Use of The Spanner® Temporary Prostatic Stent as an Alternative to a Urinary Catheter to Achieve Bladder Drainage in Men Unfit for Other Treatments

CIP Reference Number SRS 1.0

Rev D
January 27, 2016

Sponsor:

SRS Medical Systems, Inc.
76 Treble Cove Road, Building 3
North Billerica, MA 01862

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1 IDENTIFICATION OF THE CLINICAL INVESTIGATION PLAN

1.1 Title

Use of The Spanner® Temporary Prostatic Stent as an Alternative to a Urinary Catheter to Achieve Bladder Drainage in Men Unfit for Other Treatments

1.2 Reference Number

CIP Reference Number SRS 1.0

1.3 Version Number

Rev. A, November 13, 2015

1.4 Revision History

Table 1. CIP Revision History

Revision	Revision Date	Summary of Changes
A	**Nov 13 2015**	**Original IDE Submission**
B	**Dec 14 2015**	**Updates per FDA Request on Dec 11 2015**
C	**Dec 15 2015**	**Updates per FDA Request on Dec 15 2015**
D	**Jan 27 2016**	**Updates per IDE Approval Letter Recommendations of Dec 16 2015**

2 SPONSOR

2.1 Sponsor Contact Information

The sponsor of this study is:

SRS Medical Systems, Inc.
76 Treble Cove Road, Building 3
North Billerica, MA 01862

The sponsor will maintain a study contact list and updates will be provided to the sites and available upon request.

For inquiries and further information about the study or for reporting of serious adverse events and other emergencies, contact:

Lee Brody.
CEO
SRS Medical
(978) 932-0400
(617) 308-4056 [24 hours]
brody@srsmedical.com

2.2 Responsibilities for Ethical Conduct

All parties involved in the conduct of the clinical investigation shall share responsibility for its ethical conduct in accordance with their respective roles in the investigation and

shall be appropriately qualified by education or experience to perform their tasks and this shall be documented appropriately.

The sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any investigators or other parties participating in, or contributing to the clinical investigation. All investigators shall avoid improper influence on, or inducement of, the subject, monitor, the sponsor or other parties participating in, or contributing to the clinical investigation.

2.3 Nondisclosure Statement - Restricted Distribution of Documents

This document contains information that is confidential and proprietary to the sponsor. This information is being provided solely for the purpose of evaluating and/or conducting a clinical trial for the sponsor. You may disclose the contents of this document only to study personnel under your supervision, IRB, or duly authorized representatives of regulatory agencies for this purpose under the condition that they maintain confidentiality. The contents of this document may not be used in any other clinical trial, disclosed to any other person or entity, and/or published without the prior written permission of the sponsor. The foregoing shall not apply to disclosure required by any regulations; however, you will give prompt notice to the sponsor of any such disclosure. Any information that may be added to this document also is confidential and proprietary to the sponsor and must be kept in confidence in the same manner as the contents of this document.

3 INVESTIGATORS AND INSTITUTIONAL REVIEW BOARDS

Table 2 lists investigator candidates for this study. The IRBs will be determined on a site by site basis and will be local institutional or an independent contract institutional review boards. Contact information will be updated throughout the course of the study. The updated contact list will be kept at SRS Medical and is available upon request.

Table 2. Contact Information for Investigators

3.1 Investigator's Statement and Signature

I have read this clinical investigation plan (CIP) and agree that it contains all necessary details for carrying out the study as described. I will conduct this CIP as outlined herein, including all statements regarding confidentiality. I will make a reasonable effort to complete the study within the time discussed. I will provide copies of the CIP and access to all information furnished by the sponsor to study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the investigational device and the study. I understand that the study may be terminated or enrollment suspended at any time by the sponsor, with or without cause, or by me if it becomes necessary to protect the best interests of the study subjects. I agree to conduct this study in full accordance with this protocol, all applicable regulations, the Declaration of Helsinki and Good Clinical Practices (GCP).

_____	_____	_____
Principal Investigator's Signature	Date	Site #

4 STUDY SYNOPSIS

Study Title	**Use of The Spanner® Temporary Prostatic Stent as an Alternative to a Urinary Catheter to Achieve Bladder Drainage in Men Unfit for Other Treatments**
Study Number	**SRS 1.0**
Purpose	**To expand the indications for use by evaluating the safety and efficacy of The Spanner to manage voiding dysfunction and lower urinary tract symptoms in subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate.**
Device	The Spanner® Temporary Prostatic Stent
Current Indications for Use	The Spanner is intended for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination in subjects following minimally invasive treatment for benign prostatic hyperplasia (BPH) and after initial post-treatment catheterization.
Proposed Indications for Use	The Spanner Temporary Prostatic Stent is intended for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination for subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate.
Design	The proposed investigation is a prospective, multicenter, single-arm, open-label trial. Enrolling approximately 105 subjects who are dependent on a urinary catheter. Subjects will be fitted with a Spanner stent and the stent will be replaced at an interval of approximately 30 days for a total of up to 90 days of use. Subjects will complete the study upon removal of the Spanner stent after 90 days and one follow-up telephone call post-removal. PVR, uroflow, urinary symptoms, subject satisfaction and the occurrence of adverse events will be collected. Cystoscopy will be performed prior to the initial stent placement and after the final stent removal to determine any effects of The Spanner on lower urinary tract anatomy.
Primary Objectives	• To determine the proportion of subjects who achieve adequate bladder drainage over 90 days, defined as a post-void residual (PVR) of ≤150 ml. • The pre-specified success criterion for this study is that ≥50 percent of subjects will achieve adequate bladder drainage over 90 days.

Secondary Objectives	• To measure the effects of the Spanner stent on bladder drainage, defined by the proportion of subjects who achieve a post-void residual of:
	  ○ ≤150 ml over 30 days.
	  ○ ≤250 ml over 30 days.
	  ○ ≤250 ml over 90 days.
	• To measure the effects on maximum flow rate as assessed by Uroflow
	• To measure the effects on the International Prostate Symptom Score

Key Inclusion Criteria	• Age > 45 years; • Subject in urinary retention and catheterized (indwelling or intermittent) < 180 days; • Subject has a documented diagnostic history of detrusor contractility (>= 15 cmH2O) , • Subject has a negative Urinalysis on Visit 1; • Subject not a candidate for pharmacologic, minimally invasive or surgical prostate treatments; • Subject is experiencing catheter-induced discomfort

Key Exclusion Criteria	• Current or recent urinary tract disease; • Surgery altering the normal uro-genital anatomy or abnormal urethral anatomy that affect the function of the lower urinary tract; • History of conditions associated with neurogenic bladder, including spinal cord injury, multiple sclerosis, or Parkinson's disease; • Use of anticholinergic medication; • Known or suspected prostate cancer; • Prior pelvic irradiation therapy; • Prostatic urethral length < 4 cm or > 9 cm • Intravesical enlargement of the median lobe of the prostate. • Prior penile prosthesis

5 THE INVESTIGATIONAL DEVICE

5.1 Intended Purpose

The Spanner is intended for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination in subjects following minimally invasive treatment for benign prostatic hyperplasia (BPH) and after initial post-treatment catheterization.

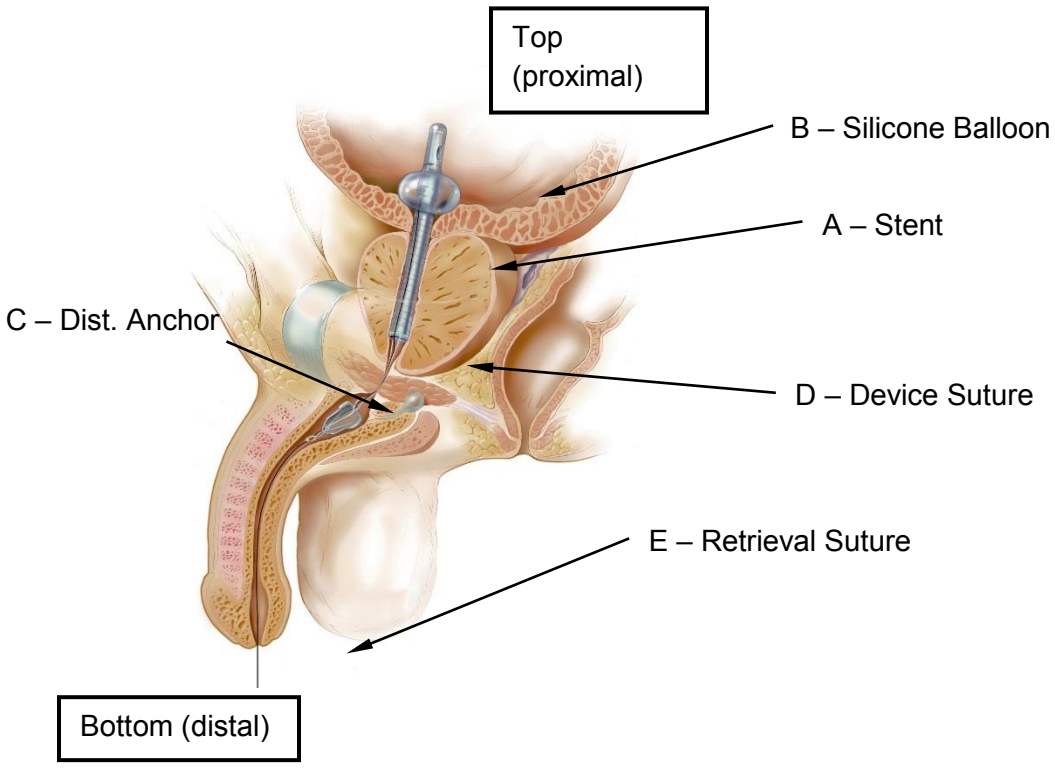
5.2 Proposed Expanded Indications For Use

The Spanner Temporary Prostatic Stent is intended for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination for subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate.

5.3 Device Description

The Spanner temporary prostatic stent is a sterile, single use, disposable intraurethral device. The Spanner is available in 20F diameter, 6 sizes (lengths 4, 5, 6, 7, 8, and 9 cm). The Spanner stent is positioned in the prostatic urethra from the bladder neck to the top (proximal side) of the external urinary sphincter (see **Figure 1**). The stent portion (A) of the Spanner is made of silicone. The stent is held in position by a silicone balloon (B) and in the bulbar urethra by a soft, silicone, distal anchor (C). A stainless steel wire-form is encapsulated into the body of the distal anchor to maintain its shape. The distal anchor is attached to the stent by means of a silicone coated device suture (D). The length of the connecting suture is such that it traverses the external sphincter, positioning the anchor on the bottom (distal side) of the sphincter to prevent migration inward to the bladder, while allowing normal sphincter function to occur. A retrieval suture (E) is attached to the device suture below the distal anchor. A stainless steel balloon plug, which is inserted into the balloons deflation port, is located at the end of the retrieval suture. The retrieval suture is provided in sufficient length to extend through the urethra, exterior of the penis. To remove the device, gentle traction is applied to the retrieval suture to remove the balloon plug and deflate the balloon. After pausing a few seconds to allow balloon deflation, the device is withdrawn by slowly pulling on the retrieval suture. To facilitate device insertion and balloon inflation, the Spanner stent is mounted on an Insertion Tool. The Spanner stent system also includes an accessory, the Surveyor®, which is used for proper Spanner size selection. A detailed description of the Spanner stent, Insertion Tool, and Surveyor device configurations is provided below.

Figure 1: Spanner Stent (positioned in the prostatic urethra)



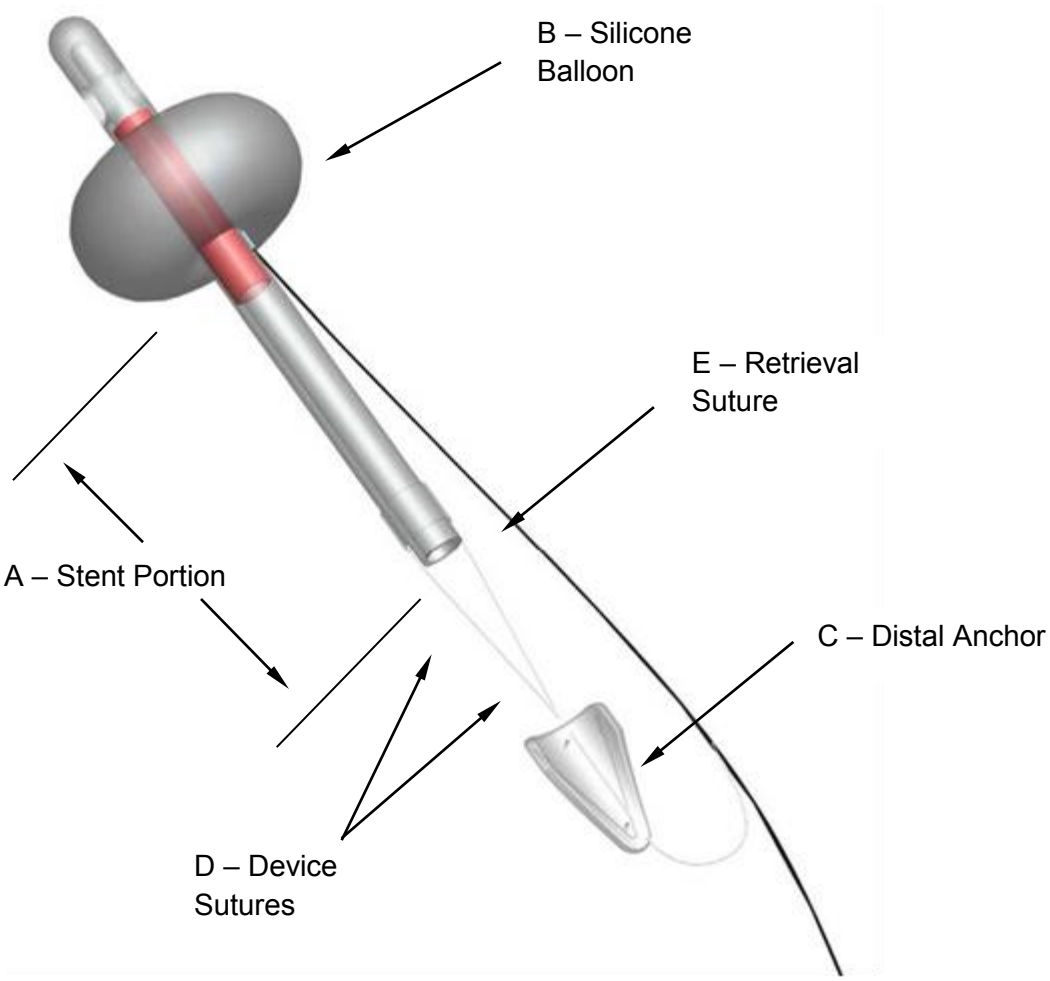
5.4 Stent Configuration

The Spanner, shown in **Figure 2** comprises a stent portion, proximal balloon anchor, device sutures, and a distal anchor. The stent is provided in a range of lengths. The combined length of the actual stent portion (A) and the device suture portion (D) determine the device size, which are 4, 5, 6, 7, 8 & 9 centimeters in length respectively. The balloon (B) and distal anchor (C) are identical on all device sizes.

The stent portion (A) is made of silicone. The stent is held in position by a silicone balloon on its proximal end (B) and a soft, silicone, distal anchor (C) on the distal end. Silicone-coated device sutures (D) attach the distal anchor to the stent. A retrieval suture (E) is attached to the device sutures. The retrieval suture is designed to extend through the urethra and the urethral meatus.

Figure 2: Spanner Stent

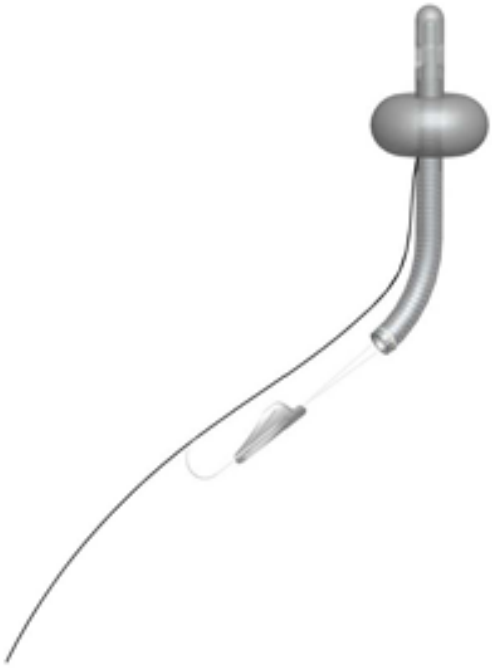
(Figure is not to scale)



Spanner sizes 6, 7, 8, and 9 include a distal curve to the stent to align with the prostatic urethral anatomy (**Figure 3**).

Figure 3: Spanner Stent with Distal Curve

(Figure is not to scale)

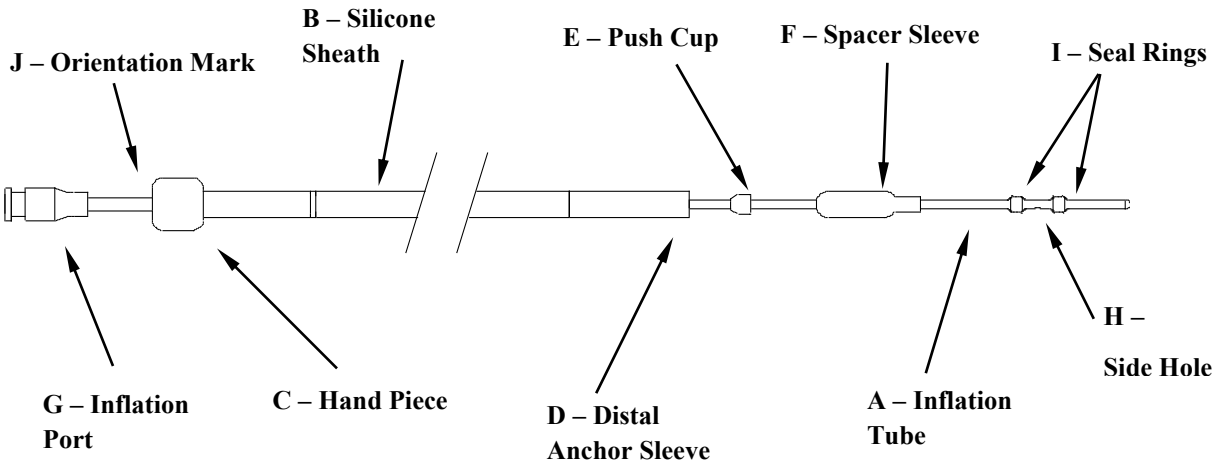


5.5 The Spanner Insertion Tool

To facilitate device insertion and balloon inflation, the Spanner stent is mounted on a sterile, single use Insertion Tool, shown in **Figure 4.** A polyurethane inflation tube (A) extends the length of the Insertion Tool. A silicone sheath (B) surrounds the inflation tube. The sheath is reinforced with a stainless steel coil and attached to the hand piece (C). The proximal end of the sheath, the distal anchor sleeve (D), houses the Spanner stent distal anchor until it is deployed. The push cup (E) is used for anchor deployment. The spacer sleeve (F) provides a smooth transition between the stent and distal anchor when loaded on the Insertion Tool. The inflation tube lumen extends from an inflation port (G) on the distal end to a side hole (H) located on the proximal end. The side hole is bounded by two seal rings (I).

The hand piece of the Insertion Tool includes a coudé tip orientation mark (J). The coudé tip orientation mark is used as a reference during insertion. The Spanner is inserted with coudé tip directed to the subject's anterior.

Figure 4: Insertion Tool



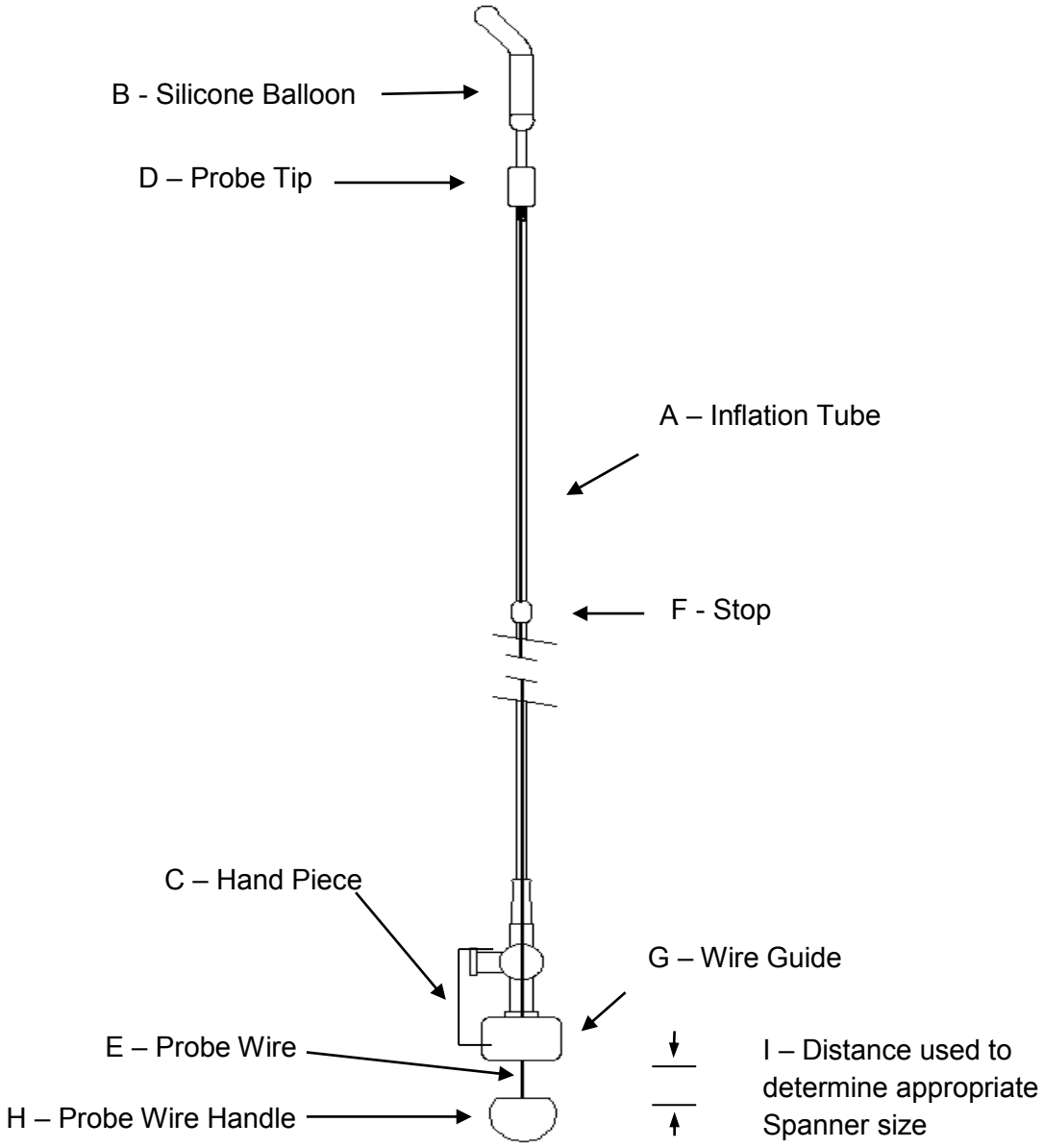
(Figure not to scale)

5.6 Surveyor

The Spanner stent system also includes an accessory that is provided separately, the Surveyor®. The Surveyor, shown in **Figure 5**, is a sterile, single use device used to assess the length of the urethra from the top (proximal side) of the bladder neck to the bottom (distal side) of the external sphincter in order to select the appropriate Spanner stent size. The Surveyor has a coudé-tip. The Surveyor consists of a polyurethane inflation tube (A) with a silicone balloon (B) on the proximal end and a hand piece assembly (C) on the distal end. The Surveyor lumen, which extends from an inflation port stopcock on the hand piece assembly to the balloon, is used to inject fluid to inflate the balloon. A short PTFE[1] probe tip (D) (approximately 1 cm length) encircles the inflation tube and is able to slide freely along the tube length between the balloon and the stop. A stainless steel probe wire (E) is attached to the probe tip and extends along the length of the Surveyor and through the stop (F) and wire guide (G), where it is attached to a probe wire handle (H). The gap (I) between the probe wire handle and wire guide indicates the length from the bladder neck to the distal side of the external sphincter; this length, in conjunction with the Spanner Selector card, is used to select the appropriate size Spanner.

[1] PTFE: Polytetrafluoroethylene a.k.a. Teflon®

Figure 5: Surveyor Device



5.7 Manufacturers

Manufacturer:

SRS Medical Systems, Inc.
76 Treble Cove Road, Building 3
North Billerica, MA 01862
FDA Establishment Registration Number: 1223851

Contract Manufacturer:

ProMed Pharma LLC
15600 Medina Road
Suite 100
Minneapolis, MN 55447
FDA Establishment Registration Number: 3003335547

Contract manufacturer ProMed Pharma LLC (ProMed) is the sole manufacture of The Spanner and Surveyor (accessory). The ProMed cleanroom meets ISO 14644:1999 class 7 cleanroom requirements and is The Spanner and Surveyor manufacturing facility and manufacturing documentation is annually inspected by FDA.

5.8 Model Matrices

The Spanner stent is provided in one diameter (20 Fr) in lengths ranging from 4 to 9 cm, in 1 cm increments. **Table 3** identifies the part, catalog and device identifier numbers for each Spanner stent size. Surveyor information is provided in **Table 4.**

Table 3. Spanner Sizes

Description	Diameter (F)	Size/ Length (cm)	Device Part Numbers	Catalog Number	Device Identifier Number
Spanner with Insertion Tool/High Flex Stent	20	4	2009004-4HA	SPNR-4HA	00890477000005
		5	2009004-5HA	SPNR-5HA	00890477000012
		6	2009004-6HA	SPNR-6HA	00890477000029
		7	2009004-7HA	SPNR-7HA	00890477000036
		8	2009004-8HA	SPNR-8HA	00890477000043
		9	2009004-9HA	SPNR-9HA	00890477000050

Table 4. Surveyor Device				
Description	**Tip configuration**	**Device Part Number**	**Catalog Number**	**Device Identifier Number**
Surveyor Urethral Measurement Device	**Coudé**	**2007900-02**	**SURV-02**	**00890477000067**

5.9 Traceability

Device traceability will be accomplished by device Lot Number.

5.10 Intended Purpose and Population

The Spanner is being evaluated for use to manage voiding dysfunction and lower urinary tract symptoms in subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate.

The Spanner Temporary Prostatic Stent is intended for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination for subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate.

5.11 Materials Contacting Tissues or Body Fluids

All materials used to construct The Spanner stent, Insertion Tool, and Surveyor are commonly used in commercially available urological devices and are shown in **Attachment F.**

5.12 Urologist Experience and Training Requirements

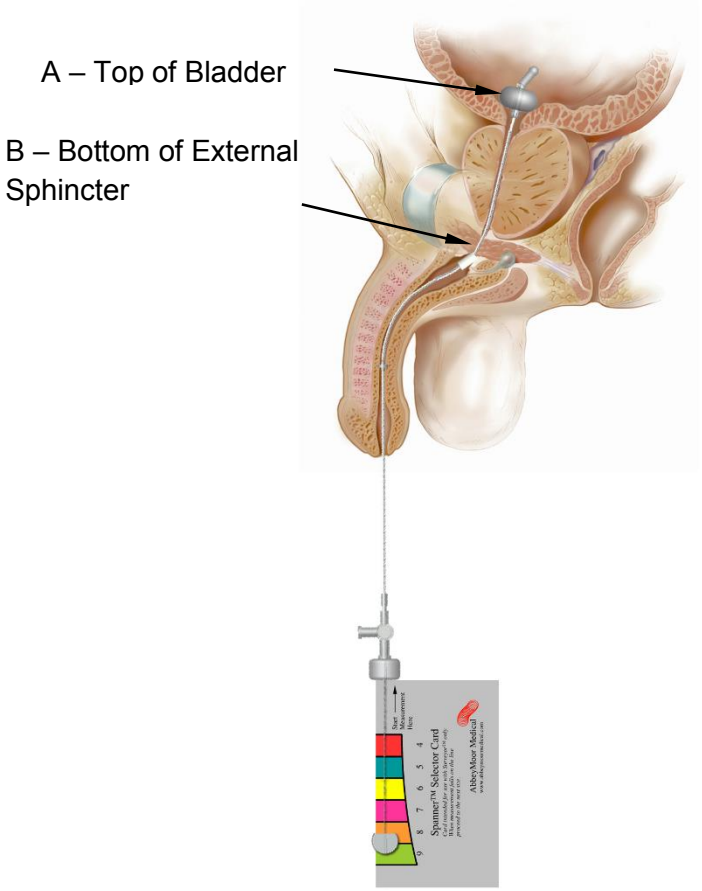
Urologists and their staff participating in the clinical study will receive device training by Sponsor personnel on use of The Spanner and Surveyor prior to use in this clinical investigation.

5.13 Procedures

The appropriate Spanner size for the subject is determined using the Surveyor accessory device. The Surveyor (see **Figure 6**) is a tool used to assess the distance from the top (proximal side) of the bladder neck (A) to the bottom (distal side) of the external sphincter (B). This distance corresponds to the distance from the Spanner balloon to the distal anchor when the Spanner resides in situ. The Surveyor is introduced into the urethra and slowly advanced into the bladder. After entering the bladder a balloon located near the end of the Surveyor is inflated with 5cc sterile water. Gentle traction seats the Surveyor balloon on top of the bladder neck. A small probe (similar to a piston with its own “push rod”) slides along the Surveyor inflation tube through the length of the pendulous urethra to the level of the bottom (distal side) of the external sphincter. Components of the Surveyor, external of the subject, replicate the position of the probe relative to the bottom of the external sphincter. The Spanner Selector Card is then used in conjunction with the Surveyor to select the appropriate

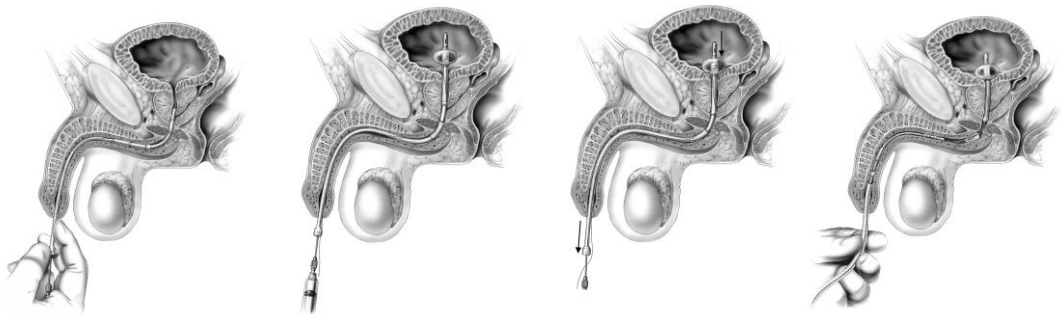
Spanner size. The Surveyor balloon is subsequently deflated and the device is withdrawn.

Figure 6: Surveyor (positioned in prostatic urethra) & Spanner Selector Card



The selected Spanner is mounted on the Insertion Tool (provided in the Spanner package) and coated with a water soluble lubricant. The stent is then inserted into the urethral meatus, and utilizing tactile feedback, advanced along the pendulous urethra until the proximal tip and proximal balloon of the Spanner are positioned well within the bladder (**Figure 7**). The balloon is inflated with 5cc of sterile water. Continuous gentle traction is applied on the Insertion Tool to seat the Spanner balloon on top of the bladder neck and deploy the anchoring device distal to the external sphincter in the bulbar urethra. Once the balloon is seated and the anchoring device deployed, the Insertion Tool is withdrawn from the urethra.

Figure 7. Inserting the Spanner

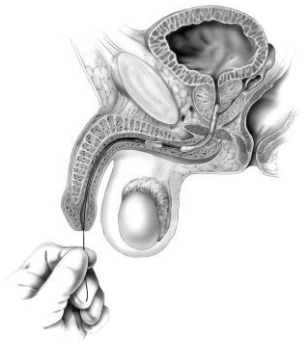


Only the device sutures pass through the sphincter area allowing the man's external sphincter to function normally, controlling urination and continence. The stent is held in place using the proximal balloon in the bladder neck to prevent expulsion and the distal anchor, distal of the external sphincter, to prevent migration.

The Spanner may be worn for up to 30 days, after which it is removed by simply pulling the retrieval suture to first deflate the balloon and then subsequently withdraw the device (**Figure 8**).

Detailed procedures for using the Spanner stent, Insertion Tool, and Surveyor are provided in the Instructions for Use (see **Attachment A**).

Figure 8. Removing the Spanner



6 JUSTIFICATION FOR THE CLINICAL INVESTIGATION

6.1 Study Background and Justification

This investigational plan describes a proposed clinical trial for The Spanner® Temporary Prostatic Stent. The Spanner is designed to provide a temporary means to relieve obstruction of the bladder outlet while maintaining volitional voiding ability.

The Spanner is a PMA Approved Device (PMA 060010) and has been on the US market continuously since December 2006. The Spanner is approved for temporary use (up to 30 days) to maintain urine flow and allow voluntary urination in subjects following minimally invasive treatment for benign prostatic hyperplasia (BPH) and after initial post-treatment catheterization. This clinical trial is intended to provide additional clinical data to support an expanded indication to a particularly needy subject population.

In the proposed investigation, The Spanner is being evaluated for use to manage voiding dysfunction and lower urinary tract symptoms in subjects who are not candidates for pharmacologic, minimally invasive or surgical treatment of the prostate. These subjects often have no alternative to relieve urinary retention other than a urinary catheter. Urinary catheters passively drain the bladder by placing a tube into the bladder that extends past the meatus and draining the urine into an external drainage bag or toilet. The proposed investigation evaluates the safety and effectiveness of using The Spanner as an alternative to a urinary catheter for these subjects. The Spanner is a completely internal stent that provides a means for these subjects to achieve normal micturition and avoid the known and serious complications that occur due to the urinary catheter's external components. The fully internal design of The Spanner also has been shown to improve subject quality of life.

6.2 Relevant Pre-clinical Testing

The Spanner is a PMA Approved Device (PMA 060010) and has been on the US market continuously since December 2006. Non-clinical device testing performed includes biocompatibility/toxicology, sterilization, shelf life/distribution, and design verification.

6.3 Prior Clinical Studies

The safety and effectiveness of The Spanner was evaluated in a prospective, randomized, multi-center clinical investigation (IDE G020140). This clinical trial is intended to provide additional clinical data to support an expanded indication to a particularly needy subject population.

The Spanner has not been withdrawn from marketing in any country for reasons relating to device safety and effectiveness.

7 RISKS AND BENEFITS OF THE INVESTIGATIONAL DEVICE AND CLINICAL INVESTIGATION

7.1 Anticipated Clinical Benefits

Men suffering from urinary retention due to an enlarged prostate and who are unfit for pharmacologic, minimally invasive or surgical treatment often have no alternative to relieve urinary retention other than catheterization. The Spanner is a completely internal stent that provides a means for these subjects to achieve normal micturition and avoid the known and serious complications that occur due to the urinary catheter's external components. The fully internal design of The Spanner has also been shown to improve subject quality of life.

7.2 Anticipated Adverse Device Effects

Based on the device design and intended use, the intended subject population, and experience with similar urological devices, the following list of potential risks and adverse events may be related to use of the device.

- Micturition burning/pain;
- Urinary frequency;
- Urgency;
- Perineal/urethral pain;
- Bacteriuria;
- Symptomatic urinary tract infection;
- Urinary retention with no reported migration or clotting;
- Urinary retention associated with migration;
- Urinary retention associated with clotting;
- Urinary incontinence;
- Pain – trauma activated;
- Ejaculation failure;
- Dyspareunia – painful sex;
- Urinary hesitation;
- Ulceration, erosion, or trauma of the bladder or urethra;
- Dysuria, pain or spasm of the bladder or urethra;
- Microscopic or gross hematuria or bleeding;
- Elevated post void residual urine;
- Purulent urethral discharge;
- Encrustation of the device or device sutures;
- Irritation of the bladder or urethra from contact with the device;
- Upper tract deterioration.

7.3 Anticipated Device Deficiencies

The following are device deficiencies that may occur during the conduct of the investigation. All device deficiencies should be reported as Adverse Events, as described in Section 21.

- Device malfunction including balloon deflation or non-deflation, balloon breakage, breakage of the removal suture or the suture connecting the stent to the distal anchor;
- Migration of the device or the removal suture;
- Expulsion of the device.

7.4 Risks Associated With Participation in the Clinical Investigation

In addition to device related risks, participants will receive a cystoscopy at visits one and four. Cystoscopy is a commonly performed urological procedure. Adverse effects can include infection, bleeding and pain associated with the cystoscopy.

Some of the possible side effects of anesthetic medication in the urethra include allergic reactions which may include coughing, difficulty swallowing, rash, hives, or swelling. Other possible side effects include high or low blood pressure, stomach upset, tingling sensations in the skin, dizziness, decreased heart rate, and death.

Having blood samples taken from a vein may cause temporary pain or bruising. It is possible for the skin at the puncture site or the vein to become irritated and inflamed. On rare occasions, blood clot formation, bleeding at the puncture site, or infection could occur.

7.5 Possible Interactions with Concomitant Medical Treatments

The Spanner device is placed in the urethra and bladder neck and is a physical obstacle to potential medical treatments that involve cystoscopy of the urethra, bladder or kidneys. The Spanner would need to be removed prior to such medical treatments. The Spanner has not been evaluated for use with an MRI. If an MRI is needed, The Spanner should be removed.

7.6 Residual Risks

The residual risks have been addressed through a risk assessment performed for the device, both from a Failure Mode Effects Analysis and through prior clinical investigations. Risks associated with the device and procedure have been mitigated through numerous mechanisms including design, inspections, protocol mechanisms, physician and study personnel training, frequent subject follow up, and study monitoring. The potential benefits are significant and offset the remaining residual risks.

7.7 Mitigation of Risks

The following measures will be taken to minimize risks to subjects participating in the trial:

- Study participants will be provided thorough verbal and written instructions and warnings for use of the study device, and they will be instructed in the appropriate actions to take, including notification of the investigator in the event of adverse effects or malfunction of the study device.
- Participants will be examined and interviewed at regularly scheduled visits to determine the presence of signs or symptoms indicating possible adverse effects or malfunction of the study device.
- Urinalysis and urine cultures will be taken at prescribed intervals to monitor for hematuria, bacteriuria and symptomatic urinary tract infections.
- Renal function will be monitored in all subjects at all time points during the study by monitoring serum creatinine levels at each visit.

- Sponsor procedures will be in place to provide for timely, ongoing investigation of adverse events in order to allow appropriate actions to be taken if unanticipated events occur.
- The Sponsor will perform regular periodic visits to each participating site, reviewing all participant files to assure timely detection of unanticipated device effects or outcomes.
- Selection of experienced urologists.
- The protocol clearly defines the subject inclusion/exclusion criteria and subject treatment and follow-up that are consistent with current medical practices.
- The Spanner has been designed and developed within a quality management system that is compliant with the applicable requirements.

7.8 Risk-to-Benefit Rationale

Subjects who are bothered by utilizing a urinary catheter for bladder drainage and who are not candidates for prostatic treatments are offered a temporary alternative to their urinary catheter. Data from prior studies indicates that a high percentage of subjects who meet the inclusion criteria benefit from the procedure. For the majority of the subjects the benefit of the procedure outweighs the risks.

8 OBJECTIVES AND HYPOTHESES OF THE CLINICAL INVESTIGATION

8.1 Primary Objective

The primary objective of the clinical study is:

- To determine the proportion of subjects who achieve adequate bladder drainage over 90 days, defined as a post-void residual (PVR) of ≤150 ml.
- The pre-specified success criterion for this study is that ≥50 percent of subjects will achieve adequate bladder drainage over 90 days.

8.2 Secondary Objectives

The secondary objectives of the clinical study are:

- To measure the effects of the Spanner stent on bladder drainage, defined by:
- The proportion of subjects who achieve a post-void residual (PVR) of ≤150 ml over 30 days.
- The proportion of subjects who achieve a post-void residual (PVR) of ≤250 ml over 30 days.
- The proportion of subjects who achieve a post-void residual (PVR) of ≤250 ml over 90 days.
- To measure the effects of the Spanner stent over time on maximum flow rate (Qmax in ml/sec) as assessed by Uroflow
- To measure the effects of the Spanner stent over time on the International Prostate Symptom Score (IPSS)

8.3 Study Hypotheses

8.3.1 Primary Endpoint: Assessment of PVR over 90 days

PVR levels will be monitored throughout the 90 days of stent use to confirm that the subject is able to successfully empty his bladder. PVR levels are assessed on Visits 1, 2, 3 and 4 while stent is in place using abdominal ultrasound. The hypothesis is that over 90 days of stent use, 50% of the subjects will be able to successfully empty their bladder, as defined by PVR of $\leq$150 ml at all four visits.

8.3.2 Secondary Endpoints: Other Assessments of PVR

The monitored PVR levels at Visits 1, 2, 3, and 4 will be further assessed as follows:

- The proportion of subjects over 30 days (Visits 1 and 2) with PVR $\leq$150 ml.
- The proportion of subjects over 30 days (Visits 1 and 2) with PVR $\leq$250 ml.
- The proportion of subjects over 90 days (Visits 1-4) with PVR $\leq$250 ml.

8.4 Adverse Events

Any Adverse Events (AEs), Serious Adverse Events (SAEs) and Unanticipated Adverse Device Effects (UADEs), to be documented from time of enrollment until the last study visit.

8.4.1 Exploratory Endpoints

- Qmax scores.
- IPSS scores.

9 DESIGN OF THE CLINICAL INVESTIGATION

The proposed investigation will be a prospective, multicenter, single-arm, open-label trial.

The study will be conducted at three to ten study centers in the US. Subjects will be enrolled in the trial for a period of up to 125 days, which includes up to 20 days of post-removal follow-up prior to study discharge. The objectives of the statistical analyses are to:

- Assess the effectiveness of the device in emptying of the bladder
- Assess the safety of the device in the population under study

The study will enroll approximately 105 subjects who are dependent on a urinary catheter and meet eligibility criteria. The study will consist of a 90 day treatment period. Subjects will be fitted with a Spanner stent and the stent will be replaced at an interval of approximately 30 days (25-35 days permitted) for a total of up to 90 days of use (75-105 days permitted). Subjects will complete the study upon removal of the Spanner stent after 90 days and one follow-up telephone call post-removal.

All participants will undergo approximately 90 days of Spanner use, in the form of consecutive Spanner placements each lasting approximately 30 days (25-35 days permitted). During the 90 days, data will be collected with respect to PVR, uroflow,

urinary symptoms, subject satisfaction and the occurrence of adverse events. Cystoscopy will be performed prior to the initial stent placement and after the final stent removal to determine any effects of The Spanner on lower urinary tract anatomy.

9.1 Measures to Avoid Bias

- The investigators are independent from the sponsor and are experienced with similar procedures.
- The study uses standardized measurements for endpoints.
- The disposition of all screened subjects will be recorded.
- Analyses to address primary and secondary objectives will be performed using an intention-to-treat sample including all enrolled subjects who underwent an attempted Spanner device implant procedure.
- The study will be monitored by independent individuals qualified by education and experience.

9.2 Primary and Secondary Endpoints

Primary and secondary endpoints have already been described in CIP Section 8.

9.3 Methods and Timing for Assessing, Recording, and Analyzing Variables

Timing of testing and events is provided in Section 12.1 Study Activities Table. Data assessment and analysis is described in Section 14. Statistical Considerations. Guidance for the categorization of adverse events is provided in Section 21.6 Managing Adverse Events. Recording guidance is provided in Section 15.1 Electronic Case Report Form Completion. The requirements for conducting and reporting uroflow are defined in **Attachment B.**

9.3.1 Requirements for Diagnostic and Laboratory Tests

9.3.1.1 Urinalysis (UA), Urine Culture and Sensitivity (UC&S) and Serum Creatinine

- Test Laboratory

Testing must be completed by an accredited laboratory. Documentation of accreditation of the laboratory must be provided to the study Sponsor prior to study initiation. A copy of the laboratory normal ranges must also be supplied to the Sponsor.

- Specimen Collection, Handling & Analysis Requirements
- Clean catch, voided, mid-steam urine samples of adequate volume (50 ml minimum) should be collected in sterile containers and forwarded promptly to the testing lab. If clean catch is not practical due to urinary retention, use a straight catheter to directly drain the bladder.
- Urinalysis with microscopy – A complete microscopic examination is required in addition to the routine urinalysis. Specifically, counts of white cells (WBC), red cells (RBC) and bacteria present in the sample are required.
- Urine culture – Required when Urinalysis suggests microbial infection. For positive urine cultures, the organism identification as well as the colony count must be provided.

- Serum Creatinine- A serum creatinine blood test is required to monitor renal function throughout the study.

9.3.1.2 Post Void Residual Urine (PVR) Testing

PVR will be determined using abdominal ultrasound:

- Subjects with a minimum PVR > 350 ml will be prematurely removed from the study (see Section 21.5.8).
- Subjects with a minimum PVR greater than 250 ml (and less than 350 ml) will be scheduled for a follow-up visit within one week to monitor PVR.

9.4 Randomization

The study design is a non-randomized single-arm design.

9.5 Pooling of Study Centers

All statistical analyses will be conducted using overall analyses pooled across all study centers.

9.6 Equipment Maintenance and Calibration

During the site initiation and training visit SRS will assure maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is performed and documented.

9.7 Procedures for Replacement of Subjects

Enrolled subjects will not be replaced.

10 EXPOSURE TO INVESTIGATIONAL DEVICES AND MEDICATIONS

10.1 Exposure to the Investigational Device

Subjects will use The Spanner for approximately 90 days, in the form of three consecutive Spanner placements each lasting approximately 30 days. The current US labeling of The Spanner does not anticipate the replacement of the initial stent after 30 days.

This is a single-armed clinical study so the study subjects will not be exposed to comparators.

10.2 Recommended Medications

10.2.1 Use of Urinary Tract Medications

Urinary tract medications may be continued, discontinued or initiated during the study period. Record the use of these medications on the eCRF system. Note that the use of certain urinary tract medications (anticholinergics and BPH medications) are prohibited from use during the study.

10.2.2 Use of Antibiotic Coverage

Men participating in the study will receive antibiotic coverage throughout the study, based on the investigator's antibiotic of choice after reviewing the scheduled urine cultures. Record the use of these medications on the eCRF system.

10.2.3 Additional Medical Care

Additional medical care in the form of medical office visits or home health care may be continued, discontinued or initiated during the study period. Record all medical care on the eCRF system.

10.3 Number of Investigational Devices Needed

The total sample size of n=105 subjects will be required for the study. Each subject is scheduled to receive three consecutive Spanner stents. Therefore, the estimated number of Spanners required for this study is 315.

Each subject will be measured once using the Surveyor Urethral Measurement Device to confirm Spanner size. The estimated number Surveyors used in the study is 105.

11 SUBJECTS

11.1 Inclusion Criteria

- Age > 45 years;
- In urinary retention and catheterized (indwelling or intermittent) for less than 180 days;
- Documented diagnostic history (within 180 days of study) of detrusor contractility (>= 15 cmH2O) confirmed via pressure-flow test;
- Negative Urinalysis on Visit 1;
- Not a candidate for pharmacologic, minimally invasive or surgical treatment of the prostate;
- Charlson Weighted Index of Comorbidity Score >= 1 (see **Attachment C**);
- Willing and able to sign the Informed Consent Form
- Willing and able to complete the follow-up protocol requirements;
- Experiencing catheter-induced discomfort.

11.2 Exclusion Criteria

- Current use of a urinary catheter daily for greater than 180 consecutive days immediately preceding entering into the study;
- Positive Urinalysis on Visit 1;
- Current or recent (within the last 6 months) urinary tract disease including urethral stricture, bladder stones, and other significant urological conditions or surgery;
- Surgery altering the normal uro-genital anatomy or abnormal urethral anatomy that affect the function of the lower urinary tract;
- History of conditions associated with neurogenic bladder, including spinal cord injury, multiple sclerosis, or Parkinson's disease;

- Use of anticholinergic medication;
- Gross hematuria when catheter is removed on Visit 1;
- Known or suspected prostate cancer;
- Prior pelvic irradiation therapy;
- Prostatic urethral length < 4 cm or > 9 cm (combined length from the top proximal side of the bladder neck to the bottom distal side of the external sphincter)
- Intravesical enlargement of the median lobe of the prostate.
- Prior penile prosthesis

11.3 Subject Withdrawal or Discontinuation

Premature withdrawal of a subject from the study for any reason must be documented using the Study Completion eCRF. Where possible, a final evaluation should be carried out including all of the evaluations specified for Visit 4.

If a subject is withdrawn due to an Adverse Event, the final visit should be completed 1 week after resolution of the Adverse Event. If a subject is unable or unwilling to complete all of the required evaluations, obtain as many as possible. In addition, if the withdrawal is associated with an Adverse Event, follow the procedures described in Section 21.

Use the Unscheduled Visit eCRF to record the results of the evaluation.

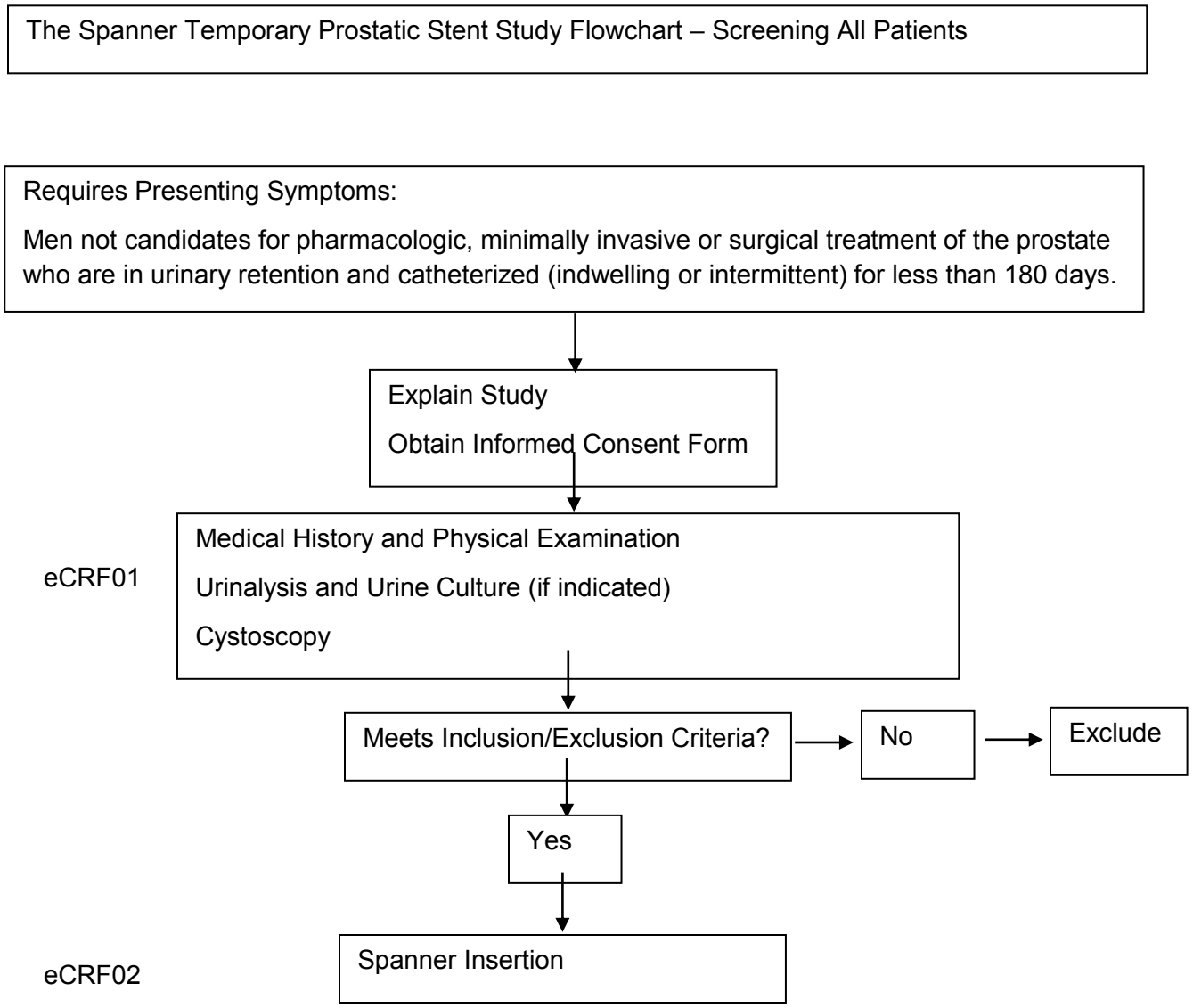
11.4 Point of Enrollment

Each study candidate to be evaluated during screening will be asked to sign an Informed Consent Form (ICF) prior to the conduct of study specific procedures. The ICF outlines the study procedures, investigational nature of the study, protocol responsibilities, and the expected risks vs. benefits of participation.

Screening is planned to be conducted entirely at Visit 1.Subjects who meet the inclusion and exclusion criteria are enrolled in the study. Device insertion is also planned to be conducted at Visit 1.

The Investigator will retain a Screening Log of those who are considered candidates for enrollment. If a subject later declines or is excluded from enrollment, the Investigator will note the reason for non-participation in the log. Potential subjects will be identified in the log by their initials only.

Figure 9. Flowchart of Subject Screening, Enrollment and Spanner Insertion



11.4.1 Positive Urinalysis Treatment and Rescreening

Subjects who are excluded as a result of a positive urinalysis may treated and rescreened at a future visit.

11.5 Expected Individual Subject Participation and Total Duration of the Clinical Investigation

The estimated time needed to meet the enrollment requirement is 4 months.

The study will consist of a 90 day treatment period. Subjects may be screened and fitted with a Spanner stent at Visit 1. The stent will be replaced at an interval of approximately 30 days (25-35 days permitted) for a total of up to 90 days of use (75-105 days permitted). Subjects will complete the study upon removal of the Spanner stent after 90 days and one follow-up telephone call post-removal.

The expected total duration of this clinical investigation is 8 months.

11.6 Number of Subjects Required

Assuming a dropout rate of 20%, the total sample size of n=105 subjects will be required for the study.

12 PROCEDURES

12.1 Study Activities Table

The study activities are listed in **Table 5.** Further descriptions of the study activities are provided in this section

Table 5. Study Activities

Activity	Visit 1 Screening, End of Catheter use (Stent #1 Placement)	Visit 2 1 Month (Stent #1 Removal. Stent #2 Placement)	Visit 3 2 Month (Stent #2 Removal. Stent #3 Placement)	Visit 4 3 Month (Stent #3 Removal)	Follow-up Phone Call
Visit Windows	**Not Applicable**	**30 ± 5 days**	**30 ± 5 days**	**30 ± 5 days**	**15-20 days post Final Stent Removal**
Informed Consent	√				
History and Physical with DRE	√				
Urinalysis with Micro	√	√	√	√	
Urine Culture & Sensitivity (If indicated)	√	√	√	√	
Uroflow	√	√	√	√	
PVR	√	√	√	√	
Subject Satisfaction Questionnaire	√	√	√	√	
IPSS		√	√	√	
Cystoscopy	√			√	
Patient is enrolled	√				
Urethral length measurement with Surveyor	√				
Stent Placement	√	√	√		
Serum Creatinine	√	√	√	√	
Adverse Events	√	√	√	√	√
Discharge					√

12.1.1 Visit 1: Screening, End of Catheter Use and Stent #1 Placement

- Obtain informed consent.
- Obtain the medical history and perform a physical examination including a digital rectal examination.
- Confirm that subject is not taking anticholinergic medication to manage bladder spasm (an exclusion criterion).
- To obtain a urine specimen:
- Remove the catheter
- Allow the subject to naturally fill his bladder
- Obtain and send a urine specimen for UA & UC&S if indicated.
- Confirm that the UA is negative.
- Perform cystoscopy and take two cystoscopy photographs: (a) of the bulbar urethra looking at a closed external sphincter, and (b) at the verumontanum looking towards the bladder.
- Subjects who meet the inclusion and exclusion criteria will be enrolled into the study.
- For directions for Spanner size selection and insertion refer to *The Spanner Physician Instructions for Use* (see **Attachment A**). Use the Surveyor urethral measurement device to determine the appropriate size Spanner.
- Insert the Spanner.
- Place cystoscope into bulbar urethra and confirm the proper location of the distal anchor. If the Spanner was incorrectly sized, the stent can be removed and replaced with the proper size. Replacement may occur one time only.
- Record any Adverse Event that occurred during sizing and Spanner insertion.
- Allow the subject to drink fluids and wait for a full bladder. Alternatively, investigator may choose to fill the bladder using cystoscopy (if cystoscopy filling is performed, note in the source and the eCRF system).
- With Stent #1 in place, perform the uroflow test followed by measurement of the PVR (abdominal ultrasound). Refer to **Attachment B** for requirements for uroflow testing.
- Provide *Subject Information Booklet for The Spanner* (see **Attachment D**) to the subject. Review each potential Adverse Event with the subject and the appropriate actions to be taken by the subject if they occur.
- Provide *Subject Emergency Removal Card* (see Attachment D) to the subject. Instruct the patient to provide the card to other care providers to inform them that the patient is wearing the Spanner.
- Obtain and send blood sample for serum creatinine.
- Have the subject complete the subject satisfaction questionnaire.
- Interview the subject for signs and symptoms of Adverse Events.
- Place test reports in the subject's study file and record in eCRF..
- Schedule the subject to return for Visit 2 (in 25-35 days).

12.1.2 Visit 2: Stent #1 Removal and Stent #2 Placement

- Have the subject complete the subject satisfaction questionnaire and an IPSS survey. Instruct the subject that he should answer the questions about symptoms related to the timeframe between visits.
- Obtain and send a urine specimen for UA & UC&S (if indicated). Place a copy of the test report in the subject's study file and record in eCRF.
- Perform a uroflow test. Measure and record the Qmax during the test. Refer to **Attachment B** for requirements for uroflow testing. Place the uroflow report in the subject's study file.
- Immediately following each uroflow test, measure the PVR using abdominal ultrasound. Record the PVR with the corresponding uroflow test. Note: If two uroflow tests were conducted PVR must be measured and reported for each test.
- Remove Stent #1
- Place Stent #2.
- Obtain and send blood sample for serum creatinine.
- Interview the subject for signs and symptoms of Adverse Events.
- Schedule the subject to return for Visit 3 (in 25-35 days).

12.1.3 Visit 3: Stent #2 Removal and Stent #3 Placement

- Have the subject complete the subject satisfaction questionnaire and an IPSS survey. Instruct the subject that he should answer the questions about symptoms related to the timeframe between visits.
- Obtain and send a urine specimen for UA & UC&S (if indicated). Place a copy of the test report in the subject's study file and record in eCRF.
- Perform a uroflow test. Measure and record the Qmax during the test. Refer to Attachment B for requirements for uroflow testing. Place the uroflow report in the subject's study file and record in eCRF.
- Immediately following each uroflow test, measure the PVR using abdominal ultrasound. Record the PVR with the corresponding uroflow test. Note: If two uroflow tests were conducted PVR must be measured and reported for each test.
- Remove Stent #2
- Place Stent #3.
- Obtain and send blood sample for serum creatinine.
- Interview the subject for signs and symptoms of Adverse Events.
- Schedule the subject to return for Visit 4 (in 25-35 days).

12.1.4 Visit 4: Stent #3 Removal

- Have the subject complete the subject satisfaction questionnaire and an IPSS survey. Instruct the subject that he should answer the questions about symptoms related to the timeframe between visits.
- Obtain and send a urine specimen for UA & UC&S (if indicated). Place a copy of the test report in the subject's study file and record in eCRF.

- Perform a uroflow test. Measure and record the Qmax during the test. Refer to Attachment B for requirements for uroflow testing. Place the uroflow report in the subject's study file and record in eCRF.
- Immediately following each uroflow test, measure the PVR using abdominal ultrasound. Record the PVR with the corresponding uroflow test. Note: If two uroflow tests were conducted PVR must be measured and reported for each test.
- Remove Stent #3
- Perform cystoscopy and take two cystoscopy photographs: (a) of the bulbar urethra looking at a closed external sphincter, and (b) at the verumontanum looking towards the bladder.
- Obtain and send blood sample for serum creatinine.
- Interview the subject for signs and symptoms of Adverse Events.
- Schedule the subject for a follow-up phone call (in 15-20 days).

12.1.5 Phone Call #1

- Via telephone, interview the subject for signs and symptoms of Adverse Events. Record information on the Adverse Event eCRF.
- Discharge subject from study.

NOTE: Any subject with an ongoing or unresolved adverse event may continue to be followed until the event is resolved. The subsequent follow up and resolution should be documented on the Adverse Event eCRF.

12.1.6 Unscheduled Visits

If the subject returns to a medical facility due to a BPH or stent related issue, then complete an Unscheduled Visit eCRF.

12.1.7 Post Study Completion - Continued Access

If, at the completion of all study visits, the Spanner is not yet approved for this indication, then the investigational device may be made available during the preparation and review of the marketing application, to allow enrolled subjects to extend their use of the device.

These continued access visits will be conducted in compliance with the clinical investigational plan, ISO 14155, and 21 CFR Parts 812, 50, 54, and 56. The study visits will be conducted by the delegated study staff using the eCRFs, including visit, unanticipated visit, and adverse event monitoring. There will be continued CRO oversight and monitoring during this entire continued access period and additional safety and effectiveness data will be collected.

Subjects must have completed the requirements of the final telephone visit described in Section 12.1.5 above before obtaining voluntary continued access. Subjects who volunteer for continued access will be required to attend monthly study visits (30 days +/- 5 days) repeating the requirements of Visit 3 (the Continued Access Visit requirements are listed below). These visits may continue until use of the Spanner is no longer clinically indicated or desired, or until the Spanner receives marketing approval for this indication, whichever is sooner.

12.1.7.1 Continuing Access Visits after Study Completion: Stent Removal and Placement

- Have the subject complete the subject satisfaction questionnaire and an IPSS survey. Instruct the subject that he should answer the questions about symptoms related to the timeframe between visits.
- Obtain and send a urine specimen for UA & UC&S (if indicated). Place a copy of the test report in the subject's study file and record in eCRF.
- Perform a uroflow test. Measure and record the Qmax during the test. Refer to Attachment B for requirements for uroflow testing. Place the uroflow report in the subject's study file and record in eCRF.
- Immediately following each uroflow test, measure the PVR using abdominal ultrasound. Record the PVR with the corresponding uroflow test. Note: If two uroflow tests were conducted PVR must be measured and reported for each test.
- Remove Stent
- Place Stent.
- Obtain and send blood sample for serum creatinine.
- Interview the subject for signs and symptoms of Adverse Events.
- Schedule the subject to return for next Visit (in 25-35 days).

12.2 Foreseeable Factors that May Compromise the Outcome of the Clinical Investigation

Use of anticholinergic medication to manage bladder spasm is an exclusion criterion. Subjects taking anticholinergic medication are asked to discontinue use of the medication for the duration of the study.

The inclusion assessment requires evidence of detrusor muscle contractility. Subjects entering the study with poor bladder contractility could result in unanticipated device failures.

13 MONITORING PLAN

13.1 Monitor Name and Address

The monitoring of study sites and the audit functions will be the responsibility of the study sponsor or their designee(s):

SRS Medical Systems, Inc.
76 Treble Cove Road, Building 3
North Billerica, MA 01862

13.2 Monitor Responsibilities

A sponsor may designate one or more appropriately trained and qualified individuals to monitor the progress of a clinical investigation. A monitor need not be a person qualified to diagnose and treat the disease or other condition for which the test article is under investigation, but somewhere in the direct line of review of the study data there will be a person so qualified.

Each monitor will be trained on monitoring per Standard Operating Procedures (SOPs), the protocol and protocol-specific monitoring plan prior to conducting any study-specific activities.

13.3 Procedures

SRS Medical is responsible to ensure that the study is monitored and to confirm proper conduct and progress of the study including adequate protection of human subjects and the integrity of the clinical study data is of the highest quality. The sponsor shall assess the extent and nature of monitoring appropriate for the clinical investigation, including the strategy for source data verification, based on considerations such as the objective, design, complexity, size, critical data points and endpoints of the clinical investigation. Results of this assessment shall be used to develop a monitoring plan.

The monitor shall have access to the source documents and other information needed to ensure investigator compliance with the clinical investigation plan and applicable rules and regulations, and to assess the progress of the clinical investigation.

Site visits will be made before the study begins, at regular intervals during the study, and at the study closeout. Communication by telephone, mail, and e-mail may be used as needed to supplement site visits. The investigator and study personnel will cooperate with the sponsor and their representatives, provide all appropriate documentation, and be available to discuss the study.

13.4 Monitoring and Audit Visits

Site visits will be made before the study begins, at regular intervals during the study, and at the study closeout. Communication by telephone, mail, and e-mail may be used as needed to supplement site visits. The Investigator and study personnel will cooperate with the sponsor and their representatives, provide all appropriate documentation, and be available to discuss the study. Adequate time and space for these visits should be allocated by the investigator.

According to the guidelines on Good Clinical Practice, the monitor will check the CRF entries against the source documents. The consent form will include a statement by which the subjects allow the sponsor's duly authorized personnel to have direct access to source data which supports data on the case report forms (e.g.: medical records, clinic charts and office notes, appointment books, original laboratory records, uroflow printouts, cystoscopy reports, etc.). These personnel, bound by professional confidentiality, will not disclose any personal identity or personal medical information outside of the realm of study data.

The monitoring and auditing visits may include but are not limited to the following:

13.4.1 Site Qualification and Site Initiation Visit

The Site Qualification Visit enables SRS Medical to determine acceptability of site for subject population, expected enrollment, appropriate space for study equipment including limited access to investigational product and availability of an accredited clinical laboratory. These visits also determine the qualification and availability of investigator, sub-Investigators, and support staff, staff's previous clinical research experience, and the monitoring requirements. This visit will be documented in a site qualification report. This visit may be completed on site or remotely. Investigation site selection rationale can be based on prior experience of the sponsor with the principal investigator or the investigation site. Previously used sites may not require an addition qualification visit however justification for their use will be documented.

During the Site Initiation Visit (or Investigator Meeting), a review of the CIP, discussion of the Investigator's Brochure and discussions on the function/use of the system/equipment with the investigator/staff will occur. Should the PI choose to delegate study related tasks to qualified personnel under their direct supervision, this will be documented on the Delegation of Authority Log that will include names, initials, signatures, functions, and designated authorizations for the principal investigator and members of the investigation site team. In addition, delegated site personnel must be trained on the study relative to the tasks that have been assigned to them and this will be documented on the training log.

Before enrolling any subjects in this study, site personnel and the investigator will be trained on the protocol, the CRFs and instructions for their completion, the procedure for obtaining informed consent, and the procedure for reporting AEs, SAEs, SADEs and UADEs.

13.4.2 Interim Monitoring Visits

Interim monitoring visits are made periodically per the monitoring plan to assess the investigator's adherence to the CIP, IRB requirements, maintenance of records and reports and review of source documents for accuracy, completeness, legibility, omissions and equipment calibration records. In cases where the site is not able to grant the monitor access to the electronic medical record, the investigational site staff will obtain copies of the electronic medical record and number the pages consecutively, sign and date the packet to indicate they are certified copies of the medical record. The monitors will acquire information to assess the progress of the study (toward meeting study objectives) and identify any concerns that stem from observation of device performance and/or review of the investigator's subject records, study management documents**,** regulatory documents, device tracking and verifying each subject has signed informed consent documents. Resolution of outstanding issues and completion of assigned tasks will be documented by the monitors. The Investigator agrees to accommodate and be available at monitoring visits conducted at a reasonable time in a reasonable manner, as needed.

13.4.3 Close Out Visit

The monitor will conduct a final Close-Out Visit at the sites for all sites. If investigational product remains at the site then a site visit is required to collect and document the return of any unused investigational products. A remote close out visit may occur at sites where investigational product has never been shipped or final device reconciliation has been completed at previous monitoring visits. Close out visits instruct the site on adherence to record retention requirements, ensure final data has been reconciled and a final monitoring report, to include the study status at the site, shall be prepared by the monitors (or designates).

Routine close-out activities shall be conducted to ensure that the principal investigator's records are complete, all documents needed for the sponsor's files are retrieved, remaining clinical investigation materials are retrieved or disposed of, previously identified issues have been resolved and all parties are notified including the EC and regulatory authorities, if required.

Ensure that:

- essential documents are complete and up to date,
- CRFs are completed,
- outstanding queries are resolved,
- the current status of all ongoing adverse events is documented,
- arrangements are made for archiving and record retention, and
- disposition of investigational devices and other clinical investigation materials is documented.

13.4.4 Site Audits

SRS Medical may choose to perform random audits throughout the study as part of implementing quality assurance. The purpose of this audit (which is independent of and separate from routine monitoring or quality control functions) is to evaluate study

conduct and compliance with the protocol, applicable regulatory requirements, and study-specific procedures. The plan for this audit may be guided by the number of subjects at the site and any identified problems (such as non-compliance to the protocol). Non-compliance to the protocol and applicable regulatory requirements by the investigator/institution will lead to prompt action by SRS Medical to secure compliance. If the monitoring and/or auditing identify serious and or persistent non-compliance by the investigator/institution, SRS Medical may terminate the investigator/institution participation in the study.

14 STATISTICAL CONSIDERATIONS

This study is a multi-center, prospective, open-label, single-armed clinical study.

14.1 Level of Significance, Power and Sample Size

A hypothesis test that the proportion of successes in the treatment group is statistically significantly greater than 50% will be computed. In order to have an 80% chance of showing that the success proportion in the Spanner group is statistically significantly greater than 50%, assuming that the device can achieve a 65% success rate, with α=0.05, a sample size of n=85 completers will be needed for the study. The sample size calculation was based on an exact binomial one sample test.

14.2 Expected Drop-out Rates

Assuming a dropout rate of 20%, the total sample size of n=105 subjects will be required for the study. A hypothesis test that the proportion of successes in the treatment group is statistically significantly greater than 50% will be computed.

14.3 Primary Effectiveness Variable and Pass/Fail Criteria

The primary effectiveness endpoint is the success/failure of the subject to have a successful urinary void at all four study visits: (a) upon initial placement of the first stent (Visit 1), and (b) at all three visits in which the subject has a stent placed for 30 days (Visits 2, 3 and 4).

The primary effectiveness endpoint will be marked as a failure for a subject if any of the following occur:

- PVR of >150 ml at any visit (Visits 1, 2, 3, and 4)
- The subject withdraws from the trial

14.4 Secondary Effectiveness Variable

The secondary effectiveness variables for this study are:

- PVR through the first removal visit is ≤150 ml of urine (Visits 1 and 2)
- PVR through the first removal visit is ≤250 ml of urine (Visits 1 and 2)
- PVR through the third removal visit is ≤250 ml of urine (Visits 1-4)

14.5 Exploratory Effectiveness Variable

The exploratory effectiveness variables for this study are:

- Qmax measurement
- IPSS Total Symptom Score

Qmax measurements will be taken from the initial stent placement forward (Visits 1, 2, 3 and 4), while the IPSS instrument will be administered from the initial stent removal forward (Visits 2, 3, and 4). Qmax and IPSS scores will be the change from baseline values (Visit 1 for Qmax and Visit 2 for IPSS).

14.6 Safety Variables

Safety variables that will be recorded are:

- Treatment emergent adverse events deemed to be related to the implantation procedure

- Treatment emergent adverse events deemed to be related to the device
- All other adverse events

14.6.1 Analysis Populations

The following analysis populations will be defined.

- Intent-to-Treat (ITT) Population – The ITT population will consist of any enrolled subject who underwent an attempted Spanner device implant procedure.
- Per Protocol (PP) Population – The PP population will consist of all subjects who are enrolled in the study, have been implanted with a Spanner device, and have completed all study visits with no major protocol deviations while enrolled in the study[2].
- Safety Population – The safety population will consist of all subjects who are enrolled in the study.

The analysis of the primary and secondary efficacy endpoints will be conducted on ITT and PP populations. The primary analysis set will be the ITT analysis. All safety analyses will be conducted on the safety population.

The study subjects to be excluded from the PP analysis set and the reasons for their exclusion will be determined and documented prior to statistical analysis. These decisions will not be outcome-data driven.

14.6.2 Analysis of Baseline and Demographic Characteristics

Baseline and demographic characteristics will be summarized for all subjects in the safety population. Continuous variables will be displayed via summary statistics (mean, median, sample size, standard deviation, minimum, and maximum). Categorical variables will be summarized via counts and percentages.

14.6.3 Analysis of the Primary Effectiveness Variable

The following hypotheses will be tested at a one-sided $\alpha=0.025$ level of significance:

$H_{a0}: p_s \leq 50\%$ vs. $H_{a1}: p_s > 50\%$

where p_s is the proportion of subjects with maintenance of successful voiding during the Spanner implantation period. This hypothesis will be tested using a one-sample exact binomial test. Summary statistics (counts and percentages) will be computed on the primary endpoint along with a 95% confidence interval on the treatment group success proportion.

[2] A major protocol deviation is defined as any protocol deviation that may affect the primary endpoint.

14.7 Analysis of the Secondary Effectiveness Variables

The statistical analysis of the secondary effectiveness variables will be described in the Statistical Analysis Plan (SAP) document for the study. The SAP will be completed and signed by the Sponsor before the enrollment of the first subject in the study.

14.8 Analysis of Safety Variables

All adverse events (AEs) will be observed for each subject from enrollment until termination from the study. A treatment emergent adverse event is defined as an adverse event whose start date is on or after the procedure date. If the procedure date and/or the AE start date are missing, the AE will be considered treatment emergent.

Prior to analysis, all adverse events (AEs) will be coded using the Common Terminology Criteria for Adverse Events (CTCAE). All AEs will be listed.

14.8.1 Interim Analyses

No formal interim analyses will be conducted during this study.

14.9 Specification of subgroups for analysis

None planned

14.10 Reporting Deviations from the SAP

Any deviations from the planned statistical analysis will be described and justified in the Final Study Report, if required.

14.11 Treatment of Missing Data, Including Lost to Follow-up and Withdrawals

For endpoint evaluations subjects with missing data due to missed visit, lost-to-follow-up or study withdrawal will have their missing data imputed using a multiple imputation method. Unless otherwise specifically noted, no statistical techniques will be used to impute missing values in other analyses of study data.

14.12 The Number of Subjects at Each Center

The study will be carried out at up to 10 clinical centers with a maximum of 45% of subjects enrolled at any one clinical center.

15 DATA MANAGEMENT

15.1 Electronic Case Report Form Completion

Electronic case report forms (eCRFs) shall be developed to capture the data for each enrolled subject as required by the CIP. The eCRFs shall include information on the condition of each subject upon entering, and during the course of the clinical investigation, and exposure to the investigational device.

It is the responsibility of the investigator to complete and maintain adequate and accurate eCRFs, which have been designed by the sponsor to record all observations and other pertinent data to the clinical investigation. All information provided on the eCRFs must have source documentation in the subject's chart in order to verify the data.

Any discrepancies shall be explained in writing. All observations relevant to the clinical evaluation will be entered on the appropriate eCRFs for each subject enrolled in the clinical study. All eCRFs will be signed by the Investigator or their designee.

Once eCRFs have been reviewed by the monitor and collected from the study site, all corrections will be addressed through the query system provided with the data capture system. The monitor or Sponsor will issue the queries to the site personnel at or between monitoring visits.

All documents, eCRFs, photos or other subject data provided to SRS Medical will be de-identified. The subject ID number, date and visit will be written on each document. All clinical data should be provided to the sponsor within 1 week of the visit/procedure/test or sooner if requested.

15.2 Data Confidentiality

Data is anonymized on data collection forms. Information sent to the sponsor is identified only by the assigned study ID number, initials, and age.

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited with the exceptions noted below. Subject confidentiality will be further ensured by utilizing identification code numbers to correspond to data in the study records and databases. The investigator will maintain a separate personal identification list or master list (which matches subject study identification numbers with their names) to enable records to be identified. This list will be maintained and stored in a secured location. The list will be accessed only by research study staff and will be destroyed after study completion as recommended by the IRB and Health Information Protection guidelines and national regulation.

Medical information may be given to the subject's personal physician or to other appropriate medical personnel responsible if required for the welfare of the subject if the subject provides such consent.

15.3 Access to Data

The Investigator / institution will permit trial related sponsor monitoring, audits, IRB review and regulatory inspection, providing direct access to all related source data / documents. Electronic case report forms and all source documents, including progress notes and copies of laboratory and medical test results will be available for review by the sponsor, the IRB and the FDA. Subjects will be informed that the IRB and the FDA will have access to this information when requested for inspection.

During regular business hours and upon reasonable prior notice to the site the sponsor's authorized representative(s) and governmental regulatory authorities shall, to the extent permitted by law, be permitted to:

- Examine and inspect the site's facilities for performance of the study to monitor compliance with the protocol; and
- Inspect and copy all data and work products relating to the study (with a de-identifying process after copying, to ensure no identified material leaves the institution).

Site shall cooperate with any other regulatory authority with appropriate jurisdiction, and with sponsor's prior notice, allow them access to applicable records and data.

15.4 Data Review, Database Cleaning and Queries

The sponsor clinical personnel or designee(s) will review the data for legibility, completeness, and logical consistency. Requests for data clarification or correction are forwarded to the investigative site for resolution.

All documents and data shall be produced and maintained in a way that assures control and traceability. Where relevant, the accuracy of translations shall be guaranteed and documented. All documents, and subsequent versions, related to a clinical investigation shall be identifiable, traceable and appropriately stored to provide a complete history of the clinical investigation. SRS Medical or designee's standard operating procedures, work procedures and forms for data management, treatment of data, source data verification, data archiving and retention procedures will be used in the conduct of the trial.

Written procedures shall be implemented to:

a) establish and document requirements for the electronic clinical data system to receive and process data,

b) verify and validate that the requirements for the electronic clinical data system can be consistently met,

c) ensure attributability, completeness, reliability, consistency and logic of the data entered,

d) ensure accuracy of reports,

e) ensure that data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail),

f) maintain a security system that prevents unauthorized access to the data, both internally and externally,

g) maintain a list of individuals who have access to the electronic data system as well as the dates of access and privileges granted to each user,

h) ensure that all completed CRFs are signed by the principal investigator or authorized designee,

i) maintain adequate backup, retention and retrievability of the data, and

j) train users on proper use of the system.

15.5 Database Development

SRS Medical will perform or oversee all technical functions to design and program a database system to house the eCRF data that is compliant with 21 CFR Part 11 and relevant FDA guidance documents:

- Computerized Systems Used In Clinical Investigations
- E6 Good Clinical Practice: Consolidated Guidance

SRS Medical databases will incorporate data entry and verification, time-stamped audit trails, protection of human subjects, restricted access, visit and eCRF tracking, and data security at the component level. SRS Medical will configure the database to allow data entry and record management from data collected on paper case report forms into electronic data entry screens.

15.6 Database Validation

Validation techniques used by SRS Medical are consistent with FDA's guidelines applicable at the time of this study protocol. Each database must pass a series of standard tests that demonstrate the usability and correctness of the database system to approved specifications.

15.7 Record Retention Period

Investigators are required to maintain the records listed below in an orderly, retrievable file during and after the investigation for the following period: 3 years after the date that (1) the data is no longer needed for an FDA submission or (2) the date the investigation is completed or terminated whichever is longer. The Investigator is advised to contact the Sponsor to confirm the status of the device *prior to discarding* records.

- All reports required in Section 21.
- All correspondence about the study with another investigator, the Sponsor, the IRB, and FDA.
- Documents evidencing each subject's informed consent and reasons for use of a device without informed consent (if applicable).
- Each subject's completed case report forms and source documents such as medical records and results of diagnostic tests.
- The protocol and protocol amendments (if applicable) with documents showing the dates and reasons for any deviation from the protocol (if applicable).
- Any additional records required by the reviewing IRB.

16 AMENDMENTS TO THE CIP

SRS will submit a supplemental application to the FDA and obtain approval for changes in the investigational plan that may affect the scientific soundness of the investigation or the rights, safety, or welfare of the subjects. SRS will receive IRB approval when the change involves the rights, safety, or welfare of subjects.

17 DEVIATIONS FROM THE CIP

Investigators are required to conduct this study in accordance with the signed Investigator's Agreement this investigational plan, applicable laws and FDA regulations, and any conditions of approval imposed by the reviewing IRB and FDA. CIP deviation is defined as failure to follow, intentionally or unintentionally, the requirements of the protocol and associated documents. The investigator is not allowed to deviate from the CIP except with prior approval or under emergency circumstances. All deviations shall be documented on an eCRF and explained, regardless the reason for the deviation.

17.1 Notification Requirements

According to FDA regulation 21 CFR 812.150(a)(4), an investigator shall notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life and physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than five working days after the emergency occurred. This information must also be included in the final study report to the IRB. Except in such an emergency, prior approval by the sponsor and the IRB are required for any change in or deviations from a plan. If these changes or deviations could affect the scientific soundness of the plan or the rights, safety or welfare of human subjects, FDA approval is also required in accordance with 21 CFR 812.35(a). If the investigator uses a device without informed consent, the investigator shall report this to the IRB within 5 working days of the occurrence.

17.2 Corrective and Preventive Actions and Principal Investigator Disqualification Criteria

If noncompliance with the study protocol or Investigator's Agreement is found during a site visit, a discussion regarding the non-compliance will occur with the investigator or his/her staff at the time, determining corrective action, and obtaining the investigator's concurrence. Shipment of additional devices will not occur until nonconformities are addressed. Documentation of the activity will be included on the monitoring visit report.

Serious repetitive violations of the study protocol or Investigator's Agreement may warrant exclusion from the study. Serious violations include, but are not limited to:

- enrolling subjects without informed consent
- enrolling subjects who do not meet the inclusion/exclusion criteria
- failure to follow procedures called out by the protocol
- failure to report adverse events
- failure to submit the reports required under 21 CFR 812.150(a) or maintain the records required under 21 CFR 812.140 (a)

A decision for exclusion will be made by Clinical Affairs, Regulatory Affairs and SRS management, and documented in the administrative file. The investigator and the reviewing IRB for the site will be notified in writing. FDA will be notified of any such action and the reason for the action. Unused investigational device supplies will be withdrawn from an excluded site.

17.3 Procedure for Analyzing CIP Deviations

SRS Medical will analyze the documented deviations based on frequency and significance, and identifying any necessary corrective and/or preventive action (e.g. amending the CIP or to terminate the study early) internally and with the clinical investigator(s) and report them in the CRFs and in the final report.

If significant non-compliance is identified, prompt action to either secure compliance, or discontinue shipments of the device to the PI and terminate the site's participation in the study will be performed if applicable. In circumstances of study termination, SRS

Medical will also require that the PI return the investigational devices, unless this action would jeopardize the rights, safety, or welfare of a subject.

18 INVESTIGATIONAL DEVICE DOCUMENTATION AND SHIPPING

18.1 Labeling

The investigational system shall bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor, and the quantity of contents, if appropriate. The label, or other labeling, shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

19 STATEMENTS OF COMPLIANCE

19.1 Statements of Compliance

This clinical investigation shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki[3]. These principles protect the rights, safety and well-being of human subjects, which are the most important considerations and shall prevail over interests of science and society. These principals shall be understood, observed and applied at every step of the investigation.

This study will be conducted in compliance with clinical investigational plan, ISO 14155, and 21 CFR Parts 812, 50, 54, and 56.

The clinical investigation shall not begin until the required approval/favorable opinion from the IRB and FDA approval of this CIP has been obtained via an IDE Application.

Any additional requirements imposed by the regulatory authorities or the IRB shall be followed as appropriate

19.2 Insurance

Until the termination of the clinical trial or up to one year past explant of the last study participant, whichever is sooner, SRS Medical shall maintain comprehensive general liability insurance, including product liability insurance, underwritten by a reputable insurance carrier in an amount not less than 2 Million USD per occurrence and 2 Million USD in the aggregate.

20 INFORMED CONSENT PROCESS

The Informed Consent Form (ICF) includes the description for subject privacy for the study. The template includes all aspects of the clinical investigation that are relevant to the subject's decision to participate in the clinical investigation. This template must be customized for each investigational site to receive IRB approval of the ICF and final approval of the ICF by SRS Medical or designee.

[3] Declaration of Helsinki, available at http://www.wma.net

The consent form will be translated into the native language as required by local law, will not waive or appear to waive the subject's legal rights, and will be written in non-technical terms that would be understandable to subjects. The Principal Investigator (PI) or designee cannot seek the consent of prospective study subjects until the IRB has approved the current version of the Investigational Plan and the ICF.

Prior to initiation of any study specific procedures, including screening and questionnaires, informed consent must be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The IRB and SRS Medical approved ICF will be signed and dated by the subject. A PI shall seek the consent only under circumstances that provide the prospective subject sufficient opportunity to consider all aspects of the study and whether or not to participate in the study and that minimize the possibility of coercion or undue influence. The subject will have the benefits and risks explained to them and will be given the opportunity to ask questions of the personnel conducting the study. The ICF will be signed and dated by both the subject and the person conducting the consent process (PI or designee). The signed ICF must be filed in the hospital/clinic medical chart or with the study subject documentation and be available for monitoring and auditing. A copy of the signed ICF must be given to the subject for their records.

If new information about the study or the medical device becomes available during the course of the study, the information will be provided to new and existing subjects, and if relevant, request existing subjects to confirm their continued participation in the study by signing a new informed consent.

Due to the level of subject participation required for testing or training in the study, it is anticipated that all subjects will be able to make their own informed decision regarding participation and no vulnerable subjects will be enrolled in this study and the study device will not be used in emergency situations.

21 ADVERSE EVENTS, ADVERSE DEVICE EFFECTS AND DEVICE DEFICIENCIES

21.1 Definitions

21.1.1 Adverse Event- (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. (ISO 14155:21011(E)).
Note 1: this definition includes events related to the investigational medical device or the comparator. Note 2: This definition includes events related to the procedures involved. Note 3: For users or the persons, the definition is restricted to events related to investigational medical devices

An AE can be any unfavorable and intended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product whether or not related to the investigational product (E6 Guidance).

All Device Deficiencies, whether resulting in a symptom or not, should be reported as an AE.

An adverse event maybe further characterized as an ADE:

21.1.2 Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device (ISO 14155:2011(E)). *Note1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from user error or from intentional misuse of the investigational medical device.*

21.1.3 Anticipated Adverse Events

- Adverse event that was previously identified in nature, severity, or degree of incidence in the investigational /plan or application including supplementary plan or application or investigator's brochure.
- Any normal expected post-treatment complaints or symptoms that involves a clinically significant change in severity or duration of symptoms, or requires clinical intervention that is different from ordinary postoperative care: i.e. temporary abdominal pain, regurgitation or vomiting associated with eating.
- Complications associated with anesthesia, cystoscopy of blood draw.
- An anticipated adverse event may be either serious or non-serious

21.1.4 Serious adverse event (SAE)

An SAE is an event that has led to any of the following:

- Led to death
- Led to a serious deterioration on the health of a subject that either resulted in:
- A life-threatening illness or injury, or
- A permanent impairment of body structure or body function, or
- in-patient hospitalization (hospital admission) greater than 24 hours or prolonged hospitalization
- medical or surgical intervention to prevent life-threatening illness, permanent impairment of body structure or body function
- Led to fetal distress, fetal death or congenital abnormality or birth defect. (ISO 14155:21011(E)).

21.1.5 Serious Adverse Device Effect (SADE):

An SAE may be further characterized as a serious adverse device effect (SADE) if it is related to the use of the investigational device.

21.1.6 Unanticipated Adverse Device Effects (UADE):

UADE are defined as any serious adverse effect on health or safety or any life-threatening problem, or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including supplementary plan or application), or

any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CRF 812.39s).

21.1.6.1 Unanticipated Serious Adverse Device Effect (USADE):

A UADE may be further defined as a USADE if it is related to the use of the investigational device.

21.1.7 Not Considered Adverse Events

The following are not considered to be adverse events:

- **Pre-existing Conditions:** Any current condition that is recorded as a pre-existing condition on a case report form is not considered an adverse event unless there is a worsening of that condition in terms of nature, severity, or degree of incidence.

21.2 AE Assessment, Documentation and Reporting

Complete an Adverse Event eCRF. Provide a complete description of the nature, severity and circumstances of the Adverse Event including results of physical examinations, diagnostic tests, treatments given, outcome of treatments and the subject's final condition.

Reports to the Sponsor.

Report all Serious Adverse Events, and Unanticipated Adverse Device Events to the Sponsor as soon as adequate information about the adverse event is available, but no later than 5 working days from the date the Investigator first became aware of the event. Notify the Sponsor by completing, or partially completing, Adverse Event eCRF.

Reports to the IRB.

Investigators are required to report all Unanticipated Adverse Device Events (See 21.3 for definition) to the reviewing IRB no later than 10 working days from the date that the Investigator first became aware of the event. In addition, the Investigator must comply with any other reporting requirements of the reviewing IRB.

21.3 Reporting Device Deficiencies.

If a device deficiency is suspected, The Spanner should be evaluated to determine if removal or replacement is necessary. All device deficiencies related to the identity, quality, durability, reliability, safety or performance of an investigational medical device shall be documented throughout the clinical investigation and appropriately managed by the sponsor. All Device Deficiencies, whether resulting in a symptom or not, should be reported as an Adverse Event and an Adverse Event eCRF should be completed.

21.4 Foreseeable Device Deficiencies/Malfunctions

List is provided in Section 7 of this CIP, Anticipated Device Deficiencies.

21.5 Managing Adverse Events and Device Deficiencies

The following guidelines are recommended for managing Adverse Events and complications that may occur during the study. As these are only guidelines, the final decision for appropriate management of Adverse Events rests on the investigator's clinical judgment. Contact the SRS Medical for additional guidance on a case-by-case basis.

- If a device deficiency is known or suspected, The Spanner should be evaluated to determine if removal is necessary.
- If a device is removed in either in association with an adverse event or a device deficiency, then the subject is to attend the next scheduled visit.
- If the subject has no unresolved adverse events, then the subject should complete the study visit, including replacement of the stent and resume the study visit schedule.
- If the subject has unresolved adverse events, then complete as much of the study visit as possible, but do not place the stent. The subject should resume the study schedule and be reassessed at the next visit for the possibility of stent placement.

21.5.1 Bacteriuria

Bacteriuria will be considered as present if the urine culture indicates a single organism with a colony count >100,000 CFU and the subject is asymptomatic.

No treatment is required for asymptomatic bacteriuria and the subject may continue in the trial. Only the initial occurrence of bacteriuria should be reported on the Adverse Event eCRF. If the event persists with the same organism to the next visit, it would still be considered the same event. If bacteriuria with a new organism is present at a subsequent visit, it would be classified as a new event. If the bacteriuria converted to a symptomatic urinary tract infection, it would also be considered a new event (see below).

21.5.2 Symptomatic Urinary Tract Infection

The criterion below will be used to determine if a subject has a symptomatic UTI. The criterion is based on a publication from the Center for Disease Control[4].

Symptomatic UTIs should be treated by the physician. If the physician determines that The Spanner should be removed as part of the treatment of a symptomatic UTI, the subject should continue in the study and attend the next study visit. Spanner devices removed for symptomatic UTIs need not be returned to the Sponsor.

Criterion for a symptomatic UTI:

Subject has at least ***one*** of the following signs or symptoms:

- • fever (>38°C)
- • suprapubic tenderness*****
- • costovertebral angle pain or tenderness*****

[4] Urinary Tract Infection (Catheter-Associated Urinary Tract Infection [CAUTI] and Non-Catheter-Associated Urinary Tract Infection [UTI]) and Other Urinary System Infection [USI]) Events, January 2015

- • urinary frequency*
- • urinary urgency*
- • dysuria*

AND,

Subject has a urine culture with no more than two species of organisms, at least one of which is a bacteria of ≥100,000 CFU/ml.

On a stent removal visit, if a subject has one of the above signs or symptoms **and** a positive urinalysis on that visit, the removal of stent is postponed as follows:

- Urine sample sent for Urine Culture and Sensitivity (as scheduled)
- The Subject will be scheduled for a follow-up visit to remove or replace the stent at a minimum of 72 hours after the initiation of treatment of the UTI.

*With no other recognized cause

21.5.3 Hematuria

Transient gross hematuria from the trauma of The Spanner insertion may occur during the follow up period. If this occurs, Spanner removal is not required but the incident should be reported as an Adverse Event.

If persistent gross hematuria or an event with significant frank bloody urine occurs in the follow up period, The Spanner should be removed. Cystoscopy should be performed as soon as possible and practical after removal of The Spanner to determine the source of bleeding and whether or not it is related to use of The Spanner. An Adverse Event should be recorded and the device returned to the Sponsor. The subject should continue in the study and attend the next study visit.

21.5.4 Pain or Perceived Bladder or Urethral Spasm

Severe pain. If a study subject experiences persistent severe pain believed to be related to The Spanner, it should be removed. Following removal of The Spanner, a cystoscopy should be performed as soon as possible and practical to determine whether trauma or injury to the urethra, bladder or bladder neck is the probable source of the pain. An Adverse Event should be recorded and the device returned to the Sponsor. The subject should continue in the study and attend the next study visit.

Moderate-mild pain or discomfort, perceived bladder or urethral spasm. The decision to remove The Spanner is left to the discretion of the subject and investigator. An Adverse Event should be recorded. If the device is removed due to the symptoms, it must be returned to the Sponsor. *Note: If the device is removed, the subject should continue in the study and attend the next study visit.*

21.5.5 Meatal Irritation and Discomfort

Meatal Irritation. Irritation is defined as an inflammatory response at the meatus. The decision to remove The Spanner is left to the discretion of the subject and investigator.

An Adverse Event should be recorded. If the device is removed due to the symptoms, it must be returned to the Sponsor. *Note: If the device is removed, the subject should continue in the study and attend the next study visit.*

Meatal Discomfort. The decision to remove The Spanner is left to the discretion of the subject and investigator. An Adverse Event should be recorded. If the device is removed due to the symptoms, it must be returned to the Sponsor. *Note: If the device is removed, the subject should continue in the study and attend the next study visit.*

21.5.6 Migration or Expulsion of the Device

Migration- If migration of the Spanner is suspected, perform an x-ray or cystoscopy, if possible, to document the location of the device prior to attempting removal.

Subsequently, the device should be removed, either by locating and grasping the retrieval suture to remove the device or, if the retrieval suture cannot be located, by retrieving the device cystoscopically. In either case, care should be taken to assure that the proximal balloon is deflated prior to withdrawing the device through the urethra and that all of the device components are removed. (If possible, the balloon may be deflated by cystoscopically locating the suture that is attached to the proximal balloon and pulling it to remove the balloon drain plug to allow the balloon to empty. Alternately, the balloon may be ruptured cystoscopically using a cautery tool or wire guide.)

Record a Device Deficiency eCRF and return the device to the Sponsor. Provide a detailed description of any damage to the device that is known to have occurred as a result of removing the device (i.e. balloon punctured, suture between stent and distal anchor cut).

The subject should continue in the study and attend the next study visit.

Expulsion - Record a Device Deficiency eCRF and return the device to the Sponsor. Provide a detailed description of any damage to the device that is known to have occurred as a result of removing the device (i.e. balloon punctured, suture between stent and distal anchor cut). The subject should continue in the study and attend the next study visit.

Urinary Retention- If urinary retention occurs, and there is a question of whether the retention is related to bladder performance, an urodynamic evaluation should be considered to determine if bladder performance is contributing to urinary retention.

For urinary retention in a subject, cystoscopy or an x-ray should be performed prior to removal of The Spanner to verify whether device migration or inadequate stenting is the cause of the urinary retention. Subsequently, the device should be removed. After Spanner removal, the subject should be evaluated to determine voiding capability and urinary catheter bladder drainage instituted if needed.

An Adverse Event should be recorded and the device returned to the Sponsor. The subject should continue in the study and attend the next study visit.

21.5.7 Occlusion of the Device Drainage Lumen or Device Malfunction

If occlusion or malfunction of the device is suspected, The Spanner should be removed. A Device Deficiency eCRF should be completed and the device returned to the Sponsor. The subject should continue in the study and attend the next study visit.

21.5.8 Criteria for Spanner Removal and Re-establishment of Bladder Drainage: Clinically Significant Post Void Residual Urine

For purposes of the clinical trial, PVR > 350 ml on two measurements taken within a few hours will be considered as significant and requiring intervention. If the subject has a PVR > 350 ml on two measurements taken within a few hours at any scheduled or visit, or at other medical visit, the intervention should include the removal of The Spanner, the re-establishment of bladder drainage (CIC or Foley) and the premature withdrawal of the subject from the study.

21.6 Emergency Sponsor Contact Information for Reporting SAE and SADE

Lee Brody
SRS Medical
Telephone: (978) 932-0400 / (617) 308-4056 [24 hours]
Email: brody@srsmedical.com

21.7 Data Monitoring Committee,

A Data Monitoring Committee has not been established.

22 VULNERABLE POPULATION

This study will not recruit nor enroll subjects from vulnerable populations nor under emergency conditions.

23 SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

23.1 Procedure for Suspension or Premature Termination

The sponsor may suspend or prematurely terminate either a clinical investigation in an individual investigation site or the entire clinical investigation for significant and documented reasons. A principal investigator, IRB, or regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the investigation sites for which they are responsible. If suspicion of an unacceptable risk to subjects arises during the clinical investigation, or when so instructed by the IRB or regulatory authorities, the sponsor shall suspend the clinical investigation while the risk is assessed. The sponsor shall terminate the clinical investigation if an unacceptable risk is confirmed.

The sponsor shall consider terminating or suspending the participation of a particular investigation site or investigator in the clinical investigation if monitoring or auditing identifies serious or repeated deviations on the part of an investigator.

If suspension or premature termination occurs, the sponsor shall justify its decision in writing and promptly inform the other parties with whom they are in direct communication. The principal investigator and sponsor shall keep each other informed of any communication received from either the IRB or the regulatory authority.

If, for any reason, the sponsor suspends or prematurely terminates the investigation at an individual investigation site, the sponsor shall inform the responsible regulatory authority as appropriate and ensure that the IRB is notified, either by the principal investigator or by the sponsor. If the suspension or premature termination was in the interest of safety, the sponsor shall inform all other principal investigators.

If suspension or premature termination occurs,

a) the sponsor shall remain responsible for providing resources to fulfil the obligations from the CIP and existing agreements for following up the subjects enrolled in the clinical investigation, and

b) the principal investigator or authorized designee shall promptly inform the enrolled subjects at his/her investigation site, if appropriate. The method and the timing of this communication will depend on the circumstances and the perceived risks. All subjects must have the device removed and attend a 1 month follow-up visit.

c) the study is not blinded so there need not be criteria for breaking the blind.

23.2 Procedure for Resuming the Clinical Investigation After Temporary Suspension

When the sponsor concludes an analysis of the reason(s) for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the sponsor shall inform the principal investigators, the IRBs, and, where appropriate, the regulatory authority of the rationale and provide them with the relevant data supporting this decision.

Concurrence shall be obtained from the IRBs and, where appropriate, regulatory authorities before the clinical investigation resumes. If subjects have been informed of the suspension, the principal investigator or authorized designee shall inform them of the reasons for resumption.

24 PUBLICATION POLICY

24.1 Confidentiality Agreement

All goods, materials, information (oral or written) and unpublished documentation provided to the investigators, inclusive of this protocol and the case report forms are the exclusive property of SRS Medical. They may not be given or disclosed by the Investigator or by any person within his authority either in part or in totality to any unauthorized person without the prior written formal consent of SRS Medical.

24.2 Subject Confidentiality

The investigators and sponsor commit to maintaining the confidentiality of individual data of subjects involved in the study. All case report forms and related documents will be submitted using unique, confidential numbers assigned by SRS Medical and the site. All documents submitted to SRS Medical should be maintained by the investigator in strict confidence.

Each subject's data will be completely de-identified in the final reports and subsequent publications.

24.3 Ownership of Data and Use of Study Results

All clinical data gathered during the study will be pooled in a common database that is the property of SRS Medical. The results of the clinical study may not be published or presented at scientific meetings without the written approval of SRS Medical.

24.4 Publication Policy

At this time no publication or presentation is planned however the study will be published upon completion. At that time each investigator must agree that no publications or abstracts will be submitted that will jeopardize a multi-center publication. However, investigators may submit a request to SRS Medical to publish their single center experience if desired.

The investigator agrees to inform the sponsor in writing and to submit all manuscripts at least 30-45 days prior to submission and abstracts at least seven days prior to submission. This allows the sponsor to protect proprietary information and to provide comments and give its approval prior to any submission of data, abstracts or manuscripts. Also, this assures that the sponsor has submitted the supplement pre-market approval application, if it requires certain confidentiality of data before its publication.

24.5 Clinical Trial Registration

This study will be submitted for inclusion in the clinical trial registry at http://www.ClinicalTrials.gov.

In accordance with the national regulations, the intent to carry out a clinical investigation, as well as the results thereof, will be made available.

25 INSTITITIONAL REVIEW BOARD (IRB)

25.1 IRB Approval

The protocol and the informed consent document must have the initial and annual approval, as required by each IRB. The signed approval letter must identify the documents approved (i.e., list the investigator's name, the protocol number and title, the date of the protocol and informed consent document, and the date of approval of the protocol and the informed consent document). Any written information to be provided to the subject (e.g., subject education materials and/or subject information packet) and any advertisement used to recruit subjects must also be reviewed by the IRB. The sponsor

will not ship clinical supplies until a signed approval letter from the IRB has been received and a contractual agreement has been signed by the sponsor and the clinical site.

25.2 Continuing Communication with the IRB

The following information shall be provided to the IRB in accordance with their requirements:

- serious adverse events,
- requests for deviations, and reports of deviations,
- progress reports, including safety summary and deviations,
- amendments to any documents already approved by the IRB;
- if applicable, notifications of suspensions or premature termination,
- if applicable, justification and request for resuming the clinical investigation after a suspension,
- clinical investigation report or its summary.

As a minimum, during the clinical investigation, the following information shall be obtained in writing from the IRB prior to implementation:

- approval/favorable opinion of amendments,
- approval of the request for deviations that can affect the subject's rights, safety and well-being or the scientific integrity of the clinical investigation,
- approval for resumption of a suspended clinical investigation, if applicable.

26 INVESTIGATOR RESPONSIBILITIES

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as protecting the rights, safety, and welfare of subjects. An investigator must conduct the investigation in accordance with the signed agreement with SRS Medical, the investigational plan, ISO 14155 standard and other applicable country laws, including data protection laws, the latest version of the Declaration of Helsinki and any conditions of approval imposed by an IRB

The principles of the Declaration of Helsinki have all been implemented in this study by means of a subject informed consent process, IRB approval, training on the study, preclinical testing, risk benefit assessment, etc.

26.1 Qualification of the Principal Investigator

The principal investigator shall:

a) be qualified by education, training and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this International Standard; evidence of such qualifications of the principal investigator and key members of the investigation site team shall be provided to the sponsor through up-to-date CVs or other relevant documentation,

b) be experienced in the field of application and trained in the use of the investigational device under consideration,

c) disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results, and

d) be knowledgeable with the method of obtaining informed consent.

26.2 Qualification of investigation site

The principal investigator shall be able to demonstrate that the proposed investigation site:

a) has the required number of eligible subjects needed within the agreed recruitment period, and

b) has one or more qualified investigators, a qualified investigation site team and adequate facilities for the foreseen duration of the clinical investigation.

26.3 Study Agreement

A Study Agreement shall be entered into effect by the PI [and/or investigational site] as per the local legal requirements, and returned to SRS Medical prior to the start of any study activities. The PI indicates approval of the protocol and any amendments by signing and dating the agreement. Amendments to the protocol shall be agreed upon between SRS Medical and the PI and be recorded with a justification of the amendments.

26.4 Communication with the IRB

The principal investigator shall:

a) provide the sponsor with copies of any clinical-investigation-related communications between the principal investigator and the IRB,

b) obtain the written and dated approval/favorable opinion of the IRB for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required,

d) perform safety reporting,

e) promptly report any deviations from the CIP that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IRB, CIP or national regulations. In particular circumstances, the communication with the IRB can be performed by the sponsor, partly or in full, in which case the sponsor shall keep the principal investigator informed.

26.5 Informed Consent Process

The principal investigator shall ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent, and ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

26.6 Compliance with the CIP

The principal investigator shall indicate his/her acceptance of the CIP in writing and conduct the clinical investigation in compliance with the CIP and propose to the sponsor any appropriate modification(s) of the CIP or investigational device or of the use of the

investigational device. He shall refrain from implementing any modifications to the CIP without agreement from the sponsor, IRB and regulatory authorities, if required, and document and explain any deviation from the approved CIP that occurred during the course of the clinical investigation. At the end of the study he will sign the clinical investigation report.

The investigator is also responsible for ensuring that IRB approval of the protocol, informed consent and any other written information provided to the subject is in place before obtaining written consent from a subject. This approval should be in the form of a letter and identify the version or date of the documents approved. The approval letter should be accompanied by an IRB roster or letter of compliance to allow verification that the PI, other site study staff or SRS Medical personnel are members of the IRB. If they are members of the IRB, written documentation is required stating that they did not participate in the approval process. If the IRB imposes any additional requirements (e.g. safety reports, progress reports, etc.), SRS Medical will prepare the required documents and provide them to the PI for reporting to the IRB. The PI must inform SRS Medical of any change in status of IRB approval once the site has started enrollment in the study. If any action is taken by an IRB with respect to the study, that information will be forwarded to SRS Medical by the PI.

It is the responsibility of the Investigator to complete and maintain adequate and accurate eCRFs, which have been designed by the sponsor to record all observations and other pertinent data to the clinical investigation. The investigator shall assure the accuracy, completeness, legibility and timeliness of the data reported to the sponsor on the CRFs and in all required reports. Where copies of the original source document as well as printouts of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document. Source documents shall be created and maintained by the investigation site team throughout the clinical investigation. Ensure that all clinical-investigation-related records are retained as specified and make them available as requested during monitoring visits or audits, Allow and support the sponsor to perform monitoring and auditing activities, be accessible to the monitor and respond to questions during monitoring visits, allow and support regulatory authorities and the IRB when performing auditing activities.

In addition, the investigator shall only permit an investigational device to be used under his or her direct supervision only with subjects that are enrolled in the clinical study and shall not use an investigational device on any person not authorized to receive it. Use of the investigational device is to be used only in accordance with this Clinical Investigational Plan and instructions for use. Upon SRS Medical request, study completion, or termination of this study (or the investigator's part of the study), the investigator shall return to SRS Medical any remaining supply of the investigational device system.

Upon request, the investigator shall disclose sufficient accurate financial information to SRS Medical, and promptly update this information if any relevant changes occur during the course of the study and for 1 year after study completion. The PI should provide SRS Medical with a recently signed and dated curriculum vitae (CV) from all key

members of the investigational site study team as listed on the study delegation task list (dated within 3 years of the date of site activation). The sponsor will avoid improper influence on, or inducement of the subject, monitor and investigator or other parties participating in, or contributing to, the study by implementing the subject informed consent process, study agreements and IRB approval of the study.

The investigator shall ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation. New members of the investigation site team may be added during the study. New personnel should only start their assignment after receiving adequate training in the clinical investigation requirements and this training shall be documented. The names, initials, signatures, functions, and designated authorizations of new personnel shall be documented. He shall ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented.

26.7 Medical Care of Subjects

The principal investigator shall:

a) provide adequate medical care to a subject during and after a subject's participation in a clinical investigation in the case of adverse events,

b) inform the subject of the nature and possible cause of any adverse events experienced,

c) inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required,

d) provide the subject with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment,

f) ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation,

g) if appropriate, subjects enrolled in the clinical investigation shall be provided with some means of showing their participation in the clinical investigation, (contact address and telephone numbers shall be provided),

h) inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation, and

i) make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from the clinical investigation while fully respecting the subject's rights.

26.8 Safety Reporting

The principal investigator shall

a) record every adverse event and observed device deficiency, together with an assessment,

b) report to the sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect;

c) report to the IRB serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the IRB,

d) report to regulatory authorities serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations, and

e) supply the sponsor, upon sponsor's request, with any additional information related to the safety reporting of a particular event.

27 RESPONSIBILITIES OF THE SPONSOR

SRS Medical or designee(s) will perform the following:

27.1 Clinical Quality Assurance and Quality Control

Quality assurance and quality control principles shall apply to the processes of the clinical investigation. The sponsor shall implement and maintain written clinical quality procedures to ensure that the clinical investigation is designed, conducted and monitored, and that data are generated, documented, recorded and reported in compliance with this International Standard, the CIP, any subsequent amendment(s), and any other applicable standards and regulatory requirements.

They shall maintain records to document the compliance of all parties involved in the clinical investigation, ensure that the auditing requirements are met, if applicable, and justify and document significant exceptions to the requirements of the International Standards.

Clinical quality assurance and quality control may be integrated in the sponsor's overall quality system.

27.2 Clinical Investigation Planning and Conduct

Prior to commencement of the clinical investigation, the sponsor shall:

a) define, establish and allocate all the roles and responsibilities related to the clinical investigation in one or more written agreements,

b) select appropriately qualified principal investigators,

c) receive disclosures of conflict of interest from principal investigators and investigators, where required by national regulations,

e) ensure the members of the investigation site team and their designated authorization(s) are identified in a log with delegated responsibilities detailed,

f) designate or appoint one or more monitors, or otherwise assume the responsibilities of the monitor(s),and

g) ensure documentation of training, experience and scientific or clinical knowledge for all the relevant parties involved in order to adequately conduct the clinical investigation, including training, on

- the use of the investigational device(s),
- device accountability procedures ,
- CIP,
- eCRFs and instructions for completion,
- the written informed consent form and process as well as other written information provided to subjects, and
- sponsor's written procedures, International Standards and any applicable regulatory requirements;

h) ensure that, in multicenter investigations, all investigators and all other parties involved are given instructions on uniformly assessing and documenting clinical and laboratory findings,

i) ensure that any clinical-investigation-related activities of sponsor representative(s) at the investigation site(s) are described in the CIP and the informed consent form, and that these activities occur in such a way that they do not bias the data integrity,.

27.3 Preparation of Documents and Materials

Prior to commencement of the clinical investigation, the sponsor shall:

a) prepare contacts and essential documents and ensure they are approved by the relevant persons by dated signature.

b) assure the accuracy of translations, where relevant,

c) ensure that a supply of investigational devices is available in a timely manner for the clinical investigation. Investigational devices shall not be made available to the principal investigator until all requirements to start the clinical investigation are met,

d) provide a clinical liability insurance,

e) document any financial arrangements between the principal investigator or the investigation site and the sponsor,

f) submit any required application(s) to begin the clinical investigation in a given country to the appropriate regulatory authorities for review, acceptance or permission.

g) ensure that IRB's approval/favorable opinion is obtained and documented, and that appropriate provisions are made to meet any conditions imposed by the IRB, and

h) ensure that any modification(s) required by the IRB or regulatory authority are made and documented by the principal investigator and have gained the approval/favorable opinion of the IRB or regulatory authority.

27.4 Conduct of the Clinical Investigation

The sponsor shall be responsible for:

a) accountability of investigational devices throughout the clinical investigation,

b) documenting correspondence with all parties involved in the clinical investigation, including IRBs and regulatory authorities,

c) ensuring that the clinical investigation is appropriately monitored by determining the extent and nature of monitoring, including the strategy for source data verification, based on considerations such as the objective, design, complexity, size, critical data points and endpoints of the clinical investigation,

d) reviewing the monitoring reports and following up any actions required in the monitoring reports,

e) taking prompt action to secure compliance with all clinical investigation requirements, and

f) submitting progress reports, including safety summary and deviations, when requested, to all reviewing IRBs and the regulatory authorities.

27.5 Monitoring

The purpose of clinical investigation monitoring is to verify that the conduct of the clinical investigation complies with the approved CIP, subsequent amendment(s), the FDA and International Standards, and the applicable regulatory requirement(s). Monitoring activities may be conducted by the Monitor or the Sponsor.

27.5.1 Qualifications of the Monitor

Monitors shall be:

a) qualified in the field of the International Standards through training and experience as well as scientific or clinical knowledge;

b) knowledgeable on the use of the investigational device(s) and relevant requirements, CIP and informed consent process

c) trained on the sponsor's clinical quality assurance and quality control system as well as any special procedures for monitoring a specific clinical investigation.

Training shall be documented in the sponsor's files.

27.5.2 Assessment of the Investigation Site

The monitor shall assess each investigation site to verify that the principal investigator has:

a) adequate qualifications;

b) adequate resources, including facilities, laboratories, equipment and a qualified investigation site team;

c) access to an adequate number of subjects.

27.5.3 Initiation of the Investigation Site

The monitor shall initiate each investigation site to ensure that the principal investigator and investigation site team:

a) have received and understood the requirements and contents of:

- CIP,
- IRB,
- the informed consent form,
- eCRFs,
- the instructions for use,
- any written clinical investigation agreements, as appropriate,

b) have access to an adequate number of investigational devices,

c) have been trained in the use of the investigational device, and

d) are familiar with the responsibilities of the principal investigator.

27.5.4 Interim Monitoring Visits On-site

The monitor shall perform interim on-site monitoring visits to verify that:

a) compliance with the CIP, any subsequent amendment(s), this International Standard and regulatory requirements is maintained; deviations shall be discussed with the principal investigator(s) or authorized designee, documented and reported to the sponsor,

b) only authorized individuals are participating in the clinical investigation,

c) the investigational device is being used according to the CIP or instructions for use and that, where modifications are required to the device, its method of use or the CIP, these are reported to the sponsor,

d) investigation site resources, including laboratories, equipment and the investigation site team, remain adequate throughout the duration of the clinical investigation,

e) the principal investigator continues to have access to an adequate number of subjects and investigational devices,

f) signed and dated informed consent forms have been obtained from each subject at the point of enrollment or before any clinical-investigation-related procedures are undertaken,

g) source documents and other clinical investigation records are accurate, complete, up to date, stored and maintained appropriately,

h) eCRFs and queries are complete, recorded in a timely manner, and consistent with source documents,

i) appropriate corrections, additions or deletions are made to the eCRFs, dated, explained if necessary and initialed by the principal investigator or by his/her authorized designee; the monitor shall not make corrections, additions or deletions to the eCRFs,

j) all adverse events and device deficiencies are reported to the sponsor, and all serious adverse events and device deficiencies that could have led to a serious adverse device effect are reported to the sponsor without unjustified delay,

k) all serious adverse events and deviations are reported to the IRB, if required,

m) all other required reports, notifications, applications, submissions and correspondence are maintained in the investigator's files and are accurate, complete, timely, legible, dated and identify the clinical investigation,

o) current laboratory normal values, laboratory certifications, accreditations, or other validations are present in the investigator's file, if required,

p) subject withdrawal has been documented; the monitor shall discuss this with the principal investigator or his/her authorized designee,

q) subject non-compliance with the requirements stated in the informed consent has been documented; the monitor shall discuss this with the principal investigator or his/her authorized designee,

r) the principal investigator and investigation site team are informed and knowledgeable of all relevant document updates concerning the clinical investigation, and

s) any corrective and preventive actions, as needed, have been implemented and are effective.

27.5.5 Close-out Activities

The monitor shall perform close-out activities.

27.5.6 Monitoring Reports

All monitoring activities shall be documented in a written report to the sponsor and shall include:

a) the date, investigation site identification, name of the monitor and name of the principal investigator or other individuals contacted, and

b) a summary of what the monitor reviewed and his/her observation(s) with regard to the completion of previous action items, significant findings, facts, deviations, conclusions, and recommended actions to be taken to secure compliance.

A copy of the monitoring report or a summary of key findings shall be shared with the principal investigator in writing.

27.6 Safety Evaluation and Reporting

The sponsor is responsible for the classification of adverse events and ongoing safety evaluation of the clinical investigation and shall:

a) review the investigator's assessment of all adverse events and determine and document in writing their seriousness and relationship to the investigational device; in case of disagreement between the sponsor and the principal investigator(s), the sponsor shall communicate both opinions to concerned parties,

b) review all device deficiencies and determine and document in writing whether they could have led to a serious adverse device effect; in case of disagreement

between the sponsor and the principal investigator(s), the sponsor shall communicate both opinions to concerned parties,

c) report or ensure the reporting, to the IRB by the principal investigator(s), of all serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by national regulations or by the IRB,

d) report to regulatory authorities, within the required time period, all serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by national regulations,

e) report all relevant safety information to the DSMB, if established, according to written procedures,

f) in the case of a multicenter clinical investigation, inform all principal investigators in writing of all the serious adverse device effects at all investigation sites that have been reported to the sponsor, and ensure that they are reported to their EC, if required by national regulations or by the IRB, whichever is more stringent,

g) ensure that the IRB and the regulatory authorities are informed of significant new information about the clinical investigation, and

h) in case of serious adverse device effects and device deficiencies that could have led to serious adverse device effects, determine whether the risk analysis needs to be updated and assess whether corrective or preventive action is required.

27.6.1 Clinical Investigation Close-out

The sponsor shall:

a) ensure all clinical investigation close-out activities are properly conducted,

b) provide a statistical analysis of the data,

c) produce a clinical investigation report and

d) ensure that the clinical investigation report, whether for a completed or prematurely terminated clinical investigation, is provided to the EC, participating investigators and regulatory authorities, as required by national regulations.

27.7 Outsourcing of Duties and Functions

The sponsor may transfer any or all of the duties and functions related to the clinical investigation, including monitoring, to an external organization (such as a CRO or individual contractor), but the ultimate responsibility for the quality and integrity of the clinical investigation data shall reside with the sponsor. All requirements in the International Standards applying to a sponsor shall also apply to the external organization inasmuch as this organization assumes the clinical-investigation-related duties and functions of the sponsor.

The sponsor shall specify in writing any clinical-investigation-related duty or function assumed by the external organization, retaining any clinical-investigation-related duties and functions not specifically transferred to, and assumed by, the external organization.

The sponsor shall be responsible for verifying the existence of and adherence to written procedures at the external organization.

27.8 Communication With Regulatory Authorities

The sponsor shall, if required:

a) notify or obtain approval from regulatory authorities in the country where the clinical investigation is conducted,

b) report on the progress and status of the clinical investigation, and

c) perform safety reporting

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ATTACHMENT A: DEVICE LABELING

3007035	Physician's IFU for The Spanner and Surveyor
3007026	The Spanner Selector Card
1007364-X	Label, Spanner
1007365-X	Label, Surveyor

ATTACHMENT B: SPANNER STUDY PROCEDURE FOR UROFLOW TESTING

REQUIREMENT FOR A VALID UROFLOW TEST

Enrollment Period – Visits 1, 2, 3 and 4:

Once the participant is consented in the study they will have two attempts within a few hours to obtain PVR of 150 ml or less.

Subjects will be withdrawn from the study only if they have a PVR of 350 ml or more on both attempts.

TEST ENVIRONMENT

The test should be conducted in a quiet, non-rushed environment in a location that provides for subject comfort and privacy.

EQUIPMENT SET UP

Prior to testing, verify correct operation and maintenance of the uroflowmeter. Complete any calibration or equipment set up recommended by the equipment manufacturer.

ORIENTATION OF THE SUBJECT TO UROFLOW TESTING

To reduce the influence of the test equipment and test environment on subject performance during testing, subjects participating in the study should be given an orientation prior to their first uroflow test under the study protocol.

The orientation should consist of instruction on how to void into the test equipment and a simulated use demonstration (i.e. pouring water into the test set up) to show the subject how to do the test and how the equipment operates (e.g. if any operation of the equipment, like printing, occurs during testing). Any instructions or precautions related to the specific uroflow equipment that will help achieve a technically good test should be reviewed with the subject.

SUBJECT TESTING

- Have the subject drink two to four 8 oz. glasses of water.

Hand out the *How to Perform a Voiding Test* Sheet to the subject, asking him to review it prior to testing. Copies for distribution to study participants are provided in the individual case report form notebooks. (See sample on following page.)

- Instruct him to return for testing when he has a full bladder and strong urge to void.

RECORDING THE TEST RESULT

Record the values from the uroflow printout where indicated on the eCRF. In addition, due to the limitations of the uroflow equipment to account for artifacts, the investigator's manual reading of the uroflow graph is optional based on investigator discretion. Record the investigator reading on the eCRF with the corresponding machine values, which must include Qmax in ml/s. Label the report with the test date, subject initials and ID number. Place the uroflow test reports and graphs in the subject notebook.

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SAMPLE OF STUDY PARTICIPANT HANDOUT

How to Perform a Voiding Test

For Study Participants

The voiding test is very useful to your physician's assessment of your voiding problems and it is an important test in the study. The way in which you perform the test influences its usefulness. Here are some reminders of things "to do" and "not to do" to help get the best test result.

1. Drink two to four large glasses of water 1-2 hours before testing to make sure that you have a full bladder for the test.

2. Wait until your bladder feels full and you have a fairly strong urge to urinate before you report for testing.

3. To void get into a comfortable, steady position in front of the test equipment. Avoid bumping or jarring the test equipment during the test.

4. When you perform the test, do your best to direct your urine stream into the center of the collecting container. Do not direct your stream onto the sides of the collecting container.

5. Take as long as you need to empty your bladder.
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ATTACHMENT C: CHARLSON WEIGHTED INDEX OF COMORBIDITY

Table 3. Weighted index of comorbidity

Assigned weights for diseases	Conditions
1	Myocardial infarct
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumor
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	AIDS

ATTACHMENT D: STUDY SUBJECT MATERIALS

1007335 Subject Information Booklet for The Spanner

1007336 Subject Emergency Removal Card

ATTACHMENT E: CASE REPORT FORMS

CRF01	Case Report Form – Screening Visit 1
CRF02	Case Report Form – Spanner Insertion Visit 1
CRF03	Case Report Form – Stent #1 Removal & Stent #2 Placement Visit 2
CRF04	Case Report Form – Stent #2 Removal & Stent #3 Placement Visit 3
CRF05	Case Report Form – Stent #3 Removal Visit 4
CRF06	Case Report Form – Follow-up Interview
CRF11	Informed Consent
CRF12	IPSS Survey
CRF13	Subject Questionnaire
CRF21	Adverse Event Form
CRF22	Protocol Deviation Form
CRF23	Study Completion Form
CRF24	Unscheduled Visit Form
CRF25	Device Deficiency Form

ATTACHMENT F: MATERIALS IN CONTACT WITH TISSUES OR BODY FLUIDS

Spanner Stent Materials and Route of Biocontact			
Material	**Grade/Formulation (where applicable)**	**Where Used?**	**Biocontact**
Silicone Rubber	NuSil MED1-4213, NuSil MED2-4213	Silicone Adhesives	Direct Tissue
	NuSil MED-4720	Balloon Cover Slip	Direct Tissue
	NuSil MED-4830	Proximal Tube Assembly Distal Anchor Assembly	Direct Tissue
	NuSil MED 4725/4735 blend, Parylene N coated	Check Valve	Indirect Tissue
	NuSil MED-4870/MED-4770	Inner Sleeve	Indirect Tissue
Stainless Steel	304, 304V	Plug Distal Anchor Assembly	Direct Tissue
Epoxy	USP Class VI Tra-Con , Inc., Tra-Bond FDA2	Epoxy	Direct Tissue
Fluorosilicone Fluid	NuSil Med 420	Lubricant	Direct Tissue
Nylon	Type 6/6 non-absorbable	Device Suture Suture (black suture dyed with Hematein (logwood) black)	Direct Tissue
Polyester	2/0 green surgical suture	Access Tether (Shore Line)	Direct Tissue

Insertion Tool Materials and Route of Biocontact			
Material	**Grade/Formulation (where applicable)**	**Where Used?**	**Biocontact**
Silicone Rubber	St Gobain Tygon 3350 Tubing	Silicone Sleeve	No Tissue Contact
	NuSil MED-4234	Sealing Ring	Direct Tissue
	GE Silicone LSR 4030	Spacer Sleeve	Direct Tissue
	NuSil MED1-4213, MED 2-4213	Silicone Adhesive	Direct Tissue
	Wacker Silicones R-4105/60	Push Tube	Direct Tissue
	NuSil MED 4970, Wacker Silicones ELR Plus 4105/70 K20R	Anchor Sleeve Subassembly	Direct Tissue
Stainless Steel / Metals	304V	Coil Needle Tip Anchor Sleeve Assembly Stiffener Wire	Indirect Tissue
	Brass with Nickel Plating	Needle Tip Luer Connector	Indirect Tissue
Polyurethane	Dow Pellethane 2363-55DE, 30% BaSO4	Inflation Tube	Direct Tissue
Polyurethane Colorant	30% BaSO4, White	White Colorant for Inflation Tube	Direct Tissue
Polycarbonate	LEXAN 104-1111, USP Class VI	Push Cup	Direct Tissue
		Tube Barb Barrel Hand piece	Indirect Tissue

Insertion Tool Materials and Route of Biocontact			
Material	**Grade/Formulation (where applicable)**	**Where Used?**	**Biocontact**
Acetal Homopolymer	21CFR 117.2490 or ASTM 4181, Class I, Grade I	Plunger Stop	No Tissue Contact
Platinum Primer	NuSil CF2-135	Primer, Silicone	Direct Tissue
Epoxy	USP Class VI Tra-Con , Inc., Tra-Bond FDA2	Epoxy	Direct Tissue
Ink	Nontoxic Permanent Marker (ASTM D4236)	Push Cup	Direct Tissue

Surveyor Materials and Route of Biocontact			
Material	**Grade/Formulation (where applicable)**	**Where Used?**	**Biocontact**
Silicone Rubber	NuSil MED1-4213, NuSil MED2-4213	Adhesive	Direct Tissue
	GE LSR 4030	Subassembly Proximal Tip	
	NuSil MED-4720	Balloon	
Stainless Steel	304V	Stiffener	No Tissue Contact
		Ferrule Probe Wire	Direct Tissue
Polycarbonate	LEXAN 104-1111, USP Class VI	Probe Wire Handle Stopcock Wire Guide	Indirect Tissue
		Stop	Direct Tissue
Platinum Primer	NuSil CF2-135	Primer, Silicone	Direct Tissue
High Density Polyethylene	Lupolen 6021D	Stopcock	Indirect Tissue
Epoxy	USP Class VI Tra-Con , Inc., Tra-Bond FDA2	Epoxy	Direct Tissue
Aliphatic Polyether-based Polyurethane	TecoFlex, EG-65D-B20	Catheter Tubing (a.k.a. Inflation Tube)	Direct Tissue
Polyurethane Colorant	20% $BaSO_4$, White	White Colorant for Catheter Tubing	Direct Tissue
PTFE (a.k.a. Teflon)	USP Class VI or ASTM D1710, Type I Grade I, Class D	Probe Tip	Direct Tissue

ATTACHMENT G: ABBBREVIATIONS

AE – Adverse Event
ADE – Adverse Device Effect
BPH – Benign Prostatic Hyperplasia
CIP – Clinical Investigation Plan
DD – Device Deficiency
DRE – Digital Rectal Examination
DSMB – Data and Safety Monitoring Board
EC – Ethics Committee
eCRF – Electronic Case Report Forms
CTCAE - Common Terminology Criteria for Adverse Events
FMEA – Failure Mode Effects Analysis
GCP – Good Clinical Practice
ICF – Informed Consent Form
IPSS – International Prostate Symptom Score
PI – Principal Investigator
PTFE - Polytetrafluoroethylene a.k.a. Teflon®
PVR – Post Void Residual
Qmax – Maximum Flow Rate
RBC – Red Blood Count
SAE – Serious Adverse Event
SADE – Serious Adverse Device Effect
UA – Urinalysis
UC&S – Urine Culture and Sensitivity
UADE – Unanticipated Adverse Device Effect
USADE – Unanticipated Serious Adverse Device Effect
WBC – White Blood Count