Serenity Medical

Instructions for Use

River Stent System™

Humanitarian Device. Authorized by Federal law for use in the treatment of idiopathic intracranial hypertension in adult patients who have failed medical therapy. The effectiveness of this device for this use has not been demonstrated.

℞ only

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1 Device Description

The River Stent System™ consists of the following:

- Self-expanding nickel titanium (nitinol), open-cell tapered stent.
- Delivery catheter made up of the inner catheter assembly and outer catheter assembly.

Figure 1 shows an overview of the fully assembled River Stent System and the relative position of the components within the system. The delivery catheter consists of the inner and outer catheter subsystem which are two coaxial catheter assemblies. The River Stent is preloaded within the delivery system. The outer catheter assembly captures the stent within two marker bands (marker band #2 and marker band #3) of the inner catheter assembly. The stent is delivered to the sinus by withdrawing the outer catheter assembly while maintaining position of the inner catheter assembly.

Fully Assembled River Stent System

Components of the River Stent System

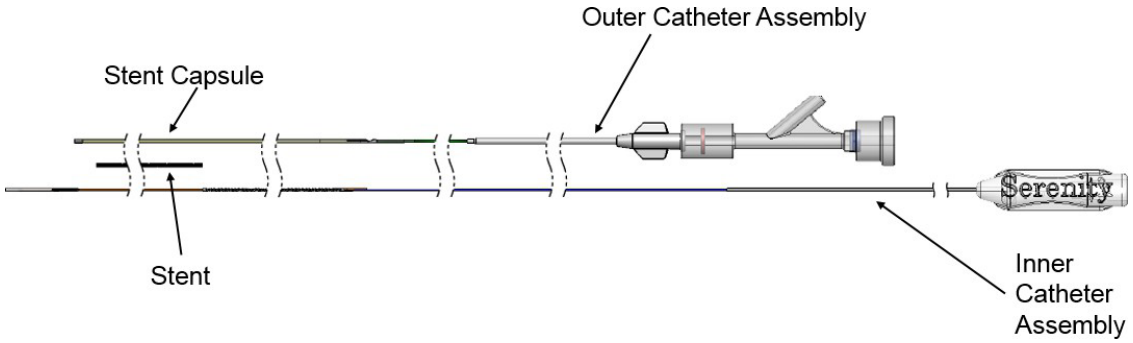


Figure 1: River Stent System

Figure 2 indicates the locations of the radiopaque markers at the distal end of the catheter system (inner and outer catheter assembled). The length of the stent is identified by the proximal radiopaque marker band (marker band #3) and the middle marker band (marker band #2). The tip of the delivery catheter system is marked by the distal most marker band (marker band #1) which is 5 mm from the tip of the catheter.

The tip of the outer catheter is also marked with a radiopaque polymer. When loaded, the radiopaque tip of the outer catheter system overlays directly over the middle marker band (marker band #2). As the outer catheter is withdrawn, the tip of the outer catheter can be observed to withdraw proximally by tracking the radiopaque tip of the outer catheter assembly.

The proximal end of the outer catheter assembly is a Y-hub with a rotating Tuohy hemostasis valve and a female Luer hub.

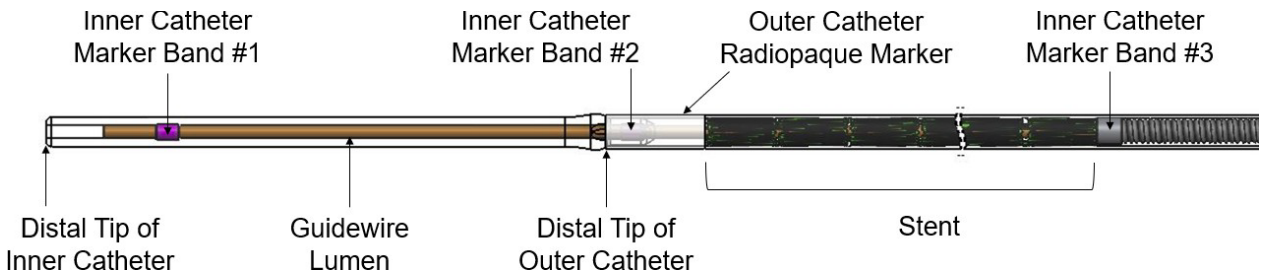


Figure 2: Position of Radiopaque Markers at Distal End of River Stent System

1.1 How Supplied

- STERILE – DO NOT RESTERILIZE – SINGLE USE ONLY. This device is supplied sterile and for single use only. It is sterilized by ethylene oxide.
- Package contents: One (1) River Stent System, product literature, patient implant card.

1.2 Materials

- The River Stent is intended as a permanent implant and is made of nitinol (nickel-titanium alloy).
- The River Stent System is not made with latex or bis (2-ethylhexyl) phthalate (DEHP) materials.

1.3 Packaging and Storage

The River Stent System is placed inside a protective, plastic dispenser and packaged in a pouch and single unit carton. The device will remain sterile unless the package is opened, damaged, or the expiration date has passed. Store at controlled room temperature in a dry place. Do not use the device beyond the labeled “Use-By” date on the package.

2 Intended Use

The River Stent System™ is intended for stenting of venous sinus stenosis in patients with idiopathic intracranial hypertension who have failed medical therapy.

3 Indications for Use

The River Stent System™ is indicated for stenting of the venous sinus in adult patients (22 years of age or older) with idiopathic intracranial hypertension (IIH) who have failed medical therapy, have a significant stenosis of the venous sinus (> 50% stenosis and pressure gradient ≥ 8 mmHg), and have an upstream venous sinus diameter between 5 mm and 8.5 mm. Patients must also meet one or both of the following criteria:

- Intractable headache (severe impact with score > 59 on the Headache Impact Test (HIT)-6 scale) and papilledema or a history of papilledema and medical therapy failure for IIH for at least 6 months. Patients who are obese [body mass index (BMI) ≥ 30] must also have completed a weight management program including behavioral therapy, nutritional counseling, and/or medication support for at least 6 months, without achieving adequate relief of their IIH symptoms.
- Moderate to severe papilledema (Frisén grade ≥ 2), transient visual obscuration, or 6th nerve palsy who have failed medical therapy and in the opinion of the treating ophthalmologist are losing vision or at risk of losing vision.

4 Contraindications

Use of the River Stent System is contraindicated for use in:

- Patients in whom anticoagulant, anti-platelet therapy or thrombolytic drugs are contraindicated.
- Patients with thrombophilic disorder or anticardiolipin syndrome.

- Patients with known hypersensitivity to nitinol and/or its components (e.g., nickel, titanium).
- Patients with known allergy to contrast or anesthetic drug despite pre-medication.
- Patients with anatomy that does not permit passage or deployment of the River Stent.
- Patients with an active bacterial infection.
- Patients with a pre-existing stent at the target transverse-sigmoid sinus.
- Patients with renal insufficiency not on dialysis.

5 Warnings

- The device is provided sterile and for single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing, or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious diseases(s) from one patient to another. Contamination of the device may lead to patient injury, illness, or death.
- Do not use the device if the package is open or damaged, or if there are abnormalities in the sterile barrier (e.g., broken seal, torn or breached barrier).
- If the center of the temperature indicator is black, it means that the device was exposed to a temperature of 60 ºC or more. Do not use if the temperature indicator is completely black as the stent may have been compromised.
- Do not expose the delivery catheter system to organic solvents (e.g., alcohol) as structural integrity and/or function of the device may be compromised.
- The River Stent System is shipped with the Tuohy Borst valve in the OPEN position. Care should be taken not to pre-deploy the stent. It is imperative to tightly rotate the rotating hemostatic valve prior to introduction of the River Stent System into the guide catheter to prevent premature stent delivery.
- Should unusual resistance be felt at any time during access, the River Stent with its delivery catheter should be removed as a single unit. Applying excessive force during catheterization of the transverse-sigmoid sinus with the River Stent System can potentially result in loss or damage to the River Stent and delivery catheter.
- Do not reposition the River Stent in the transverse-sigmoid sinus. The River Stent must be entirely deployed once its deployment has started.
- Do not torque the delivery catheter while advancing or retracting the River Stent System.
- The delivery catheter should be used only to deliver the River Stent into the transverse-sigmoid sinuses and should not be used as a support mechanism to advance a guide catheter. The marker at the distal end of the stent on the delivery catheter should not be advanced beyond the torcula. Using the device as a secondary guide catheter support or advancing the distal end marker beyond the torcula may result in device failure including device breakage that may result in injury to the patient.

6 Precautions

- The device should only be used by physicians that have experience with neurointerventional techniques in the vascular system.
- Carefully inspect the device prior to use to verify that it was not damaged during shipment. Do not use kinked or damaged components.
- Do not use the device beyond the labeled “Use-By” date indicated on the product label.

- Use a J-shaped guidewire (soft tip) to avoid involuntary catheterization of a cortical vein during sinus catheterization and over-the-wire exchange.
- Before insertion of the River Stent System, appropriate antiplatelet and anticoagulant therapy should be administered.
- Appropriate stent size selection is important to ensure stent apposition to the vessel wall.
- Exercise caution when crossing the deployed River Stent with adjunctive devices such as guidewires, catheters, microcatheters or balloon catheters to avoid disrupting the device geometry and device placement.
- The device should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is required.
- The River Stent is delivered under fluoroscopic guidance. Computed tomography angiographic procedures may be used to visualize the anatomy. Operators should take precautions to limit radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying radiographic equipment parameters where possible.
- The delivery system is not designed for the use of power injection. Use of power injection may adversely affect device performance.
- Once the stent is delivered, it cannot be recaptured.
- The stent has not been tested for safety or probable benefit as overlapping stents.
- The safety and probable benefit of the River Stent System has not been established in:
    - Patients with dural arteriovenous fistula or other arteriovenous lesion affecting cerebral blood flow.
    - Pregnant patients.

7 Magnetic Resonance Imaging (MRI) Safety Information

 MR Conditional	The River Stent is MR Conditional. A patient with the River Stent may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.
Parameter	**Condition of Use/Information**
Nominal Values of Static Magnetic Field (T)	1.5-Tesla (T) or 3.0-T
Maximum Spatial Field Gradient (T/m and gauss/cm)	40-T/m (4,000-gauss/cm)
Type of Radiofrequency (RF) Excitation	Circularly Polarized (CP) (i.e., Quadrature-Transmission)
Transmit RF Coil Information	There are no transmit RF coil restrictions. Accordingly, the following may be used: body transmit RF coil and all other RF coil combinations (i.e., body RF coil combined with any receive-only RF coil, transmit/receive head RF coil, transmit/receive knee RF coil, etc.).
Operating Mode of MR System	Normal Operating Mode

Maximum Whole Body Averaged Specific Absorption Rate (SAR) (W/kg)	2-W/kg (Normal Operating Mode)
Limits on Scan Duration	Whole body averaged SAR of 2-W/kg for 60 minutes of continuous RF exposure (i.e., per pulse sequence or back-to-back sequences/series without breaks).
MR Image Artifact	The presence of this implant produces an imaging artifact. Therefore, carefully select pulse sequence parameters if the implant is located in the area of interest. The River Stent may create local field inhomogeneity and susceptibility artifacts during magnetic resonance venography (MRV), which may degrade the diagnostic ability to assess vessel lumen patency.

8 Potential Adverse Effects

Possible adverse events associated with use of the device may include, but are not limited to, the following:

- Access site complications
- Allergic reaction to contrast agent, procedure medications, pre- and post-procedural medications (anti-platelet or anticoagulant agents), or nitinol
- Embolism (air, thrombus, device/stent or other)
- Death
- Headache
- Hematoma
- Hemorrhage/bleeding
- Infection
- Neurological insufficiencies including stroke and death
- Pain
- Renal insufficiency or failure secondary to contrast medium
- Thrombosis and stent restenosis or thrombosis
- Vessel injury (perforation, dissection, rupture, erosion, spasm, or other)

Patients will experience radiation exposure from use of fluoroscopy during device delivery and computed tomography imaging procedures which may be used to visualize the vascular anatomy. Potential risks associated with radiation exposure may include, but are not limited to, alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia. The probability of adverse event occurrence increases as procedure time and the number of procedures increase.

9 Clinical Study Summary

9.1 Study Design

The clinical evidence supporting the safety and probable benefit of the River Stent System was derived from “The River Trial – Clinical Evaluation of the Serenity River Stent System to Treat Idiopathic Intracranial Hypertension.” “The River Trial” was a prospective, non-randomized, single-arm, multicenter study to demonstrate the safety and probable benefit of the River Stent System when used to treat subjects with IIH who have failed medical therapy. A total of 39 subjects were enrolled at 5 sites in the United States (U.S.). Study follow-up occurred pre-discharge, 1 week to 1 month, 3 months, 6 months, and 1-year post-procedure. Annual follow-up will continue through 5 years post-procedure.

9.2 Study Population

Patients were eligible to enroll in the study if they were > 18 years old with a diagnosis of IIH per the modified Dandy criteria, cerebrospinal fluid (CSF) opening pressure > 25 cm H_2O, and clinical symptoms of headaches (HIT-6 score > 59 refractory to medical therapy or medication intolerance ≥ 4 weeks) or visual field (VF) loss (perimetric mean deviation -6 dB to -30 dB in one or both eyes with papilledema Frisén grade > 1 despite at least 2 weeks of medical therapy). Radiological examination or retrograde catheter venography (RCV) must show bilateral transverse-sigmoid venous sinus stenosis > 50% or unilateral stenosis of the dominant sinus with contralateral hypoplastic sinus, and no stenosis of the

superior sagittal sinus. In the absence of the study, the subject would have been offered a surgical intervention by optic nerve sheath fenestration (ONSF), CSF shunting procedure, or venous sinus stenting with an off- label device. Angiographic inclusion criteria included a pressure gradient > 8 mmHg across the transverse-sigmoid sinus stenosis by catheter manometry and venographic evidence of sinus stenosis > 50%. Key protocol exclusions included patients presenting with de novo papilledema and severe visual field deficits (VF loss ≥ 15 dB) requiring immediate surgical treatment, patients with a current or scheduled CSF shunt, patients with prior intracranial sinus stent implant, and patients with no measurable visual acuity at one meter in the study eye. Full inclusion and exclusion criteria for the study are outlined below.

Inclusion Criteria

Subjects must meet all of the following criteria to be eligible for participation in the study:

1. Subject is > 18 years old and has given informed consent.
2. Diagnosis of IIH per modified Dandy criteria.
3. CSF opening pressure is > 25 cm H_2O.
4. Radiological examination (magnetic resonance venography (MRV) or computed tomographic venography (CTV)) or retrograde catheter venography (RCV) shows bilateral transverse-sigmoid venous sinus stenosis (> 50%) or unilateral stenosis of the dominant sinus with contralateral hypoplastic sinus and no stenosis of the superior sagittal sinus.
5. Presence of IIH clinical symptoms:

   a. Headaches: Score > 59 (severe impact) on the HIT-6 scale, refractory to medical therapy (e.g., acetazolamide 1000 mg BID (bis in die; twice daily), topiramate 100 mg BID, or other headache medication), or medication intolerance for ≥ 4 weeks;

   OR

   b. Visual field loss: defined by perimetric mean deviation (PMD) between -6 dB and -30 dB in one or both eyes (with papilledema Frisén grade > 1) despite at least 2 weeks of medical therapy with acetazolamide 1000 mg BID, or if the visual field deteriorates by more than 2 dB during treatment, or treatment intolerance.

   Note that if only one eye fulfills criteria for visual field loss, and only one eye has grade 2 or higher papilledema, then they must be the same eye. This is to prevent the inclusion of a patient where one eye has severe visual field loss with atrophy (with no chance of improvement) and the other has papilledema but only mild visual field loss.
6. In the absence of this study, the subject would have been offered a surgical intervention by ONSF, CSF shunting procedure, or venous sinus stenting with an off-label device.

Angiographic Inclusion Criteria

7. Catheter manometry shows a pressure gradient > 8 mm Hg across the transverse-sigmoid sinus stenosis.
8. Venographic evidence of sinus stenosis (> 50%).

Exclusion Criteria

Subject must be excluded from participation in this study if any of the following criteria were met:

1. Subject presenting with de novo papilledema and severe visual field (VF) deficit (VF loss ≥ 15 dB) that requires immediate surgical treatment without prior attempt of medical therapy.
2. Subject has no measurable visual acuity at one meter in the study eye.
3. Currently has or plans to have an implanted CSF shunt.
4. History of previously implanted intra-cranial sinus stent.
5. Transverse-sigmoid sinus vessel size < 5 mm or > 10 mm.
6. Creatinine > 1.5 mg/dl and/or creatinine clearance < 60 mL/min (except if patients are already on hemodialysis).
7. Allergic to imaging contrast media (iodine or gadolinium) despite premedication.

8. Allergic to nitinol or nickel.
9. Contra-indication to general anesthesia.
10. Contra-indication to aspirin, clopidogrel or other anticoagulant.
11. Hypercoagulable state (Factor V Leiden, protein C or S deficiency, anticardiolipin antibodies, Lupus anticoagulant, B2-glycoprotein-1 antibodies, or hyperhomocysteinemia).
12. Currently requiring full anti-coagulation for other medical reasons, such as atrial fibrillation (AF), artificial cardiac valves, deep vein thrombosis, pulmonary embolism, etc.
13. History of stroke or transient ischemic attack (TIA).
14. History of AF or other risks of stroke.
15. History of deep vein thrombosis or pulmonary embolism.
16. History of severe chronic obstructive pulmonary disease (COPD) or other severe respiratory disease.
17. History of severe carotid atherosclerotic disease.
18. History of heart failure, dilated cardiomyopathy, or congenital heart conditions, etc. that are at high thrombogenic risk.
19. History of uncontrolled diabetes.
20. Use of tetracycline derivative, retinoid, or vitamin A during the last 3 months except topical applications which are allowed.
21. Cerebral vascular lesions (arteriovenous malformation (AVM), arteriovenous fistula, aneurysms, significant stenosis of extra- or intra-cranial vessels other than the targeted venous sinus stenosis, intracranial artery dissection, etc.).
22. Patient has vision loss due to other disease (e.g., cataract, macular degeneration, glaucoma, etc.).
23. Inability to provide reliable and reproducible visual field examinations (> 15% false positive errors and/or failure to maintain fixation for eye monitoring).
24. For female subject of childbearing potential, pregnant or not willing to use contraception for 12 months.
25. Presence of a physical, mental or social condition that could prevent adequate one-year follow-up (homelessness, drug dependency, anticipation of moving far away, life threatening disease, terminal illness).
26. Anatomical anomaly of the venous sinus which would prevent safe catheterization and stenting (e.g., multi-channel sinus).
27. Currently enrolled in a premarket investigational study. Enrollment in a post market study that does not impact the River™ Stent procedure or device is allowed.

All 39 enrolled subjects were treated with the River Stent and 34 completed the 1 year visit. Two subjects had an alternate IIH procedure (CSF shunt) after the 6-month visit and were exited from the study.

The cohort was mostly female (38/39) with average age of 35 years and average body mass index of 35.4 kg/m^2. There were 34 subjects enrolled based on headache criteria, 4 based on visual criteria, and one subject who did not meet headache or visual eligibility criteria at study entry. 14 of the 39 subjects enrolled had a history of papilledema but no baseline papilledema in either eye. 25 of the 39 subjects enrolled had some degree of papilledema (Frisén grade ≥ 1) at baseline in at least one eye. 14 subjects had papilledema Frisén grade 1 in the worst eye, 11 had papilledema Frisén grade 2 and 2 subjects had papilledema Frisén grade 3 in the worst eyes. All 4 of the 4 subjects enrolled based on visual criteria had Frisén grade 2 in both eyes. Of the 34 subjects enrolled based on headache criteria, 14 had no baseline papilledema, 14 had Frisén grade 1 at baseline and 6 had Frisén grade > 1 at baseline. The one subject who did not meet headache or visual eligibility criteria had papilledema with Frisén grade 3 in one eye and grade 2 in the other. See Table 4 below.

Subject Accountability

Subject accountability is shown in Table 1. A total of 39 subjects were enrolled and treated in the study and 34 completed the 1-year visit. Two subjects exited the study early, prior to 1 year, with both subjects undergoing a CSF shunt procedure at 6 months. Three subjects missed the 1-year visit. Of the 34 subjects who completed the 1-year visit, 8 subjects did not undergo the RCV and manometry (RCVM) assessment necessary to assess the primary probable benefit endpoint. In total, 22 subjects met all the selection criteria and had all the elements for calculation of the primary probable benefit endpoint including RCVM, HIT-6, and reliable visual fields and known primary probable benefit events. As of the database cut-off date, four

additional subjects exited the study after the 1-year visit due to loss to follow-up.

Table 1. Subject Accounting by Follow-Up Visit and Endpoint

Characteristic	Number of Subjects
mITT (Modified Intent-to-Treat)	39
River Stent attempted	39
River Stent implanted	39
Follow-Up Visits Completed	
3-month visit	38
6-month visit	37
1-year visit	34
Primary Safety Endpoint[1]	37
Subjects with 1-year visit completed	34
Subjects with alternate IIH surgical procedure (CSF shunt) at 6-months due to recurrent IIH symptoms	2
Subjects who missed 1-year visit but was contacted by phone by study site for major adverse event data collection for primary safety	1
Primary Probable Benefit Endpoint[2]	22
Met all inclusion criteria and had all the elements for calculation of the primary probable benefit endpoint, including RCVM, HIT-6, and reliable visual fields	20
Withdrew at 6-months due to alternate IIH surgical procedure (CSF shunt placement)	2
Missing Data for Elements of Primary Probable Benefit Endpoint at 1-Year	17
Missed 1-year visit (lost to follow-up)	3
Missing RCVM (at 1-year)[3]	12
Missing HIT-6[4]	2
Missing visual field data[4,5]	4
Unreliable visual field data[5]	5
Did not meet headache or visual field eligibility criteria	1
Subjects with Data for Key Secondary Endpoints at 1-Year	
CSF opening pressure[2]	22
Stent patency	26
Headache (HIT-6)	34
Papilledema (Frisén grade)	32

[1]37 subjects contributed to the primary safety endpoint, 3 of which did not complete the 1-year visit but had confirmed primary safety events.
[2]Four out of 20 subjects with primary probable benefit endpoint data available at 1-year did not have 1-year CSF opening pressure data.
[3]This includes: 3 lost to follow-up, 7 refused the procedure, 2 with CSF shunt who reached primary safety endpoint and were not offered the procedure.
[4]CSF shunt subjects did not collect 1-year probable benefit endpoint data.
[5]One subject with missing visual field data and one subject with unreliable visual field data also was missing RCVM at 1-year.

Table 2. Subject Demographics and Baseline Characteristics

Characteristic	Value
Age at Enrollment (Years)	
Mean ± Standard Deviation (SD) (N)	35.7 ± 12.01 (39)
Median	31.0
Min, Max	19, 65
Female Gender, n/N (%)	38/39 (97.4%)
Race / Ethnic Origin, n/N (%)[1]	
Asian	2/39 (5.1%)

Characteristic	Value
Black or African Origin	8/39 (20.5%)
Caucasian	24/39 (61.5%)
Hispanic or Latino	8/39 (20.5%)
Native American or Alaskan Native	1/39 (2.6%)
Other	4/39 (10.3%)
Body Mass Index (kg/m^2)	
Mean ± SD (N)	35.42 ± 7.975 (39)
Median	34.00
Min, Max	20.0, 56.5
Study Enrollment by Symptoms, n/N (%)	
Headache Group (HIT-6 score > 59)	34/39 (87.2%)
Ophthalmic Group (PMD: -6 dB to -30 dB)	4/39 (10.3%)
No Symptom Group	1/39 (2.6%)
Study Eye, n/N (%) (Ophthalmic Group Only)	
Right	0/4 (0.0%)
Left	2/4 (50.0%)
Both	2/4 (50.0%)

Abbreviations: dB, decibels; HIT-6, Headache Impact Test – 6; PMD, perimetric mean deviation.
[1]Some subjects reported more than one race / ethnic origin.

Table 3. Enrollment by Criteria [mITT]

	Headache Criteria (HIT-6 score > 59)	
Ophthalmic Criteria (PMD: -6 dB to -30 dB)	**Headache Present n/N (%)**	**Headache Absent n/N (%)**
Ophthalmic Present n/N (%)	4/39 (10.3%)[1]	0/39 (0.0%)
Ophthalmic Absent n/N (%)	34/39 (87.2%)[2]	1/39 (2.6%)[3]

Abbreviations: dB, decibels; HIT-6, Headache Impact Test – 6; PMD, perimetric mean deviation.
[1]4/4 subjects enrolled based upon ophthalmic criteria had bilateral papilledema Frisén grade 2 at baseline.
[2] 6/34 subjects enrolled based upon headache criteria had papilledema with Frisén grade > 1 at baseline and 14/34 subjects had papilledema with Frisén grade = 1 at baseline.
[3]One subject did not qualify for the study based on inclusion 5 requiring the presence of IIH clinical symptoms with specified criteria for headache or visual field loss. This subject had bilateral papilledema (Frisén grade 2 in one eye and Frisén grade 3 in the other eye) at baseline.

Table 4. Papilledema at Baseline

	Frisén > 1	**Frisén = 1**	**Frisén = 0**	**Total**
Headaches group	6	14	14	**34**
Visual field defect group	4	0	0	**4**
No group	1	0	0	**1**
Total	**11**	**14**	**14**	

9.3 Study Procedures

Baseline and follow-up assessments included:

- Physical exam
- Laboratory assessments
- Neuro-ophthalmological assessments
- Headache Impact Test (HIT-6)
- Tinnitus Functional Index (TFI)
- Quality of life (QoL) assessments: SF-12, NEI-VFQ-25, EQ-5D

Subjects received pre- and post-procedure antiplatelet therapy in the form of aspirin and clopidogrel.

All enrolled subjects underwent the stent placement procedure successfully. The average time from device insertion to catheter removal was 21.8 minutes. Intra-procedural sinus stenosis and pressure measurements are summarized in Table 5.

Table 5. Venous Sinus Stenosis and Pressure Measurements

Venous Sinus Measurement	Mean ± SD (N)
Stenosis Measurements (Before Stenting)	
Downstream diameter (mm)	7.42 ± 1.126 (39)
Upstream diameter (mm)	7.46 ± 1.715 (39)
Stenotic diameter (mm)	3.77 ± 6.541 (39)
Length of stenosis (mm)	19.86 ± 11.743 (38)
Trans-stenotic Pressure Gradient (mmHg)	
Pre-stenting	16.1 ± 10.82 (35)
Post-stenting	1.7 ± 1.58 (39)
Percent Stenosis (%)	
Pre-stenting	61.6 ± 6.77 (39)
Post-stenting	24.9 ± 11.83 (39)

9.4 Safety and Probable Benefit Results

Primary and secondary endpoint analyses are based on a modified intent-to-treat population which includes all enrolled subjects who had the investigational device attempted.

9.4.1 Primary Safety Endpoint

The primary safety endpoint is the major adverse event (MAE) rate at 1 year post River Stent procedure, which was defined as a composite of: moderate or severe stroke (National Institutes of Health Stroke Scale (NIHSS) > 3), neurological death, perforation of sinus or cerebral vein, thrombosis of sinus or cerebral vein, device distal embolization, need for target vessel revascularization or need for IIH alternate procedure (new venous sinus stenting, CSF shunting, or ONSF).

The primary safety endpoint was met (Table 6). The MAE rate at 1 year was 5.4% (2/37) [95% confidence interval: 0.7%, 18.2%] with 2 subjects requiring a CSF shunt placement after the 6-month visit. The upper 95% confidence limit is lower than the pre-specified performance goal of 51.7% for standard of care CSF shunting procedures ($p < 0.0001$, one-sided exact binomial test). The primary safety analysis included one subject who missed the 1-year visit but was followed by the site for primary safety endpoint data and excluded two subjects who missed the 1-year follow-up visit. As a worst-case analysis, subjects who missed the 1-year visit were counted as experiencing an MAE. The upper 95% confidence limit for the worst-case analysis was lower than the performance goal.

Table 6. Primary Safety Endpoint – MAE Rate at 1 Year

Primary Safety Endpoint	Subjects % (n/N)	95% CI [LCL, UCL]	Performance Goal	p-value[1]
Total MAE rate	5.4% (2/37)	0.7%, 18.2%	51.7%	< 0.0001
Worst-case MAE rate[2]	10.3% (4/39)	2.9%, 24.2%	--	--

Abbreviations: CI, confidence interval; LCL, lower confidence limit; UCL, upper confidence limit.
[1]One-sample exact binomial test.
[2]Subjects with missing data counted as having MAE.

A post hoc analysis including the addition of clinically significant vision loss in the endpoint definition (defined as loss of > 3 lines of best-corrected acuity or PMD loss > 5dB) also supported the safe use of the device.

9.4.2 Primary Probable Benefit Endpoint

The primary probable benefit endpoint was a composite at 1 year of:

- Absence of significant (> 50%) stenosis of the stented sinus and of new significant (>

50%) stenosis of the other cerebral venous sinuses on retrograde catheter venography (RCV).
AND

- Decrease of trans-stent pressure gradient (difference between the pressure measured in the torcula, proximal to the stent, and the pressure measure in the sigmoid sinus, proximal to the stent) to less than 8 mmHg.
  AND
- Clinically relevant improvement in the main clinical outcome per specific inclusion criteria and stabilization or better of the other:
  - Headaches: Improvement in the HIT-6 scale by ≥ 5 points and improvement or stabilization of visual field.
    OR
  - Ophthalmic: Improvement in visual field by ≥ 30% of the baseline value in the study eye (or at least one eye, with stabilization or better of the other eye, if a subject has 2 study eyes) and improvement or stabilization of headaches.

Assessment of stenosis was based on findings from an independent imaging core laboratory. A total of 27 subjects had RCVM at 1 year. 22 of 39 subjects (56.4%) treated with the River Stent had data available at the 1-year visit for all elements of the primary probable benefit outcome. For these 22 subjects with data available for all elements of the primary probable benefit outcome, results show that 54.5% (12/22) of subjects met the probable benefit endpoint which was a composite of multiple indicators of therapeutic benefit (Table 7). A sensitivity analysis utilizing multiple imputation was performed to evaluate the impact of missing data (Table 7). Results of this analysis were consistent with the primary results. As a worst-case analysis, the primary probable benefit endpoint was also evaluated without adjustments for missing data for the mITT cohort, with 30.8% (12/39) of subjects meeting the primary probable benefit endpoint. The individual components of the primary probable benefit endpoint are shown in Table 8 for subjects with 1-year RCVM data.

Table 7. Primary Probable Benefit Endpoint at 1 Year

Primary Probable Benefit Endpoint	Subjects % (n/N)	95% CI [LCL, UCL]
Prespecified Endpoint		
mITT with observed reliable visual field data and all elements to calculate probable benefit endpoint	54.5% (12/22)	32.2%, 75.6%
Additional Analyses for Sensitivity of Primary Probable Benefit Analysis		
mITT with multiple imputation (missing at random assumption)	55.4%	38.6%, 71.9%
mITT, all 39 subjects implanted with River Stent (worst-case analysis)	30.8% (12/39)	17.0%, 47.6%

Abbreviations: CI, confidence interval; LCL, lower confidence limit; UCL, upper confidence limit.

Table 8. Individual Components of Primary Probable Benefit Endpoint

Primary Probable Benefit Endpoint Component	Subjects, % (n/N)
Absence of significant (> 50%) stenosis on RCV	**88.9% (24/27)**
Of the stented sinus	100% (27/27)
Of new significant > 50% stenosis of other cerebral venous sinuses	88.9% (24/27)
Decrease of trans-stent pressure gradient < 8 mmHg	**88.9% (24/27)**
Clinically relevant improvement	**73.1% (19/26)**
Headaches: improvement in HIT-6 by 5 points and improvement or stabilization of visual field	76.0% (19/25)
Ophthalmic: improvement in visual field by 30% in the study eye and improvement or stabilization of headaches	0.0% (0/1)

Abbreviations: HIT-6, Headache Impact Test – 6; mITT, modified intent to treat; RCV, retrograde catheter venography.
Note: Component-level results are presented based on data availability. Of 39 subjects, 3 missed the 1-year visit and 2 withdrew at 6 months due to alternative IIH treatment (CSF shunt), resulting in 34 subjects eligible across components. For components 1 and 2, 7 additional subjects lacked RCV assessments (n=27). For component 3, 8 additional subjects had missing or unreliable visual field data (n=26).

9.4.3 Key Secondary Endpoints

New Venous Sinus Stenosis

There were 27 subjects who had RCVM at 1 year. New venous sinus stenosis was reported in 11.1% (3/27) of these subjects at 1 year, including one new stenosis of the transverse sinus and two superior sagittal sinus stenosis; all 3 stenoses were adjacent to the torcula. One additional subject had a shunt placed after 6 months for a new venous sinus stenosis in the superior sagittal sinus for a total new venous sinus stenosis rate of 14.3% (4/28). There was no in-stent stenosis observed in the cohort.

CSF Opening Pressure, Neuro-ophthalmology Evaluations, and Quality of Life

Results for CSF opening pressure, neuro-ophthalmology evaluations, and quality of life measures are summarized in Table 9 for the cohort.

Table 9. Summary of Secondary Outcomes

Variable	Baseline (BL)	3 Month	6 Month	1 Year	Change (1 Year – BL)
CSF Opening Pressure (cm H_2O)	32.9 ± 6.92 (39)	NA	NA	15.7 ± 7.40 (22)	-33.5 ± 36.36 (22)
HIT-6	69.5 ± 6.12 (39)	58.4 ± 11.84 (36)	56.5 ± 10.55 (37)	56.5 ± 10.49 (34)	-12.9 ± 9.57 (34)
Frisén Grade[1]	0.9 ± 0.81 (78)	0.1 ± 0.39 (76)	0.0 ± 0.20 (74)	0.0 ± 0.28 (64)	NR
ETDRS[1]	86.6 ± 6.28 (78)	87.2 ± 7.88 (76)	87.3 ± 7.15 (72)	87.5 ± 6.82 (64)	-0.4 ± 4.65 (64)
Visual Field PMD, Reliable (dB)[1]	-1.927 ± 5.1289 (60)	-1.813 ± 5.8810 (65)	-1.306 ± 5.0226 (63)	-0.772 ± 2.7704 (54)	0.116 ± 1.7676 (54)
Visual Field PMD, Reliable and Unreliable (dB)[1]	-2.543 ± 6.1377 (78)	-1.933 ± 5.7411 (76)	-1.369 ± 4.9511 (74)	-1.630 ± 5.0512 (64)	-0.395 ± 3.4496 (64)
Retinal Nerve Fiber Layer Thickness (µm)[1]	110.2 ± 29.21 (78)	96.1 ± 12.90 (76)	94.4 ± 12.70 (74)	96.8 ± 10.22 (60)	-12.3 ± 27.80 (60)
Tinnitus Function Index	50.09 ± 28.717 (37)	28.63 ± 25.392 (37)	29.57 ± 25.639 (36)	24.27 ± 23.880 (34)	-26.83 ± 32.977 (32)
Transient Visual Obscuration Present	14/39 (35.9%)	2/38 (5.3%)	1/37 (2.7%)	1/32 (3.8%)	NA
Diplopia Present	13/39 (33.3%)	6/38 (15.8%)	3/37 (8.1%)	2/32 (6.3%)	NA
Short-Form (SF)-12 Physical Component Summary	33.3 ± 10.21 (37)	42.1 ± 13.31 (37)	46.3 ± 11.54 (37)	45.0 ± 10.53 (34)	11.5 ± 11.19 (34)
SF-12 Mental Component Summary	29.8 ± 12.48 (37)	42.7 ± 14.91 (37)	39.7 ± 13.62 (37)	44.7 ± 12.21 (34)	14.7 ± 15.42 (34)
NEI-VFQ-25 Composite	61.8 ± 22.44 (39)	77.6 ± 19.82 (38)	80.3 ± 20.20 (37)	83.3 ± 18.28 (34)	20.6 ± 18.99 (34)
NEI-VFQ-25 with NO-10	58.6 ± 23.04 (39)	73.6 ± 21.05 (38)	78.0 ± 20.60 (37)	80.1 ± 19.11 (34)	20.5 ± 19.07 (34)
EQ-5D VAS	53.0 ± 18.86 (37)	65.1 ± 20.96 (37)	69.4 ± 18.55 (37)	71.9 ± 18.42 (34)	NR

Mean ± standard deviation (n) or n/N (%) shown.
Abbreviations: ETDRS, Early Treatment Diabetic Retinopathy Study; NEI-VFQ-25, 25-item National Eye Institute Visual Function Questionnaire; NO-10, 10-item neuro-ophthalmic supplement; NR, not reported; NA, not applicable; PMD, perimetric mean deviation.
[1]n for this measure indicates number of eyes.

Medication Usage

The average daily medication dose for acetazolamide and topiramate decreased at 1 year as compared to baseline (Table 10). Of the subjects taking the medication at baseline who had information on IIH medication usage at 1 year, 47% (8/17) and 29% (2/7) stopped taking acetazolamide and topiramate, respectively, by 1 year.

Table 10. Medication Daily Dose

IIH Medication	Baseline N=39	1 Year N=34	Change (1 Year – BL) N=24
Acetazolamide	986.8 ± 658.67 (19)	513.9 ± 609.20 (18)	-529.4 ± 565.15 (17)
Topiramate	97.2 ± 63.05 (9)	66.7 ± 48.41 (9)	-32.1 ± 87.46 (7)
Furosemide	30.0 ± 14.14 (2)	30.0 ± 14.14 (2)	0.0 ± 0.00 (2)

Abbreviations: BL, baseline; IIH, idiopathic intracranial hypertension; NC, not calculable.
Note: IIH medication usage for each visit was determined based on the start and end dates for the medication usage. Daily dose is the mg/day based on the dose at each visit.

9.4.4 Summary of Adverse Events

Serious adverse events are summarized in Table 11. Adverse events related to the study device and/or procedure is summarized in Table 12.

Table 11. Serious Adverse Events

System Organ Class Preferred Term	Subjects, n (%) N=39	Events	Related to Device	Related to Procedure	Resolved
Nervous system disorders	**2 (5.1%)**	**3**	**1**	**1**	**2**
Idiopathic intracranial hypertension[1]	2 (5.1%)	3	1	1	2
Infections and infestations	**2 (5.1%)**	**2**	**0**	**0**	**2**
Bacteremia	1 (2.6%)	1	0	0	1
Corona virus infection	1 (2.6%)	1	0	0	1
Vascular disorders	**2 (5.1%)**	**2**	**0**	**0**	**2**
Vascular stenosis	1 (2.6%)	1	0	0	1
Vein dissection	1 (2.6%)	1	0	0	1
Gastrointestinal disorders	**1 (2.6%)**	**1**	**0**	**1**	**1**
Gastrointestinal hemorrhage	1 (2.6%)	1	0	1	1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	**1 (2.6%)**	**1**	**0**	**0**	**0**
Plasma cell myeloma	1 (2.6%)	1	0	0	0

[1]One event of IIH was classified as both device and procedure related.

Table 12. Device/Procedure Related Adverse Events

System Organ Class Preferred Term	Subjects, n (%) N=39	Number of Events	Related to Device	Related to Procedure
Nervous system disorders				
Headache[1]	4 (10.3%)	4	2	4
Idiopathic intracranial hypertension[1]	1 (2.6%)	1	1	1
Paresthesia	1 (2.6%)	1	0	1
Injury, poisoning and procedural complications				
Contusion	2 (5.1%)	2	0	2
Respiratory, thoracic and mediastinal disorders				
Epistaxis	2 (5.1%)	2	0	2

System Organ Class Preferred Term	Subjects, n (%) N=39	Number of Events	Related to Device	Related to Procedure
Hemoptysis	1 (2.6%)	1	0	1
Eye disorders				
Eye pain	1 (2.6%)	1	0	1
Gastrointestinal disorders				
Gastrointestinal hemorrhage	1 (2.6%)	1	0	1
Musculoskeletal and connective tissue disorders				
Pain in extremity	1 (2.6%)	1	0	1

[1]Two headache events and one IIH event were classified as both device and procedure related.

9.4.5 Long-Term Follow-Up Data

Long-term follow-up data, including both clinical assessments and contrast-enhanced magnetic resonance venography (CE-MRV), were collected through five years post-implantation to evaluate the durability of treatment effects. The results of this extended follow-up were summarized in the mITT population using descriptive statistics.

A total of 21 subjects underwent a CE-MRV between 3- and 5-years post-implantation and data from these patients were pooled to assess long-term probable benefit. The long-term follow-up durations are shown in Table 13. Data available at 1 year and for long-term follow-up were not derived from the same subjects due to missingness at these timepoints.

Table 13. Timing of Long-Term CE-MRV

Variable	Number of Subjects (n= 21)
Year 3 to Year 4	4/21 (19.0%)
Year 4 to Year 5	9/21 (42.9%)
After Year 5	8/21 (38.1%)

9.4.5.1 Long-Term Probable Benefit Results

A long-term probable benefit endpoint was calculated, which is a composite of the following endpoints at the time of the long-term CE-MRV:

I. Clinically relevant improvement in headache defined as ≥ 5-point reduction in HIT-6;
and
II. Improvement or stable absence of papilledema;
and
III. Absence of significant (> 50%) stenosis of the stented sinus and of new significant (> 50%) stenosis of the other cerebral venous sinuses on CE-MRV.

Table 14. Long-Term Probable Benefit Endpoint

Long-Term Probable Benefit Endpoint	Subjects, % (n/N)	95% CI (LCL, UCL)
mITT	**85.71% (18/21)**	**(63.66, 96.95)**
Improvement in HIT-6 by ≥ 5 points	85.71% (18/21)	N/A
Improvement or stable absence of papilledema	100% (21/21)	N/A
Absence of significant (> 50%) stenosis on MRV	100% (21/21)	N/A

Abbreviations: CI, confidence interval; LCL, lower confidence limit; UCL, upper confidence limit.

Among the 21 mITT subjects with long-term CE-MRV data, 85.71% (18/21) met the long-term probable benefit endpoint, 18 of 21 subjects demonstrated sustained improvement in headache symptoms and 21 of 21 subjects showed resolution or stabilization of papilledema compared to their baseline. Additionally, 100% (21/21) showed no evidence of significant venous sinus stenosis at the time of follow-up imaging as deemed by the independent core lab.

9.4.5.2 Long-Term New Venous Sinus Stenosis

Two patients were found to have new stenoses at the time of their long-term CE-MRV follow-up. One patient developed a progression from mild to moderate stenosis in the contralateral transverse sinus, which remained asymptomatic. The other patient developed two new stenoses—one above the stent (end-stent stenosis) and one in the superior sagittal sinus—both of which were symptomatic. These stenoses were graded by the core lab as < 50% stenosis.

9.4.5.3 Long-Term Clinical Endpoints

Additional long-term clinical data were collected using the same metrics assessed at the 1-year follow-up. Headache impact scores (HIT-6) consistently improved by approximately 12 points from baseline across the 2- to 5-year follow-up period. Visual function measures—including ETDRS visual acuity, visual field mean deviation (PMD), and retinal nerve fiber layer (RNFL) thickness—also showed persistent gains from baseline, with improvements maintained or gradually increasing through 5 years. Patient-reported outcomes mirrored these trends: Tinnitus Function Index (TFI) scores declined by approximately 23–31 points from baseline across timepoints, and both SF-12 Physical and Mental Component Summary scores demonstrated sustained improvements of 8–17 points, indicating enhanced quality of life.

Frisén grade, diplopia, transient visual obscurations (TVOs), and EQ-5D VAS scores reflect the absolute scores at that timepoint (as opposed to change from baseline) and showed generally stable or improved values over time, supporting ongoing symptom resolution.

Table 15. Summary of Long-Term Clinical Outcomes

Variable	Baseline (BL)	2 Year – BL Change	3 Year – BL Change	4 Year – BL Change	5 Year – BL Change
HIT-6[1]	69.5 ± 6.1 (39)	-12.2 ± 10.5 (26)	-12.4 ± 9.7 (25)	-12.7 ± 9.0 (21)	-12.4 ± 9.0 (10)
Frisén Grade[2,3]	0.9 ± 0.81 (78)	0.0 ± 0.21 (46)	0.0 ± 0.14 (48)	0.0 ± 0.00 (38)	0.0 ± 0.00 (16)
ETDRS[2]	86.6 ± 6.3 (78)	0.4 ± 4.9 (40)	0.0 ± 3.8 (42)	0.8 ± 3.8 (36)	–1.2 ± 3.5 (16)
Visual Field PMD, Reliable VF (dB)[2]	-1.9 ± 5.1 (60)	0.89 ± 1.7 (41)	–0.35 ± 2.3 (44)	–0.53 ± 3.6 (37)	1.51 ± 2.0 (16)
Visual Field PMD, Reliable and Unreliable VF (dB)[2]	-2.5 ± 6.1 (78)	0.90 ± 1.8 (46)	–0.41 ± 2.5 (48)	–0.6 ± 3.6 (38)	1.51 ± 2.0 (16)
RNFL (µm)[2]	110.2 ± 29.2 (78)	0.7 ± 47.1 (46)	–8.7 ± 12.2 (48)	–8.5 ± 9.3 (38)	–9.5 ± 11.7 (16)
Tinnitus Function Index	50.1 ± 28.7 (37)	-30.9 ± 33.7 (23)	-22.7 ± 32.6 (23)	-27.0 ± 31.0 (19)	-23.6 ± 38.7 (11)
Transient Visual Obscuration Present[3]	14/39 (35.9%)	2/23 (8.7%)	3/24 (12.5%)	2/19 (10.5%)	0/8 (0.0%)
Diplopia Present[3]	13/39 (33.3%)	0/23 (0.0%)	2/24 (8.3%)	2/19 (10.5%)	1/8 (12.5%)
SF-12 Physical Component Summary[4]	33.3 ± 10.2 (37)	11.8 ± 13.3 (23)	10.5 ± 12.3 (23)	14.8 ± 12.4 (23)	8.1 ± 17.3 (19)

Variable	Baseline (BL)	2 Year – BL Change	3 Year – BL Change	4 Year – BL Change	5 Year – BL Change
SF-12 Mental Component Summary[4]	29.8 ± 12.5 (37)	15.8 ± 15.5 (23)	14.4 ± 15.4 (23)	15.2 ± 12.2 (23)	17.4 ± 12.9 (19)
EQ-5D VAS[3]	53.0 ± 18.86 (37)	72.2 ± 15.8 (26)	75.8 ± 13.8 (25)	73.0 ± 25.4 (21)	57.5 ± 30.8 (10)

Mean ± standard deviation (n) or n/N (%) shown.

[1]Measured across full population (i.e., both headache and ophthalmic group).

[2] n for this measure indicates number of eyes.

[3]Measured at single timepoints (i.e., 2 years, 3 years, 4 years, 5 years) as opposed to change from baseline.

[4]Calculated as paired data; change calculated as the mean of the year value minus the baseline value.

9.4.5.4 Weight-Loss Data

To better understand weight management efforts among participants with obesity (BMI ≥ 30), additional self-reported data were collected on prior and ongoing weight loss attempts. Most subjects reported active or previous efforts, including lifestyle changes, GLP-1 receptor agonist use (n=5), and bariatric surgery (n=4), both before and after stenting.

Table 16. Self-Reported Weight Loss Strategies

Weight Loss Strategy	Pre-Stenting Within the Last 12 Months (n = 13)	Post-Stenting Within the Last 12 Months (n = 21)
Behavioral or lifestyle modification	84.6% (11/13)	81.0% (17/21)
Medications	23.1% (3/13)	38.1% (8/21)
GLP-1 receptor agonists	0% (0/13)	62.5% (5/8)
Weight loss surgery	0% (0/13)	19.0% (4/21)
Bariatric surgery	0% (0/13)	75.0% (3/4)
Other	7.7% (1/13)	14.3% (3/21)
Total[1]	**84.6% (11/13)**	**85.7% (18/21)**

[1]Includes subjects who tried multiple weight loss strategies.

The majority of subjects reported pursuing weight loss both before (84.6%) and after treatment (85.7%), most commonly through behavioral modifications and, post-stenting, increased use of medications such as GLP-1 receptor agonists and surgical interventions. Despite these efforts, weight loss was not associated with differential outcomes—participants who lost weight and those who did not experienced similar improvements across all key clinical endpoints.

10 Directions For Use

10.1 Required Materials

Prepare the following materials using sterile technique:

- Introducer sheath (minimum size 6F, minimum inner diameter 0.078 in. or 2 mm)
- Guide catheter (minimum size 6F, minimum inner diameter 0.070 in. or 1.778 mm)
- Exchange length (> 300 cm) 0.014 in. (0.36 mm) guidewire with J shaped tip
- Microcatheter (minimum inner diameter 0.017 in.)
- 5-10 cc syringe filled with saline for flushing

10.2 Stent Size Selection

To select the River Stent size, examine the pre-treatment magnetic resonance venogram, computed tomography venogram or 3D catheter venography. Measure the perimeter of the transverse sinus at its upstream third, which will be the landing zone of the distal end of the River Stent. Select the River Stent size with distal perimeter immediately larger than the measured perimeter of the sinus based on Table 17.

Caution: Appropriate stent size selection is important to ensure stent apposition to the vessel wall.

Table 17. Stent Sizes

Catalog Number	Stent Length (mm)	Stent Proximal Diameter (mm)	Stent Distal Diameter (mm)	Stent Distal Perimeter (mm) [Low tolerance]
SRS70-0910	70	10.5	9.0	25
SRS70-0708	70	8.0	7.0	20
SRS70-0608	70	8.0	6.0	17

10.3 Directions for Use

10.3.1 Device Preparation

1. Carefully inspect the River Stent System package for damage to the sterile barrier.
2. Check the temperature indicator. Do not use the device if the center dot is black.

   Warning: If the center of the temperature indicator is black, it means that the device was exposed to a temperature of 60 ºC or more. Do not use if the temperature indicator is completely black as the stent may have been compromised.
3. Peel open the pouch using aseptic technique and place the tray containing the loaded River Stent delivery catheter into the sterile field.
4. Flush the plastic carrier tube through the Luer of the carrier tube (at the distal end) with a minimum of 5 cc of saline. Leave catheter in the carrier tube for a minimum of 30 seconds. This step will hydrate the external surface of the catheter including the distal 20 cm hydrophilic coated stent capsule and tip of the catheter. The distal 20 cm hydrophilic section must be kept hydrated if the catheter is not used immediately.

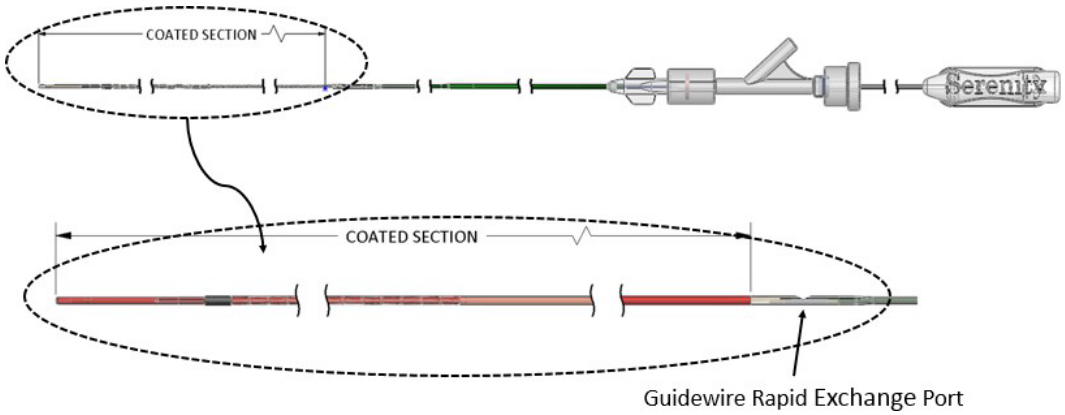


Figure 3: Hydrophilic Coated Section of the Catheter

5. Flush with saline the injection port of the rotating hemostatic valve of the loaded River Stent delivery catheter.
6. Tightly rotate the rotating hemostatic valve to secure the outer catheter to the inner catheter.

   Warning: The River Stent System is shipped with the Tuohy Borst valve in the OPEN position.

Care should be taken not to pre-deploy the stent. It is imperative to tightly rotate the rotating hemostatic valve prior to introduction of the River Stent System into the guide catheter to prevent premature stent delivery.

7. Remove the loaded River Stent delivery catheter from the tray.
8. Flush with saline the injection port of the rotating hemostatic valve until drops of saline come out of the proximal guidewire lumen of the River Stent delivery catheter.
9. Occlude the proximal guidewire exchange lumen of the loaded River Stent delivery catheter with your fingertip and again flush with saline the injection port of the rotating hemostatic valve until drops of saline come out of the distal guidewire lumen of the River Stent delivery catheter.

10.3.2 Stent Delivery Procedure

1. Use standard percutaneous technique to access the femoral vein on the side being stented with a compatible introducer sheath and guide catheter. Advance the tip of the guide catheter to the jugular sigmoid junction.
2. With the aid of a microcatheter, place a 0.014 in. exchange guidewire so that its tip is in the superior sagittal sinus.
3. Place the loaded River Stent delivery catheter over the guidewire and introduce it carefully inside the guide catheter.
4. Advance the loaded River Stent delivery catheter over the guidewire up to the sinus confluence (torcula), while ensuring that the tip of the guidewire does not move.
5. Position the River Stent so that the distal stent marker is located 5 to 10 mm below the torcula and the proximal marker is located in the vertical segment of the sigmoid sinus.

   Caution: The stent will foreshorten between 2 mm to 5.25 mm when released from the catheter delivery system.
6. Slowly pull the River Stent delivery catheter to straighten its course through the curves of the sigmoid sinus, without moving the distal stent marker.
7. To deploy the River Stent:
   a. Unscrew the rotating hemostatic valve of the loaded River Stent delivery catheter to loosen the inner and outer catheter assemblies.
   b. Ensure the orange seal within the hemostasis valve is positioned such that the catheters can move freely. If not, pull back slightly on the inner catheter and wiggle gently until the seal allows free movement.
   c. Firmly hold the handle of the inner catheter assembly and slowly pull the outer catheter to deploy the River Stent.

      Caution: Once the River Stent has started to deploy, it cannot be recaptured.
8. Remove the River Stent delivery catheter (inner and outer catheter assemblies).
9. Using standard operative procedures, perform routine venography to verify that the River Stent is fully expanded and that the transverse-sigmoid sinuses are fully patent.
10. Remove the guidewire, guide catheter, and introducer sheath from the patient.

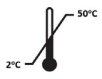
11 Disposal

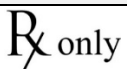
Dispose of the device in accordance with applicable local laws, regulations, and hospital procedures, including those regarding biohazards, microbial hazards, and infectious substances.

12 Patient Information

In addition to these Instructions for Use, the River Stent System is packaged with a patient implant card for the patient that contains information about the device. Patients should be instructed to always keep this card in their possession for identification of the implanted stent.

13 Symbol Glossary

Symbol	Title	Reference	Description
ISO 15223-1:2021 Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements			
	Manufacturer	5.11	Indicates the medical device manufacturer
	Date of manufacture	5.1.3	Indicates the date when the medical device was manufactured
	Use-by date	5.1.4	Indicates the date after which the medical device is not to be used
	Batch code	5.1.5	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Catalog number	5.1.6	Indicates the manufacturer's catalog number so that the medical device can be identified
	Model number	5.1.10	Indicates the model number or type number of a product
	Sterilized using ethylene oxide	5.2.3	Indicates a medical device that has been sterilized using ethylene oxide
	Do not resterilize	5.2.6	Indicates a medical device that is not to be resterilized
	Do not use if package is damaged and consult instructions for use	5.2.8	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information
	Single sterile barrier system	5.2.11	Indicates a single sterile barrier system
	Fragile, handle with care	5.3.1	Indicates a medical device that can be broken or damaged if not handled carefully
	Keep dry	5.3.4	Indicates a medical device that needs to be protected from moisture
	Temperature limit	5.3.7	Indicates the temperature limits to which the medical device can be safely exposed
	Do not re-use	5.4.2	Indicates a medical device that is intended for one single use only
	Consult instructions for use	5.4.3	Indicates the need for the user to consult the instructions for use
	Caution	5.4.4	Indicates that caution is necessary when operating the device or control close to where the symbol is placed, or that the current situation needs operator awareness or operator action in order to avoid undesirable consequences
	Non-pyrogenic	5.6.3	Indicates a medical device that is non-pyrogenic

Symbol	Title	Reference	Description
	Patient identification	5.7.3	Indicates the identification data of the patient
	Patient information website	5.7.4	Indicates a website where a patient can obtain additional information on the medical product
	Health care center or doctor	5.7.5	Indicates the address of the health care center or doctor where medical information about the patient may be found
	Date	5.7.6	Indicates the date that information was entered or a medical procedure took place
	Medical device	5.7.7	Indicates the item is a medical device
	Unique device identifier	5.7.10	Indicates a carrier that contains unique device identifier information
ASTM F2503-20 Standard practice for marking medical devices and other items for safety in the magnetic resonance environment			
	MRI conditional	7.4.6	An item with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields and the radiofrequency fields
CFR Title 21 Part 801 Labeling (FDA)			
	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician	801.109(b)(1)	Indicates the medical device is for prescription use only

Serenity Medical, Inc.
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Harrison, NY 10528 USA