specifications**

Expanded Stent Diameter (mm)	Stent Lengths (mm)	*In Vitro** Stent Deployment Pressure (atm)	Rated Burst Pressure RBP (atm)	Recommended Minimum Guiding Catheter ID (F)/(inches)/(mm)	Recommended Minimum Sheath Introducer** (F)/(inches)/(mm)
4.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
4.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
5.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
5.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
6.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
6.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
7.0	15, 18	11	14	6/0.067/1.70	5/0.071/1.80

* All data provided is based on *in vitro* testing. Assure full deployment of the stent (see *Clinician Use Information section 8.8 Stent Deployment Procedure*). Deployment pressures should be based on lesion characteristics.
** See individual manufacturer specifications for (F) equivalent.

2.0 HOW SUPPLIED

Sterile. This device is sterilized with electron beam radiation. Non-pyrogenic. Do not use if the package is open or damaged.

Storage. Store in a dry, dark, cool place.

Contents. One (1) **RX Herculink Elite Renal Stent System**, one (1) Protective / Regrooming sheath, one (1) flush tool

3.0 INDICATIONS

The RX Herculink Elite Renal Stent System is indicated for use in patients with atherosclerotic disease of the renal arteries following sub-optimal percutaneous transluminal renal angioplasty (PTRA) of a *de novo* or restenotic atherosclerotic lesion (≤ 15 mm in length) located within 10 mm of the renal ostium and with a reference vessel diameter of 4.0 - 7.0 mm. Suboptimal PTRA is defined as ≥ 50% residual stenosis, ≥ 20 mmHg peak systolic or ≥ 10 mmHg mean translesional pressure gradient, flow-limiting dissection, or TIMI [Thrombolysis In Myocardial Infarction] flow < 3.

4.0 CONTRAINDICATIONS

The RX Herculink Elite Renal Stent System is contraindicated for use in:

- Patients with a contraindication for antiplatelet/anticoagulant therapy.
- Patients who have a lesion that cannot be crossed with a wire or a balloon angioplasty catheter.
- Patients with bleeding disorders.
- Patients with a known hypersensitivity to cobalt or chrome.
- Target lesions that are resistant to complete balloon inflation.
- Stenting of an arterial vessel where leakage from the artery could be exacerbated by placement of a stent.
- Patients with a target lesion with a large amount of adjacent acute or subacute thrombus

5.0 WARNINGS

The long term safety and effectiveness of this device for use in the renal arterial system have not been established.

Should **unusual resistance** be felt **at any time** during lesion access or Delivery System removal, the introducer sheath / guiding catheter and stent system should be removed **as a single unit**. Applying excessive force to the Stent Delivery System can potentially result in loss or damage to the Stent and Delivery System components. (See *Stent / System Removal – Precautions.*)

Since the use of this device carries the associated risk of subacute thrombosis, vascular complications and / or bleeding events, judicious selection of patients is necessary.

Stenting across a major bifurcation may hinder or prevent future diagnostic or therapeutic procedures.

Once fully deployed, the stent cannot be repositioned.

Persons allergic to L605 cobalt chromium alloy may suffer an allergic reaction to this implant.

Only physicians familiar with the complications, side effects and hazards commonly associated with renal stent placement should use this device.

The **RX Herculink Elite Renal Stent System** is intended to perform as a system. The stent should not be removed for use in conjunction with other dilatation catheters, nor should the **RX Herculink Elite Renal Stent System** be used in conjunction with other stents.

The safety and effectiveness of multiple overlapping stents have not been established. However, when multiple stents are required, stent materials should be of similar composition.

6.0 PRECAUTIONS

6.1 Stent Delivery System Handling – Precautions

- **For single use only.** Do not resterilize or reuse. Note product "Use by" date.
- **Do not remove stent from its delivery balloon, as removal may damage the stent and / or lead to stent embolization.**
- Carefully inspect the RX Herculink Elite Renal Stent System prior to use to verify that the stent has not been damaged in shipment and that the device dimensions are suitable for the specific procedure. Take care to avoid unnecessary handling.
- Refer to the instructions for use supplied with any interventional devices to be used in conjunction with the RX Herculink Elite Renal Stent System, for their intended uses, contraindications, and potential complications.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during stent system removal from the packaging, placement over a guide wire and advancement through a guiding catheter or introducer sheath.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

6.2 Stent Placement – Precautions

- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the *Clinician Use Information* section.
- The inflated balloon diameter of the system used to deploy the stent should approximate the diameter of the vessel. Oversizing of the stent can result in a ruptured vessel. To ensure full expansion of the stent, the balloon should be inflated to a minimum of nominal pressure.

- Implanting a stent may lead to dissection of the vessel distal and / or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (surgical intervention, further dilatation, placement of additional stents, or other).
- Do not expand the stent if it is not properly positioned in the vessel. (See *Stent / System Removal - Precautions.*)
- Stenting across a major bifurcation may hinder or prevent future side branch access.
- Balloon pressures should be monitored during inflation. **Do not exceed Rated Burst Pressure (RBP) as indicated on product label.** Use of pressures higher than specified on product label may result in a ruptured balloon with possible vessel damage or perforation.
- Stent retrieval methods (use of additional wires, snares and / or forceps) may result in additional trauma to the vasculature and / or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.
- The RX Herculink Elite Renal Stent System is intended for deployment and post-deployment dilatation of the stent only and should not be used to dilate other lesions.
- **Do not attempt to pull an unexpanded stent back through the introducer sheath / guiding catheter; dislodgment of the stent from the balloon may occur.**

6.3 Stent / System Removal – Precautions

Should **unusual resistance** be felt **at any time** during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed **as a single unit**.

When removing the Delivery System as a single unit:

- DO NOT retract the Delivery System into the introducer sheath / guiding catheter.
- Position the proximal balloon marker just distal to the tip of the introducer sheath / guiding catheter.
- Advance the guide wire in the anatomy as far distally as safely possible.
- Secure the Delivery System to the introducer sheath / guiding catheter; then remove the introducer sheath / guiding catheter, guide wire and Delivery System as a **single unit**.

Failure to follow these steps and / or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and / or Delivery System components.

If it is necessary to retain guide wire position for subsequent vessel access, leave the guide wire in place and remove all other system components.

6.4 Post Implant – Precautions

Great care must be exercised when **crossing a newly deployed stent** with a guide wire or balloon catheter to avoid disrupting the stent geometry.

Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated that the Herculink Elite stent, in single and in overlapped configurations up to 33 mm in length, is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 or 3 Tesla
- Spatial gradient field of 2500 Gauss/cm or less
- Maximum whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) for any duration of MRI scan that would otherwise be safe for the patient without implant.

MRI at 1.5 or 3 Tesla may be performed immediately following the implantation of the Herculink Elite stent.

The Herculink Elite stent should not migrate in this MRI environment. Magnetic force on the Herculink Elite state was tested according to ASTM F2052-06e. Non-clinical testing at field strengths greater than 3 Tesla has not been performed to evaluate stent migration or heating.

Stent heating was derived by using the measured non-clinical, *in vitro* temperature rise according to ASTM F2182-09 in a GE Signa HDx 3 Tesla scanner and in a GE 1.5 Tesla coil in combination with the local specific absorption rates (SARs) in a digitized human heart model. The temperature rise was derived by a validated calculation. At overlapped lengths up to 33 mm, the Herculink Elite stent produced a non-clinical maximum local temperature rise of less than 3°C at a maximum whole body averaged SAR of 2.0 W/kg (normal operating mode) for an MRI sequence of 15 minutes. These calculations do not take into consideration the cooling effects of blood flow.

The effects of MRI on overlapped stents greater than 33 mm in length or stents with fractured struts are unknown.

Image artifact may be present when scanning the Herculink Elite stent as demonstrated in non-clinical testing performed according to ASTM F2119-07 in a GE Signa HDx 3 Tesla scanner. The image artifact (both inside and outside the device lumen) extends approximately 7 mm from the device using the spin echo sequence (TR = 500 ms; TE = 20 ms; flip angle = 90°) and 13 mm from the device using the gradient echo sequence (TR = 100 ms; TE = 15 ms; flip angle = 30°). MR image quality may be compromised if the area of interest is in the exact same area, or relatively close to, the position of the Herculink Elite stent. Therefore, it may be necessary to optimize the MR imaging parameters in the presence of Herculink Elite stents.

7.0 POTENTIAL ADVERSE EVENTS

Potential complications associated with percutaneous renal artery treatment including the use of a renal stent may include, but are not limited to, the following:

- Abscess
- Allergic reaction to Cobalt Chromium or contrast agents
- Arrhythmias (ventricular fibrillation, ventricular tachycardia, other)
- Arteriovenous fistula
- Bowel infarct
- Death
- Dialysis
- Dissection
- Drug reaction to antiplatelet agents
- Drug reaction, allergic reaction to contrast media
- Emboli (air, tissue, or thrombotic emboli) resulting in tissue ischemia/infarction
- Emergency surgery to correct vascular complications
- Emergent renal artery bypass surgery
- Extremity ischemia/amputation
- Fever
- Gastrointestinal symptoms from anticoagulation/antiplatelet medication
- Hematoma at vascular access site
- Hemorrhage requiring transfusion
- Hypersensitivity reactions
- Hypotension/hypertension
- Infection and pain at vascular access site
- Intimal tear
- Kidney infarct
- Myocardial infarction
- Myocardial ischemia
- Nephrectomy
- Peripheral neuropathy
- Pseudoaneurysm at vascular access site
- Pseudoaneurysm formation
- Renal artery thrombosis, aneurysm, rupture, perforation, occlusion, spasm, or restenosis
- Renal insufficiency or failure
- Stent migration or embolization
- Stent misplacement
- Stroke/cerebral vascular accident
- Tissue necrosis or ulceration

8.0 CLINICIAN USE INFORMATION

8.1 Clinical Studies

Results from a multi-center clinical study (IDE G060067, also known as the HERCULES study) demonstrate the safety and effectiveness of the RX Herculink Elite Renal Stent System. Specifically, the 9-month binary restenosis rate was 10.5%, meeting the performance goal of 28.6%. In addition, use of the RX Herculink Elite Renal Stent System was associated with a low rate of major adverse events (MAEs), high technical and procedural success rates, improvement in hypertension, and maintenance of renal function. An overview of the HERCULES study is presented in **Table 2**.

Table 2. Overview of the HERCULES study

Device	RX Herculink Elite Renal Stent System
Study Design	Non-randomized, prospective, single-arm, multi-center clinical study
Patients Enrolled	202 (76 male and 126 female)
Number of Sites	37 investigational sites
Primary Endpoint	Binary restenosis rate at 9 months, defined as ≥ 60% diameter stenosis, measured by duplex ultrasound (or quantitative angiography, if necessary) by an independent core laboratory. Analysis was done on a per-lesion basis.
Secondary Endpoints	MAEs: A composite safety endpoint of the following indices: death for any reason at 30 days; ipsilateral nephrectomy at 30 days; embolic events resulting in kidney damage at 30 days; and clinically indicated target lesion revascularization (TLR) up to 9 months (270 days). Change in blood pressure: Systolic and diastolic blood pressures were measured at baseline, post-procedure, 1, 6 and 9 months and the group average at each time point reported. The change at 9 months from baseline, for systolic and diastolic pressure, was calculated for each enrolled patient. Confidence intervals (95%) for the average changes were reported. In addition, systolic blood pressure was reported using categories of < 140 mmHg, ≥ 140 mmHg and < 160 mmHg, ≥ 160 mmHg and < 180 mmHg, and ≥ 180 mmHg. Change in Antihypertensive Medications: Number and type of antihypertensive medications at baseline, 1, 6, and 9 months were collected. The group average number of antihypertensive medications at each time point was reported. In addition, data was reported as a percentage of patients on 1, 2, 3, or 4 or more medications at baseline, 1, 6, and 9 months. Change in Renal Function: Defined as change in serum creatinine (sCr), it was measured at baseline, post-procedure, 1, 6 and 9 months, with the group average reported at each time point. The change at 9 months from baseline was calculated for each enrolled patient.

	Acute Device Success: The achievement of successful delivery and deployment of the assigned device(s) and successful removal of the delivery system as intended to the designated location. It was reported as a percentage of devices that were attempted to be implanted. Acute Clinical Success: Procedure success without major adverse events (MAE) or access site events requiring surgical or percutaneous intervention prior to hospital discharge. It is presented on a per subject basis. Clinically Indicated Target Lesion Revascularization: Defined as diameter stenosis ≥ 60%, as determined by the angiographic or ultrasound core laboratory, and any revascularization (including but not limited to atherectomy, embolectomy, endarterectomy, bypass surgery, repeat angioplasty, or stent implantation) to the target lesion. Freedom from clinically indicated TLR was evaluated at 9 months and is presented as time to first event on a per-lesion basis. Acute Procedural Success: The attainment of a final result of < 30% residual stenosis as determined by the angiographic core laboratory, reported as a percentage of treated lesions.
Study Hypothesis	Renal arteries treated with the RX Herculink Elite Stent will have a binary restenosis rate at 9 months that meets a performance goal of 28.6%.
Patient Follow-up	1-month clinic visit: Blood pressure measurement, anti-hypertensive medication review, laboratory (sCr, BNP assay), duplex ultrasound, laboratory, adverse events. 6-month clinic visit: Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr). 9-month clinic visit with ultrasound: Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound, angiogram (only if duplex ultrasound done at nine-month follow up visit is determined to be "not evaluable", or at the discretion of the Investigator). 12-month clinic visit: Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr). 24-month clinic visit: Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound. 36-month clinic visit: Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound.

Study Design

The primary objective of the clinical study was to assess the binary restenosis rate at 9 months after stenting, with binary restenosis determined by duplex ultrasound or angiogram. The lesion was considered restenotic if the lesion was ≥ 60% diameter prior to the 9-month primary endpoint evaluation. Specifically, the primary hypothesis was that the binary restenosis rate at 9 months on a lesion basis meets the performance goal of 28.6% (i.e., < 28.6%). Secondary analyses included MAEs (defined as death for any reason at 30 days, ipsilateral nephrectomy at 30 days, clinically-indicated target lesion revascularization up to 9 months, and embolic events resulting in kidney damage at 30 days), acute device success, acute procedural success, acute clinical success, changes in blood pressures at 9 months, change in anti-hypertensive medication in-take at 9 months, and renal function outcomes (measured by serum creatinine).

The HERCULES study was a prospective, non-randomized, multi-center, single-arm clinical study to demonstrate efficacy and safety of the RX Herculink Elite Renal Stent System (Herculink Elite) in the treatment of suboptimal post-procedural percutaneous transluminal renal angioplasty (PTRA) of atherosclerotic de novo or restenotic renal artery stenoses in patients with uncontrolled hypertension. Subjects were eligible to enroll in the study if they had a suboptimal angioplasty (defined as ≥ 50% residual stenosis, ≥ 20 mmHg systolic or ≥ 10 mmHg mean translesional pressure gradient, flow-limiting dissection or TIMI [Thrombolysis In Myocardial Infarction] flow < 3) for *de novo* or restenotic renal artery lesions (≤ 15 mm length) due to atherosclerosis originating within 10 mm of the renal ostium, a reference vessel diameter ≥ 4 mm and ≤ 7 mm, and uncontrolled hypertension (defined as systolic blood pressure [SBP] ≥ 140 mmHg or diastolic blood pressure [DBP] ≥ 90 mmHg on at least two anti-hypertensive medications). Treatment of two lesions, one per side, was allowed per patient. Patients were excluded from the study if they met any of the following conditions: only one functioning kidney, kidney transplant, had a Q-wave myocardial infarction (MI) within 30-days of the index procedure, or serum creatinine ≥ 2.5 mg/dl. Angiography was performed post stent implantation. Follow-up included ultrasound imaging at 1 month, and ultrasound (angiogram, if ultrasound was not interpretable) at 9 months. Clinical assessments (e.g., blood chemistry, blood pressure, assessment of anti-hypertensive medications) were scheduled for 1, 6, 9, 12, 24, and 36 months.

Independent core laboratories analyzed angiographic and ultrasonic imaging. The study was overseen by an independent data safety monitoring board (DSMB) comprised of physicians and a biostatistician. The committee was set up and convened at the pre-specified interim time points of the trial to evaluate the safety of the trial. A Clinical Endpoint Adjudication Committee (CEAC) adjudicated the suspected cases of peri-procedural death, ipsilateral nephrectomy and embolic events that result in kidney damage.

The principal effectiveness of the Herculink Elite was evaluated to determine if the binary restenosis rate at 9 months was less than the performance goal (PG) of 28.6% that was derived from the contemporary literature of PTRA and stenting for the atherosclerotic lesions in the aortorenal ostium. The sample size and power calculation were based on the primary endpoint of binary restenosis rate at 9 months. The PG for the binary restenosis rate at 9 months was determined to be 28.6%, based on pre-market studies of other renal artery stents used in a similar manner and which are now PMA-approved.

The primary and secondary endpoints measuring the safety and effectiveness of the device and procedure are described below.

Null Hypothesis: the 9-month binary restenosis rate, γ, is greater than or equal to 28.6%. (Interpretation: the binary restenosis rate does not meet a performance goal of 28.6%.)

Ho: $\gamma \geq 28.6\%$

Alternative Hypothesis: the 9-month binary restenosis rate, γ, is less than 28.6%. (Interpretation: the binary restenosis rate meets a performance goal of 28.6%.)

Ha: $\gamma < 28.6\%$.

The null hypothesis was tested using one-sided exact binomial test at significance level of 0.05.

For binary and categorical variables, event counts, rates and their confidence intervals were analyzed. Continuous variables were analyzed using the mean, standard deviation, and 95% confidence intervals (CI). Kaplan-Meier methodology was used to estimate the distributions of time-to-event variables.

Clinical Inclusion and Exclusion Criteria

The inclusion criteria for the HERCULES study were as follows:

- Subject is ≥ 18 years of age.
- Subject and subject's physician agree to have the subject return for all required contact following study enrollment.
- Subject has been informed of the nature of the study, and has provided written informed consent, approved by the appropriate Institutional Review Board (IRB) of the respective clinical site.
- Subject is a candidate for renal artery stenting.
- Subject has uncontrolled systolic hypertension (systolic BP ≥ 140 mmHg), or uncontrolled diastolic hypertension (diastolic BP ≥ 90 mmHg), or a combination of both in the presence of at least two (2) or more antihypertensive medications.
- Baseline sCr of ≤ 2.5 mg/dl.
- Subject has unilateral or bilateral *de novo* or restenotic after PTA (in-stent restenosis excluded) atherosclerotic lesion(s). If bilateral lesions are to be treated, the most severe lesion must be successfully treated without complications before progressing to treat the second lesion. Treatment of bilateral lesions is to occur in the same procedural event.
- Renal stenosis must be visually estimated to be ≥ 60% by angiography.
- Subject has a suboptimal PTA result, defined as one of the following:
  - ≥ 50% residual stenosis,
  - 10 mm Hg mean gradient or 20 mm Hg peak systolic gradient across the target lesion, or
  - A flow-limiting dissection (NHLBI grade D) or TIMI flow < 3.
- Renal stenosis must be visually estimated to be within 10 mm of the aortic renal border by angiography.
- Target vessel reference diameter must be visually estimated to be ≥ 4 mm and ≤ 7 mm by angiography.

- Target lesion length must be visually estimated to be ≤ 15 mm (including dissection) by angiography.
- Expected ability to deliver the stent to the lesion (absence of excessive tortuosity or calcification).
- Expected ability to fully expand the stent.

The exclusion criteria for the HERCULES study were as follows:

- Known hypersensitivity or contraindication to cobalt chromium or standard intraprocedure anticoagulant(s); sensitivity to contrast which cannot be adequately pre-treated with medication.
- Known allergy or contraindication to clopidogrel (Plavix®) or aspirin.
- Bleeding disorder or hypercoagulable disorder, or will refuse blood transfusions.
- Gastrointestinal (GI) bleeding within 30 days before the index procedure that would interfere with antiplatelet therapy.
- Renal insufficiency, defined as serum Creatinine > 2.5 mg/dl.
- Any immunosuppressive disorder, access site infection, or acute systemic infection due to any cause.
- Medical illnesses (e.g., cancer, end-stage congestive heart failure) that may cause the subject to be non-compliant with protocol requirements, confound the data interpretation, or is associated with a life expectancy of less than three years.
- Medical illnesses that would make them unlikely to respond to treatment (e.g., sickle cell nephropathy/sickle cell disease, scleroderma, arteriolar nephrosclerosis, hemolytic-uremic syndrome and vasculitis).
- Q-wave MI within 30 days before index procedure.
- Stroke or transient ischemic attack (TIA) within 30 days before index procedure.
- History of congestive heart failure and has a previously documented left ventricular ejection fraction (LVEF) < 25%.
- Subject is normotensive or has adequate control of hypertension (SBP <140 mm Hg and DBP <90 mm Hg) utilizing diet control and/or medication regimen involving only one antihypertensive medication.
- Acute thrombophlebitis or deep vein thrombosis.
- Actively participation in another drug or device trial and did not complete the required protocol follow-up period. Subject may be enrolled only once in this study and may not participate in any other clinical trial during the follow-up period.
- Unable to understand and cooperate with study procedures or provide informed consent.
- Unable to return for follow-up visits.
- Subject is pregnant.
- Subject has undergone vascular surgery, such as coronary artery bypass grafting, abdominal aortic aneurysm repair, or aorto-femoral bypass, and has not fully recovered from the effects of surgery (<3 months).
- Subject has planned staged treatment of bilateral renal artery stenosis.
- Subject has had prior surgical intervention to the target artery, or has undergone previous stent placement in the target lesion.
- Target lesion is located in a transplanted kidney.
- Kidney to be treated is < 8 cm as determined by duplex ultrasound report, computed tomography angiography (CTA) report, or magnetic resonance angiography (MRA) report within 180 days before procedure. If kidney size is

documented by more than one method, e.g. CTA and ultrasound, and one of the methods is duplex ultrasound, the kidney size as documented by duplex ultrasound shall be used to determine study eligibility.

- Subject has planned additional ancillary procedure(s) during renal stenting procedure.

Angiographic Exclusion Criteria:

- Subject has a lesion segment, including dissection, >15 mm in length.
- Requirement for more than 1 stent to treat full length of lesion and dissection.
- Target lesion has a total (100%) occlusion.
- Evidence of thrombus or mobile filling defect in the target lesion or vessel.
- Co-existing aneurysmal or occlusive disease of the abdominal aorta requiring surgical reconstruction during the follow-up period.
- Fibromuscular dysplasia.
- Subject artery has patent bifurcation within 10 mm of ostium that might be covered by placement of a stent.
- The target lesion is within the artery of a solitary functioning kidney or, the subject has a contralateral totally occluded renal artery.
- For planned treatment of bilateral lesions: the more critical lesion, i.e. lesion with the greater stenosis (which should be treated first), is either treated unsuccessfully or requires a bailout procedure. (NOTE: Less critical lesion is excluded at this point.) .

Follow-up Schedule

Clinical assessments occurred at baseline, operative/discharge and postoperative intervals at 1, 6, 9 months and 1, 2, and 3 years, as seen in **Table 3**.

Table 3. Availability of Clinical and Imaging Follow-up Data

Follow-up Period	Clinical Evaluations
1-month clinic visit	Blood pressure measurement, anti-hypertensive medication review, laboratory (sCr, BNP assay), duplex ultrasound, laboratory, adverse events.
6-month clinic visit	Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr).
9-month clinic visit with ultrasound	Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound, angiogram (only if duplex ultrasound done at nine-month follow up visit is determined to be "not evaluable", or at the discretion of the Investigator).
12-month clinic visit	Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr)
24-month clinic visit	Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound.
36-month clinic visit	Blood pressure measurement, anti-hypertensive medication review, adverse events, laboratory (sCr), duplex ultrasound.

Clinical Endpoints

With regards to safety, there were no hypothesis-driven primary or secondary safety endpoints.

With regards to effectiveness, the primary effectiveness endpoint was evaluated according to the hypothesis that renal arteries treated with the RX Herculink Elite Renal Stent will have a binary restenosis rate at 9 months on a lesion basis that meets a performance goal of 28.6%. The formulation of the hypothesis can be found in the study design section. The study was considered a success if the primary effectiveness hypothesis was met.

Accountability of PMA Cohort

Patient availability for study follow-up through 9 months is summarized in **Table 4**. The first subject was enrolled into the HERCULES study on August 31, 2007 and the last subject was enrolled on October 2, 2009. Over this period, 202 male and female subjects, who met the eligibility criteria and agreed to participate in the study and signed an informed consent, were enrolled at 37 study sites in the United States (US). Thirty-nine (39) subjects had bilateral lesions treated. Therefore, the intention-to-treat (ITT) population consists of 202 subjects and 241 lesions.

The last 9-month follow-up visit was completed on June 23, 2010. One subject did not have any post-procedure follow-up, a second subject was confirmed as lost-to-follow up at 182 days, and 4 subjects were withdrawn from the study. Through the 9 month follow-up 5 subjects expired. Three subjects had a study stent attempted without success, and a non-study stent implanted; they completed the study at the 30 day follow-up timepoint. Therefore, there were a total of 189 subjects eligible for the 9 month follow-up visit.

Table 4. Accountability of PMA Cohort

	1-month visit	6-month visit	9-month visit
Death	0	4	1
Withdrawn	0	0	4
Lost to follow-up	0	1	0
30-day follow-up complete for non-study stent	0	3	0
Eligible	202	194	189

Study Population Demographics and Baseline Parameters

Patient demographics (**Table 5**), medical history (**Table 6**), baseline blood pressure and medications (**Table 7**) and baseline lesion characteristics (**Table 8**) and baseline angiographic data (**Table 9**) were consistent with patient populations described in published literature of renal stent intervention. The mean age of the study populations was 72.1 ± 9.4, with 62.4% female gender. The key risk factors include diabetes mellitus 45.0%, hypercholesterolemia 86.1%, coronary artery disease 67.3% and current or former tobacco use 56.9%. The baseline mean creatinine was 1.2 ± 0.4 mg/dl and 61.5% of subjects had an estimated baseline glomerular filtration rate (eGFR) of < 60 ml/min per 1.73 m^2 (**Table 6**).

Table 5. Patient Demographics

Demographic	Value (N = 202 patients)
Sex	
Male	37.6% (76/202)
Female	62.4% (126/202)
Age (years, mean ± SD (range))	72.1 ± 9.4 (44 - 89)
Ethnicity	
Caucasian or White	83.7% (169/202)
Black or African American	7.9% (16/202)
Hispanic or Latino	7.4% (15/202)
Other	1.0% (2/202)
Native Hawaiian or other Pacific Islander	0.5% (1/202)
Asian	0.5% (1/202)

Table 6. Medical History

Past or Current Medical Condition	Percent Patients (number/total number)
Diabetes	
Total	45.0% (91/202)
Type I	3.5% (7/202)
Type II	41.6% (84/202)
Hypercholesterolemia	
Total	86.1% (174/202)
Requiring medication	82.2% (166/202)
Not Requiring medication	4.0% (8/202)
Coronary Artery Disease	67.3% (136/202)
Brain Natriuretic Peptide (BNP) Level (pg/ml)	181.2 ± 297.0 (192)
Renal Function	
Serum Creatinine (mg/dl)	1.2 ± 0.4 (202)
eGFR < 60 ml/min per 1.73 m^2	61.5% (123/200)
Former Smoker	44.1% (89/202)
Current Smoker	12.9% (26/202)

Table 7. Baseline Blood Pressure and Medications

Past or Current Medical Condition	Percent Patients (number/total number)
Blood Pressue	
Mean Systolic	162.3 ± 18.5 (202)
Mean Diastolic	77.7 ± 11.5 (202)
Anti-Hypertensive Medications	
1 Medication	0.5% (1/202)
2 Medications	29.2% (59/202)
3 Medications	30.7% (62/202)
≥ 4 Medications	39.6% (80/202)

Table 8. Baseline Lesion Characteristics

Characteristic	Percent Lesions (number/total number)
Lesion Location	
Right Renal Artery	52.3% (126/241)
Left Renal Artery	47.7% (115/241)
Type of Lesion	
Restenotic	0% (0/115)
de novo	100% (241/241)
Target Lesion Location	
Ostial	67.6% (163/241)
Within 10 mm of Ostium	32.4% (78/241)
Renal Arteries Treated	
Unilateral	67.6% (163/241)
Bilateral	32.4% (78/241)
Suboptimal PTA Outcome	
Residual Stenosis ≥ 50%	90.7% (214/236)
10 mmHg mean gradient or 20 mmHg peak systolic gradien	25.0% (59/236)
Flow-limiting dissection (NHLBI grade D) or TIMI flow < 3	4.7% (11/236)
Target Lesion Stenosis	81.3 ± 10.0 (241)

Table 9. Baseline Angiographic Data (core lab reported)

Measure	Mean ± SD (range, total lesions)
Lesion Length (mm)	8.5 ± 3.1 (1.8 - 22.1, n = 241)
Pre-procedure	
RVD (mm)	5.34 ± 1.1 (2.9 - 7.9, n = 241)
MLD (mm)	1.8 ± 0.7 (0.3 – 3.8, n = 241)
Percent Diameter Stenosis (%)	65.9 ± 11.4 (37.8 – 92.9, n = 241)

Safety and Effectiveness Results

Safety Results

The safety endpoint for the HERCULES study is the composite rate of freedom from major adverse events (MAEs), including all cause death, ipsilateral nephrectomy, and embolic events resulting in kidney damage, all through 30 days, and clinically indicated target lesion revascularization (TLR) up to 270 days. Through the first 30 days, there was 1 death and 2 embolic events resulting in kidney damage. The freedom from MAEs and clinically indicated TLRs at 9 months was 94.8%, as shown in **Table 10** and the Kaplan-Meier analysis (**Figure 1**).

Adverse effects that occurred in the PMA clinical study

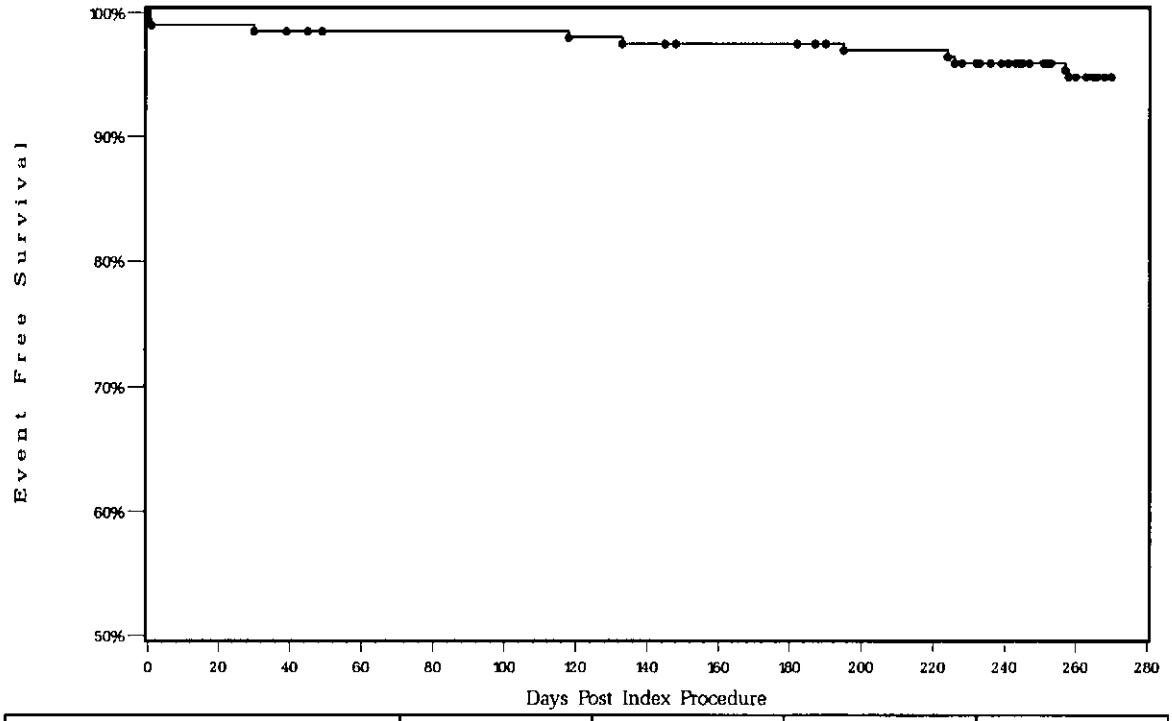
Table 10. Protocol Defined Major Adverse Events through 9 Months

MAEs Through 30-Days	**(N=202 Subjects) (N= 241 Lesions)**	**[95% CI][1]**
All-cause death	0.5%	[0.0%, 2.7%]
Device-related death	0.0%	[0.0%, 1.8%]
Embolic events resulting in kidney damage	1.0%	[0.1%, 3.5%]
Nephrectomy	0.0%	[0.0%, 1.8%]
Clinically indicated TLR	0.0%	[0.0%, 1.8%]
Stent thrombosis	0.0%	[0.0%, 1.8%]
Retroperitoneal bleed	0.5%	[0.0%, 2.7%]
Myocardial Infarction	0.0%	[0.0%, 1.8%]
Stroke	0.0%	[0.0%, 1.8%]
Events Through 9 Months (312 Days)	**(N=202 Subjects) (N= 241 Lesions**	**[95% CI][1]**
Renal Failure	1.0%	[0.1%, 3.5%]
Renal Insufficiency	2.0%	[0.5%, 5.0%]
Events Through 9 Months (312 Days)[2]	**(N=202 Subjects) (N= 241 Lesions**	**[95% CI]**
All TLR	7.4%	[3.9%, 10.9%]
Clinically Indicated TLR	5.9%	[2.6%, 9.2%]
Death	2.6%	[0.3%, 5.0%]

[1]By Clopper Pearson exact confidence interval

[2]Based on Kaplan Meier estimate

Figure 1: Freedom from Death, Ipsilateral Nephrectomy and Embolic Events Resulting in Kidney Damage through 30 Days and Clinically Indicated Target Lesion Revascularization through 270 Days (Intent-to-Treat Population)



Days Post Index Procedure	0	(0, 30]	(30, 180]	(180, 270]
Subjects at Risk	202	201	198	191
Subjects Censored	0	1	5	186
Number of Events	1	2	2	5
Event Free (%)	99.5%	98.5%	97.5%	94.8%
Standard Error (%)	0.5%	0.9%	1.1%	1.6%

Effectiveness Results

Two hundred forty-two (242) RX Herculink stents were placed to treat 241 renal artery lesions. By core lab assessment, the mean post-procedure percent diameter stenosis was 3.4% (**Table 11**). Therefore, the RX Herculink Elite Renal Stent System was effective in establishing patency at the conclusion of the procedure.

Table 11. Post-Procedure Angiographic Data (core lab reported)

Measure	Mean ± SD (range, total lesions)
Post-procedure	
MLD (mm)	5.1 ± 0.8 (3.4 - 7.3, n=240)
Percent Diameter Stenosis (%)	3.4 ± 12.5 (-43.1 - 29.8, n=240)

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Primary Endpoint

The 9-month binary restenosis rate met the performance goal (**Table 12**). The 9-month binary restenosis rate was 10.5% and the upper limit of the 95% one-sided confidence interval was 14.7%, which is below the pre-specified performance goal of 28.6% ($p < 0.0001$). These results demonstrate the effectiveness of the RX Herculink Elite Renal Stent System in treating atherosclerotic lesions of the renal arteries following suboptimal angioplasty.

Table 12. Primary Endpoint Analysis – Binary Restenosis Rate (ITT Population)

Measure	Mean ± SD (range, total lesions)
9-Month In-Stent Binary Restenosis (≥ 60%) Rate [One-Sided 95% Conf. Interval][1] One-Sided Exact Binomial Test *p*-value[2]	10.5% (22/209) [-, 14.7%] < 0.0001

[1] By Clopper-Pearson exact confidence interval
[2] One-sided p-value is computed using the exact binomial test with the objective performance criterion (OPC) of 28.6%

Secondary Endpoints

Secondary endpoint analyses included MAEs, device-related success measures (i.e., acute device success, acute procedural success, and acute clinical success), blood pressure-related outcomes (i.e., systolic and diastolic blood pressure, use of anti-hypertensive medications), and renal function (as measured by serum creatinine).

Device-related success measures ranged from 96.0% to 99.2%. Device success (successful delivery and deployment of a RX Herculink Elite stent), acute procedural success (< 30% residual stenosis post-procedure by core lab analysis), and acute clinical success (procedure success without MAE or access site event requiring surgical or percutaneous intervention prior to hospital discharge) outcomes are summarized in **Table 13**. These results support the safety and effectiveness of the RX Herculink Elite Renal Stent System in establishing renal artery patency.

Table 13. Device-related Acute Success Measures

Effectiveness	(N = 202 Subjects) (M = 241 Lesions)	[95% CI][1]
Study Device Success	96.0% (237/247)	[92.7%, 98.0%]
Procedural Success	99.2% (238/240)	[97.0%, 99.9%]
Clinical Success	98.0% (197/201)	[95.0%, 99.5%]

[1]By Clopper-Pearson exact confidence interval

Blood pressure-related outcomes demonstrated decreased systolic blood pressure from pre-procedure to 9-month follow-up. The baseline mean systolic and diastolic blood pressures were 162.3 ± 18.5 mmHg and 77.7 ± 11.5 mmHg, respectively. At 9 months mean systolic and diastolic blood pressures were 145.3 ± 21.3 mmHg and 75.4 ± 11.5 mmHg, respectively. When compared to baseline, the mean SBP was reduced at all time points (**Table 14** and **Figure 2**). The blood pressure data indicate that over 40% of subjects achieved the SBP <140 mmHg at 9 months after renal stenting. The proportion of patients with SBP < 160 mmHg was increased to 76.3% at 9 months from the 56.4% at

baseline. The proportion of patients with SBP ≥ 180 was decreased to 5.2% at 9 months from 19.3% at baseline (**Table 15** and **Figure 3**). These data demonstrate the clinical utility of the RX Herculink Elite Renal Stent System and suggest that revascularization with the RX Herculink Elite Renal Stent System does not adversely affect blood pressure outcomes.

Table 14. Blood Pressure Results

Blood Pressure	Mean ± SD (95% CI[1])	
	Systolic (mmHg)	Diastolic (mmHg)
Pre-procedure	162.3 ± 18.5 (202) [159.8, 164.9]	77.7 ± 11.5 (202) [76.1, 79.3]
Post-Procedure	141.3 ± 20.8 (197) [138.3, 144.2]	67.8 ± 11.4 (197) [66.2, 69.4]
1 Month	144.9 ± 20.6 (183) [141.9, 147.9]	75.5 ± 11.2 (183) [73.9, 77.2]
6 Months	146.7 ± 23.1 (158) [143.1, 150.4]	74.8 ± 11.2 (158) [73.1, 76.6]
9 Months	145.3 ± 21.3 (173) [142.1, 148.5]	75.4 ± 11.5 (173) [73.6, 77.1]

[1] By normal approximation

Figure 2. Summary of Systolic Blood Pressure Measurements Per Subject Analysis (Intent to Treat Population)

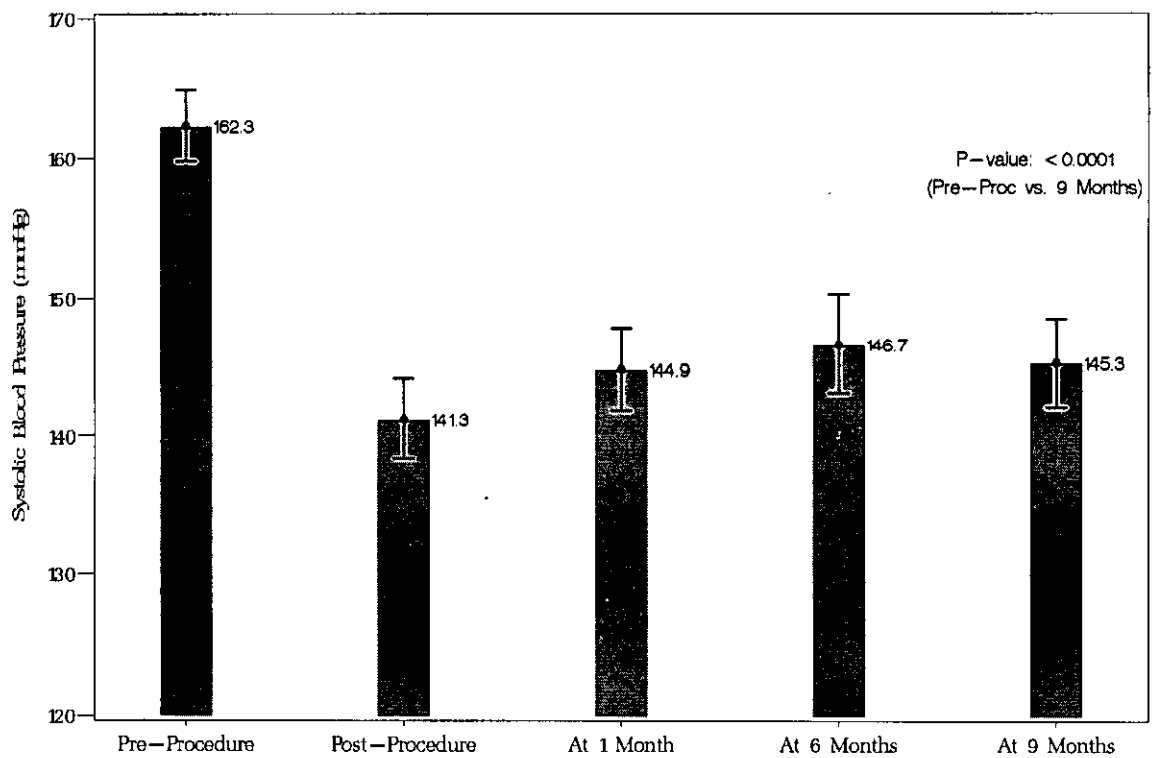
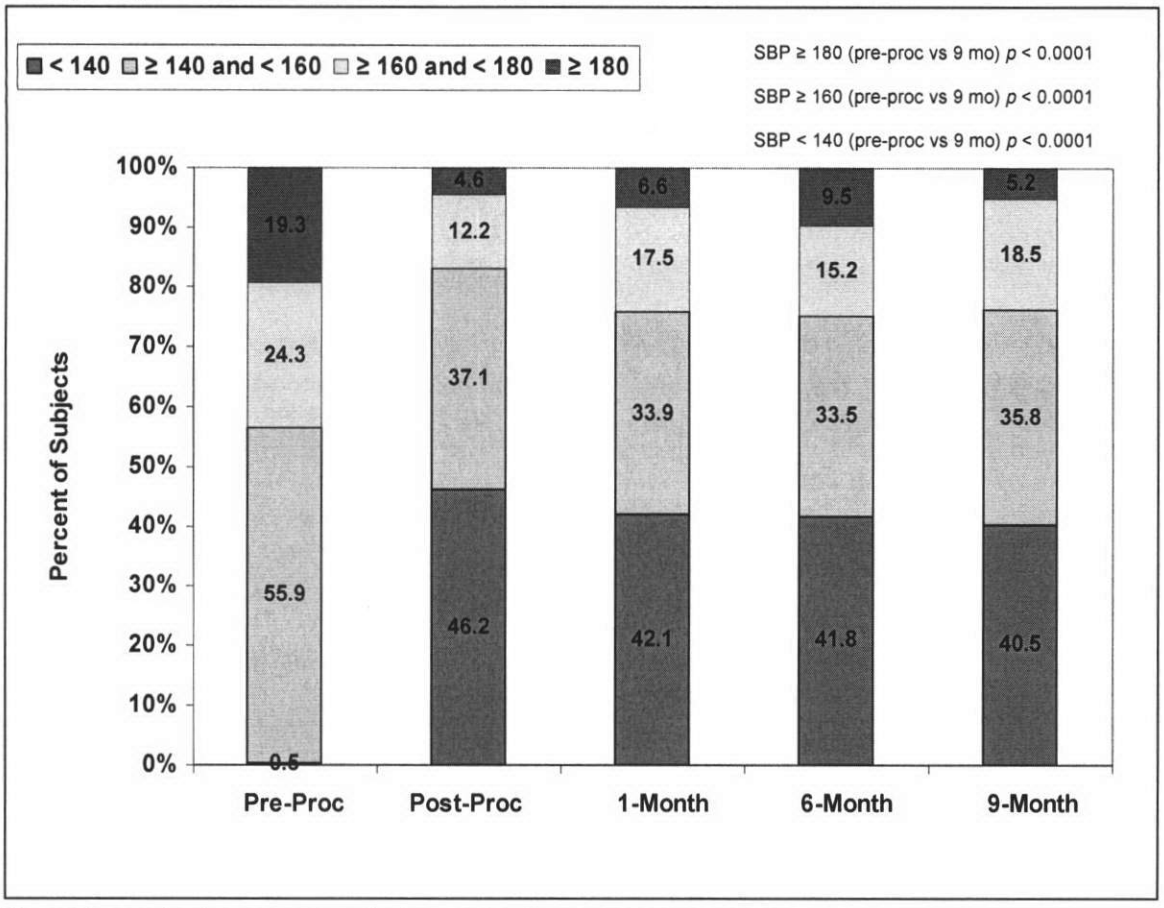


Table 15. Systolic Blood Pressure Goal Analyses

Time Period	Subjects (%) (N)	95% CI[1]
Pre-Procedure		
< 140 (mmHg)	0.5% (1/202)	[0.0%, 2.7%]
≥ 140 and < 160 (mmHg)	55.9% (113/202)	[48.8%, 62.9%]
≥ 160 and < 180 (mmHg)	24.3% (49/202)	[18.5%, 30.8%]
≥ 180 (mmHg)	19.3% (39/202)	[14.1%, 25.4%]
Post-Procedure		
< 140 (mmHg)	46.2% (91/197)	[39.1%, 53.4%]
≥ 140 and < 160 (mmHg)	37.1% (73/197)	[30.3%, 44.2%]
≥ 160 and < 180 (mmHg)	12.2% (24/197)	[8.0%, 17.6%]
≥ 180 (mmHg)	4.6% (9/197)	[2.1%, 8.5%]
30-Day		
< 140 (mmHg)	42.1% (77/183)	[34.8%, 49.6%]
≥ 140 and < 160 (mmHg)	33.9% (62/183)	[27.1%, 41.2%]
≥ 160 and < 180 (mmHg)	17.5%, (32/183)	[12.3%, 23.8%]
≥ 180 (mmHg)	6.6% (12/183)	[3.4%, 11.2%]
6-Month		
< 140 (mmHg)	41.8% (66/158)	[34.0%, 49.9%]
≥ 140 and < 160 (mmHg)	33.5% (53/158)	[26.2%, 41.5%]
≥ 160 and < 180 (mmHg)	15.2% (24/158)	[10.0%, 21.8%]
≥ 180 (mmHg)	9.5% (15/158)	[5.4%, 15.2%]
9-Month		
< 140 (mmHg)	40.5% (70/173)	[33.1%, 48.2%]
≥ 140 and < 160 (mmHg)	35.8% (62/173)	[28.7%, 43.5%]
≥ 160 and < 180 (mmHg)	18.5% (32/173)	13.0%, 25.1%
≥ 180 (mmHg)	5.2% (9/173)	[2.4%, 9.6%]

[1] By Clopper-Pearson exact confidence interval

Figure 3. Systolic Blood Pressure Measurement Change Over Time Per Subject Analysis (Intent-to-Treat Population)



Note: The p-value is not pre-specified and is for descriptive purpose only.

Change in renal function at 9 months

In addition, renal function was maintained (i.e., did not worsen) from pre-procedure to 9-month follow-up based on serum creatinine levels and eGFR, further demonstrating the clinical utility of the Herculink Elite stent and suggesting that revascularization with the Herculink Elite stent does not adversely affect renal function.

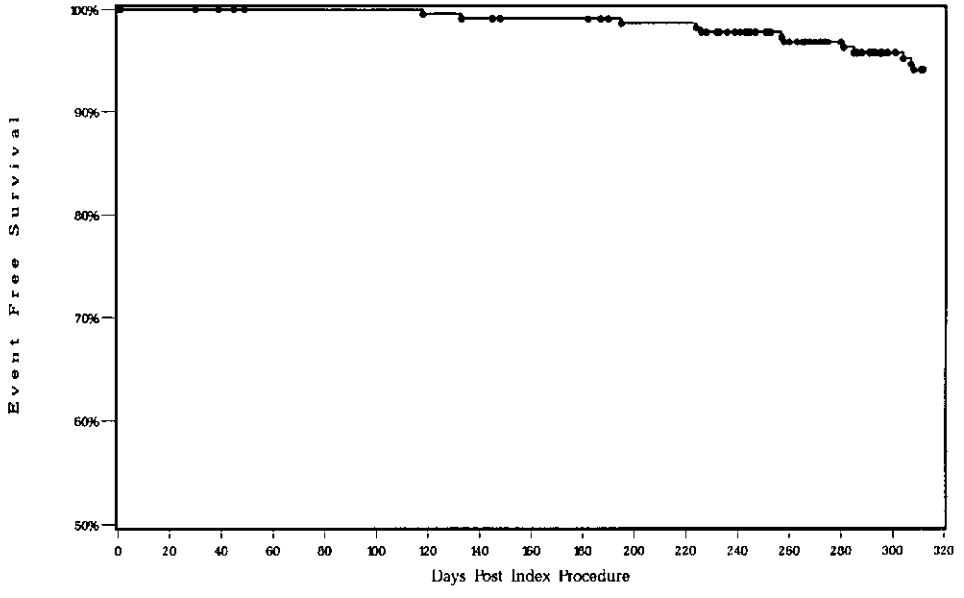
Primary and Secondary Patency

Primary and secondary patency at 9 months were 88.0% (184/209) and 95.2% (198/208), respectively.

Target Lesion Revascularization

Kaplan-Meier Survival Analysis yields a 92.6% freedom from all Target Lesion Revascularization (TLR) through 9 months. Clinically indicated TLR through 9 months was determined based on the angiographic core laboratory reported percent diameter stenosis of ≥ 60%. Kaplan-Meier Survival Analysis yields a 94.1% freedom from clinically indicated TLR through 9 months (**Figure 4**).

Figure 4. Kaplan-Meier Survival Curve – Freedom from Clinically Indicated TLR through 312 Days (Intent-to-Treat Population)



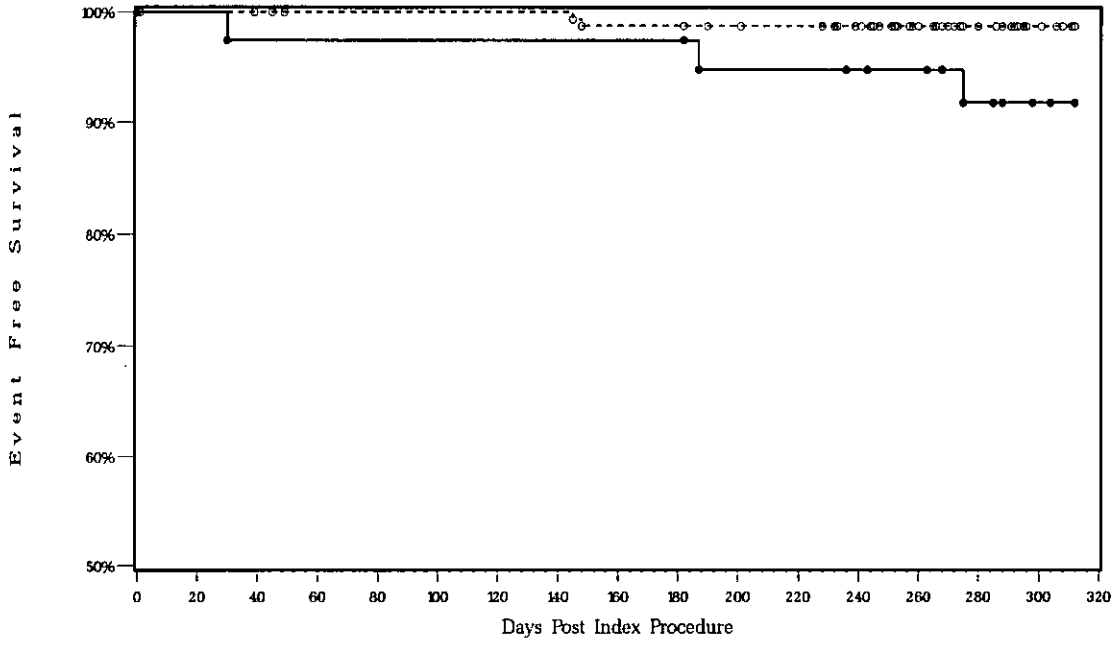
Days Post Index Procedure	0	(0, 30]	(30, 180]	(180, 270]	(270, 312]
Lesions at Risk	241	241	238	231	194
Lesions Censored	0	3	5	32	189
Number of Events	0	0	2	5	5
Event Free (%)	100%	100%	99.1%	96.9%	94.1%
Standard Error (%)	0.0%	0.0%	0.6%	1.2%	1.7%

Note: Lesions at risk gives the number of lesions at risk of an event at the start of the interval, while lesions censored and number of events are the incremental counts of lesions censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.

Subgroup Analyses

A subgroup analysis has been performed on subjects who were treated for unilateral versus bilateral lesions. Analyses at follow-up visits showed similar results between the unilateral and bilateral treatment groups. However, the Kaplan-Meier analysis showed a significant increase of mortality over the 9 months period in the bilateral group: 5.2% in bilateral vs. 1.3% in unilateral group (log rank p value = 0.0214) (**Figure 5**).

Figure 5. Subgroup Analysis - Freedom from Death through 312 Days (Intent-to-Treat Population: Bilateral vs. Unilateral)



Solid line: Bilateral Lesion Subjects (n= 39)
Dashed line: Unilateral Lesion Subjects (n= 163)

Days Post Index Procedure	0	(0, 30]	(30, 180]	(180, 270]	(270, 312]
Bilateral					
Subjects at Risk	39	39	38	38	32
Subjects Censored	0	0	0	5	31
Number of Events	0	1	0	1	1
Event Free (%)	100%	97.4%	97.4%	94.8%	91.8%
Standard Error (%)	0.0%	2.5%	2.5%	3.6%	4.5%
Unilateral					
Subjects at Risk	163	163	162	157	135
Subjects Censored	0	1	3	22	135
Number of Events	0	0	2	0	0
Event Free (%)	100%	100%	98.7%	98.7%	98.7%
Standard Error (%)	0.0%	0.0%	0.9%	0.9%	0.9%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	5.293	1	0.0214	
	Wilcoxon	4.932	1	0.0264	

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8.2 Materials Required

- Introducer sheath / guiding catheter in the appropriate size and configuration for the selected Stent Delivery System (refer to **Table 1**).
- 2 – 3 syringes (10 – 20 cc)
- 1,000 u / 500 cc normal saline
- 0.014" (0.36 mm) diameter guide wire of appropriate length
- 60% contrast diluted 1:1 with normal saline
- Inflation device
- Three-way stopcock
- Torque device (if applicable)
- Guide wire introducer

8.3 Stent Inspection Prior To Use

Prior to using the **RX Herculink Elite Renal Stent System**, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is located between the radiopaque balloon markers. Do not use if any defects are noted.

8.4 Lesion Preparation

1. Standard percutaneous technique should be used to place the introducer sheath / guiding catheter in the vessel. An appropriate sized (0.014") guide wire should be advanced across the lesion and into the common vessel.
2. Pre-dilate the lesion with an appropriate size balloon dilatation catheter to closely match the lumen diameter proximal and distal to the lesion.
3. Withdraw the balloon dilatation catheter leaving the guide wire in place.

8.5 Guide Wire Lumen Flush

1. Remove the protective cover from the tip.
2. Using the flush tool, flush the guide wire lumen with HepNS until fluid exits the guide wire exit notch.

8.6 Stent Delivery System Preparation

1. Prepare an inflation device / syringe with diluted contrast medium.
2. Attach the inflation device / syringe to the stopcock; attach to the inflation port.
3. With the tip down, orient the Delivery System vertically.
4. Open the stopcock to the Delivery System; pull negative for 30 seconds; release to neutral for contrast fill.
5. Close the stopcock to the Delivery System; purge the inflation device / syringe of all air.

6. Repeat steps 3 through 5 until all air is expelled. **Note:** If air is seen in the shaft, repeat Delivery System Preparation steps 3 through 5 to prevent uneven stent expansion.

7. If a syringe was used, attach a prepared inflation device to stopcock.

8. Open the stopcock to the Delivery System, leave on neutral.

8.7 Stent Delivery Procedure

1. Wipe the exposed guide wire with Heparinized saline to remove residual blood or contrast medium.

2. Fully open the hemostatic valve. Maintain neutral pressure on the inflation device.

3. Backload the Delivery System onto the proximal portion of the guide wire while maintaining guide wire position across the target lesion.

4. Advance the Delivery System over the guide wire to target lesion. Utilize radiopaque balloon markers to position the stent across the lesion; perform angiography to confirm stent position. If applicable tighten the hemostatic valve.

   Note: If during the process of moving the Delivery System into position you notice the stent has moved on the balloon, do not deploy the stent. The entire system should be **removed as a single unit.** *See Stent / System Removal – Precautions* section for specific removal instructions.

5. The stent is now ready to be deployed.

8.8 Stent Deployment Procedure

CAUTION: Refer to product label for *in vitro* stent outer diameter, deployment pressure, and RBP.

1. Slowly inflate the delivery balloon to low pressure; hold until balloon inflation is observed both proximally and distally to the stent. Continue balloon expansion to the specified stent deployment pressure. Confirm complete expansion of the stent / balloon fluoroscopically. If necessary, the delivery balloon can be used to post dilate the stent to optimize stent apposition.

   Do not exceed RBP: A larger PTA catheter may be used to dilate the stent. Do not expand the 4.0 mm – 6.0 mm stents beyond 7.0 mm. Do not expand the 6.5 mm – 7.0 mm **stents beyond 8.0 mm.**

2. After stent deployment, draw negative pressure on the inflation device for 30 seconds or until the delivery balloon is fully deflated.

3. Return the inflation device to neutral pressure to allow the balloon to refold during removal through the guide catheter.

4. With the inflation device on **neutral pressure**, carefully withdraw the delivery catheter with the guide wire remaining across the lesion.

Note: Should **unusual resistance** be felt **at any time** during either lesion access, or removal of an undeployed stent, the Stent System, wire, and guiding catheter should be **removed as a single unit**. See *Stent / System Removal – Precautions* section for specific removal instructions.

5. Confirm optimal stent apposition using standard angiographic techniques. If necessary, post dilate within stent. Post dilatation balloon diameters should closely match vessel reference diameter

9.0 REFERENCES

The physician should consult current literature on current medical practice on balloon dilatation and placement of balloon expandable stents.

10.0 PATENTS AND TRADEMARKS

This product and / or its use are covered by one or more of the following United States Patents: 5,242,396; 5,421,955; 5,514,154; 5,546,646; 5,569,295; 5,603,721; 5,649,952; 5,728,158; 5,735,893; 5,738,674; 5,759,192; 5,766,238; 5,780,807; 5,916,234; 6,056,776; 6,066,167; 6,066,168; 6,131,266; 6,296,655; 6,309,412; 6,369,355; 6,419,693; 6,428,568; 6,432,133; 6,482,166; 6,485,511; 6,511,504; 6,568,235; 6,589,207; 6,596,022; 6,620,193; 6,629,991; 6,651,478; 6,689,159; 6,736,843; 6,827,734; 6,835,059; 6,840,081; 6,908,479; 7,060,218.
Additional patents pending.

Herculink Elite is a registered trademark of the Abbott Group of Companies.

Plavix is a registered trademark of Sanofi-Aventis.

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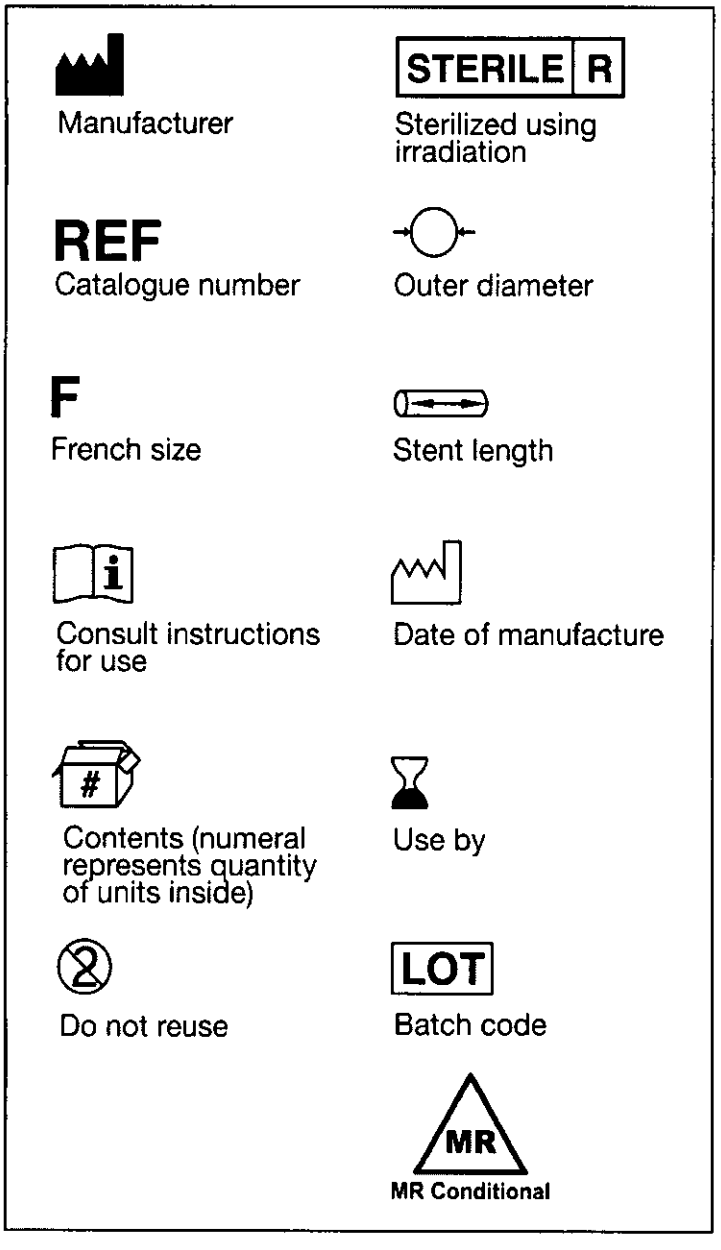
Graphical Symbols for Medical Device Labeling



RX Herculink Elite® Biliary Stent System

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

1.0 DEVICE DESCRIPTION

The **RX Herculink Elite Biliary Stent System** includes:

- A balloon expandable L605 cobalt chromium alloy stent pre-mounted on the balloon of a rapid exchange (RX) stent delivery system
- Two radiopaque markers located underneath the balloon which identify the stent position and fluoroscopically mark the working length of the balloon
- Proximal shaft markers to aid with delivery catheter position, relative to a biliary guiding catheter tip
- A third marker located approximately 30 cm from the center of the balloon that aids in locating the guide wire exit lumen and facilitating catheter removal and exchange

The delivery system can be utilized to optimize the stent wall apposition post stent deployment.

Table 1. *In Vitro Device Specifications**

Expanded Stent Diameter (mm)	Stent Lengths (mm)	*In Vitro** Stent Deployment Pressure (atm)	Rated Burst Pressure RBP (atm)	Recommended Minimum Guiding Catheter ID (F)/(inches)/(mm)	Recommended Minimum Sheath Introducer** (F)/(inches)/(mm)
4.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
4.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
5.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
5.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
6.0	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
6.5	12, 15, 18	11	14	6/0.067/1.70	5/0.071/1.80
7.0	15, 18	11	14	6/0.067/1.70	5/0.071/1.80

* All data provided is based on *in vitro* testing. Assure full deployment of the stent (see *Clinician Use Information section 8.8 Stent Deployment Procedure*). Deployment pressures should be based on stricture characteristics.

** See individual manufacturer specifications for (F) equivalent.

2.0 HOW SUPPLIED

Sterile. This device is sterilized with electron beam radiation. Non-pyrogenic. Do not use if the package is open or damaged.

Storage. Store in a dry, dark, cool place.

Contents. One (1) **RX Herculink Elite Biliary Stent System**, one (1) Protective / Regrooming sheath, one (1) flush tool

3.0 INDICATIONS

The **RX Herculink Elite Biliary Stent System** is intended for palliation of malignant strictures in the biliary tree.

4.0 CONTRAINDICATIONS

The **RX Herculink Elite Biliary Stent System** is contraindicated for use in:

- Stenting a perforated duct where the leakage from the duct can be enhanced by the prosthesis
- Patients with bleeding disorders
- Severe ascites

5.0 WARNINGS

The long term safety and effectiveness of this device in the biliary system have not been established.

Should **unusual resistance** be felt **at any time** during stricture access or Delivery System removal, the introducer sheath / guiding catheter and stent system should be removed **as a single unit**. Applying excessive force to the Stent Delivery System can potentially result in loss or damage to the Stent and Delivery System components. (See *Stent / System Removal – Precautions.*)

Stenting across a major bifurcation may hinder or prevent future diagnostic or therapeutic procedures.

Once fully deployed, the stent cannot be repositioned.

Persons allergic to L605 cobalt chromium alloy may suffer an allergic reaction to this implant.

Only physicians familiar with the complications, side effects and hazards commonly associated with biliary stent placement should use this device.

The **RX Herculink Elite Biliary Stent System** is intended to perform as a system. The stent should not be removed for use in conjunction with other dilatation catheters, nor should the **RX Herculink Elite Biliary Stent System** be used in conjunction with other stents.

The safety and effectiveness of multiple overlapping stents have not been established. However, when multiple stents are required, stent materials should be of similar composition.

6.0 PRECAUTIONS

6.1 Stent Delivery System Handling – Precautions

- **For single use only.** Do not resterilize or reuse. Note product "Use by" date.
- **Do not remove stent from its delivery balloon.**
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during stent system removal from the packaging, placement over a guide wire and advancement through a guiding catheter or introducer sheath.
- Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the delivery balloon.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

6.2 Stent Placement – Precautions

- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the *Clinician Use Information* section.
- The inflated balloon diameter of the system used to deploy the stent should approximate the diameter of the bile duct. Oversizing of the stent can result in a ruptured bile duct. To ensure full expansion of the stent, the balloon should be inflated to a minimum of nominal pressure.
- Implanting a stent may lead to dissection of the duct distal and / or proximal to the stent and may cause acute closure of the duct requiring additional intervention (surgical intervention, further dilatation, placement of additional stents, or other).
- Do not expand the stent if it is not properly positioned in the bile duct. (See *Stent / System Removal - Precautions.*)
- Balloon pressures should be monitored during inflation. **Do not exceed Rated Burst Pressure (RBP) as indicated on product label.** Use of pressures higher than specified on product label may result in a ruptured balloon with possible bile duct damage or perforation.

Do not attempt to pull an unexpanded stent back through the introducer sheath / guiding catheter; dislodgment of the stent from the balloon may occur.

6.3 Stent / System Removal – Precautions

Should **unusual resistance** be felt **at any time** during either stricture access or removal of the Delivery System post-stent implantation, the entire system should be removed **as a single unit**.

When removing the Delivery System as a single unit:

- DO NOT retract the Delivery System into the introducer sheath / guiding catheter.
- Position the proximal balloon marker just distal to the tip of the introducer sheath / guiding catheter.
- Advance the guide wire in the anatomy as far distally as safely possible.
- Secure the Delivery System to the introducer sheath / guiding catheter; then remove the introducer sheath / guiding catheter, guide wire and Delivery System as a **single unit**.

Failure to follow these steps and / or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and / or Delivery System components.

If it is necessary to retain guide wire position for subsequent biliary access, leave the guide wire in place and remove all other system components.

6.4 Post Implant – Precautions

Great care must be exercised when **crossing a newly deployed stent** with a guide wire or balloon catheter to avoid disrupting the stent geometry.

Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated that the Herculink Elite stent, in single and in overlapped configurations up to 33 mm in length, is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 or 3 Tesla
- Spatial gradient field of 2500 Gauss/cm or less
- Maximum whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) for any duration of MRI scan that would otherwise be safe for the patient without implant.

MRI at 1.5 or 3 Tesla may be performed immediately following the implantation of the Herculink Elite stent.

The Herculink Elite stent should not migrate in this MRI environment. Magnetic force on the Herculink Elite state was tested according to ASTM F2052-06e. Non-clinical testing at field strengths greater than 3 Tesla has not been performed to evaluate stent migration or heating.

Stent heating was derived by using the measured non-clinical, *in vitro* temperature rise according to ASTM F2182-09 in a GE Signa HDx 3 Tesla scanner and in a GE 1.5 Tesla coil in combination with the local specific absorption rates (SARs) in a digitized human heart model. The temperature rise was derived by a validated calculation. At overlapped lengths up to 33 mm, the Herculink Elite stent produced a non-clinical maximum local temperature rise of less than 3°C at a maximum whole body averaged SAR of 2.0 W/kg (normal operating mode) for an MRI sequence of 15 minutes. These calculations do not take into consideration the cooling effects of blood flow.

The effects of MRI on overlapped stents greater than 33 mm in length or stents with fractured struts are unknown.

Image artifact may be present when scanning the Herculink Elite stent as demonstrated in non-clinical testing performed according to ASTM F2119-07 in a GE Signa HDx 3 Tesla scanner. The image artifact (both inside and outside the device lumen) extends approximately 7 mm from the device using the spin echo sequence (TR = 500 ms; TE = 20 ms; flip angle = 90°) and 13 mm from the device using the gradient echo sequence (TR = 100 ms; TE = 15 ms; flip angle = 30°). MR image quality may be compromised if the area of interest is in the exact same area, or relatively close to, the position of the Herculink Elite stent. Therefore, it may be necessary to optimize the MR imaging parameters in the presence of Herculink Elite stents.

7.0 POTENTIAL ADVERSE EVENTS

Potential complications associated with the use of a biliary stent may include, but are not limited to, the following:

- Abscess
- Bile duct injury, including rupture and perforation
- Bile duct occlusion / obstruction
- Cholangitis
- Death
- Hypersensitivity or allergic reaction to drugs
- Infection
- Pancreatitis
- Parenchymal hemorrhage
- Peritonitis
- Sepsis
- Tumor overgrowth at the stent ends

8.0 CLINICIAN USE INFORMATION

8.1 Materials Required

- Introducer sheath / guiding catheter in the appropriate size and configuration for the selected Stent Delivery System (refer to **Table 1**).
- 2 – 3 syringes (10-20 cc)
- 1,000 u / 500 cc normal saline
- 0.014" (0.36 mm) diameter guide wire of appropriate length
- 60% contrast diluted 1:1 with normal saline
- Inflation device
- Three-way stopcock
- Torque device (if applicable)
- Guide wire introducer

8.2 Stent Inspection Prior To Use

Prior to using the **RX Herculink Elite Biliary Stent System**, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is located between the radiopaque balloon markers. Do not use if any defects are noted.

8.3 Stricture Evaluation / Biliary Drainage

Standard percutaneous transhepatic cholangiography should be performed to assess the biliary tree followed by the passage of a guide wire through the stricture and the placement of an internal / external biliary drainage catheter.

8.4 Stricture Pre-dilatation

1. Standard percutaneous technique should be used to place an introducer sheath / guiding catheter in the biliary tree. A 0.014" (0.36 mm) diameter guide wire should be advanced across the stricture and into the common bile duct.
2. Stricture and bile ducts may need to be pre-dilated with balloon dilatation. Pre-dilatation catheter diameters should closely match the duct diameter proximal and distal to the stricture to be treated.

8.5 Guide Wire Lumen Flush

1. Remove the protective cover from tip.
2. Using the flush tool, flush the guide wire lumen with normal saline until fluid exits the guide wire exit notch.

8.6 Stent Delivery System Preparation

1. Prepare an inflation device / syringe with diluted contrast medium.
2. Attach the inflation device / syringe to the stopcock; attach to the inflation port.
3. With the tip down, orient the Delivery System vertically.
4. Open the stopcock to the Delivery System; pull negative for 30 seconds; release to neutral for contrast fill.
5. Close the stopcock to the Delivery System; purge the inflation device / syringe of all air.
6. Repeat steps 3 through 5 until all air is expelled. **Note:** If air is seen in the shaft, repeat Balloon Preparation steps 3 through 5 to prevent uneven stent expansion.
7. If a syringe was used, attach a prepared inflation device to stopcock.
8. Open the stopcock to the Delivery System, leave on neutral.

8.7 Stent Delivery Procedure

1. Wipe the exposed guide wire with normal saline.
2. Maintain neutral pressure on inflation device.
3. Backload the Delivery System onto the proximal portion of the guide wire while maintaining guide wire position across the stricture.
4. Advance the Delivery System over the guide wire to target stricture. Utilize radiopaque balloon markers to position the stent across stricture; perform cholangiography to confirm stent position.

   Note: If during the process of moving the Delivery System into position you notice the stent has moved on the balloon, do not deploy the stent. The entire system should be **removed as a single unit**. See *Stent / System Removal - Precautions* section for specific Delivery System removal instructions.
5. The stent is now ready to be deployed.

8.8 Stent Deployment Procedure

CAUTION. Refer to product label for *in vitro* stent outer diameter, deployment pressure, and RBP.

1. Slowly inflate the delivery balloon to low pressure; hold until balloon inflation is observed both proximally and distally to the stent. Continue balloon expansion to the specified stent deployment pressure. Confirm complete expansion of the stent / balloon fluoroscopically. If necessary, the delivery balloon can be used to post dilate the stent to optimize stent apposition.

   Do not exceed RBP: A larger PTA catheter may be used to dilate the stent. Do not expand the 4.0 mm – 6.0 mm stent beyond 7.0 mm. Do not expand the 6.5 mm – 7.0 mm diameter stent beyond 8.0 mm.

2. After stent deployment, draw negative pressure on the inflation device for 30 seconds or until the delivery balloon is fully deflated.

3. Return the inflation device to **neutral pressure** to allow the balloon to refold during removal through the guide catheter.

4. With the inflation device on neutral pressure, carefully withdraw the delivery catheter with the guide wire remaining across the stricture.

   Note: Should **unusual resistance** be felt **at any time** during either stricture access or removal of an undeployed stent, the Stent System, guide wire and guiding catheter should be **removed as a single unit**. *See Stent / System Removal – Precautions* section for specific removal instructions.

5. Confirm optimal stent apposition using standard cholangiographic techniques. If necessary, post dilate within the stent. Post dilatation balloon diameters should closely match bile duct reference diameter.

9.0 PATENTS AND TRADEMARKS

This product and / or its use are covered by one or more of the following United States Patents: 5,242,396; 5,421,955; 5,514,154; 5,546,646; 5,569,295; 5,603,721; 5,649,952; 5,728,158; 5,735,893; 5,738,674; 5,759,192; 5,766,238; 5,780,807; 5,916,234; 6,056,776; 6,066,167; 6,066,168; 6,131,266; 6,296,655; 6,309,412; 6,369,355; 6,419,693; 6,428,568; 6,432,133; 6,482,166; 6,485,511; 6,511,504; 6,568,235; 6,589,207; 6,596,022; 6,620,193; 6,629,991; 6,651,478; 6,689,159; 6,736,843; 6,827,734; 6,835,059; 6,840,081; 6,908,479; 7,060,218.
Additional patents pending.

Herculink Elite is a registered trademark of the Abbott Group of Companies.

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