

Sentinel® Cerebral Protection System



R_x Only

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

WARNING Contents supplied STERILE using a radiation process. Do not use if sterile barrier is damaged. If damage is found, call your Claret Medical® representative.

For single patient use only. Do not reuse, reprocess, or re-sterilize as these may compromise the structural integrity of the device and/or lead to device failure, and may result in patient injury, illness, or death. Reuse, reprocessing, or re-sterilization 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 disease(s) from one patient to another. Contamination of the device may lead to injury, illness, or death of the patient.

After use, dispose of product and packaging in accordance with hospital, administrative, and/or local government policy. In the event of a product complaint or malfunction the device should be returned to Claret Medical.

PRODUCT DESCRIPTION

The Claret Medical **Sentinel Cerebral Protection System** (Sentinel System) is a percutaneously delivered dual-filter protection device, designed to capture and remove debris dislodged during transcatheter aortic valve replacement procedures. The Sentinel System utilizes a filter delivered to the brachiocephalic artery (Proximal Filter), and a second filter delivered to the left common carotid artery (Distal Filter). At the completion of the procedure, the filters and debris are recaptured into the catheter and removed from the patient.

The Sentinel System consists of a 6 French catheter with deployable Proximal and Distal Filters, an Articulating Sheath, and an integral handle assembly. Table 1 and Table 2 provide information regarding the filter sizes and Sentinel System specifications.

Table 1: Filter-Vessel Sizing Guide

REF (Model) Number for Ordering	Proximal Filter Size (mm)	Target Proximal Vessel Size (mm)	Distal Filter Size (mm)	Target Distal Vessel Size (mm)
CMS15-10C-US	15	9 – 15	10	6.5 – 10

Table 2: Sentinel System Specifications

Delivery Profile	6F
Working Length	95 cm
Articulating Sheath Length	4 cm
Guidewire Compatibility	0.014" (0.36 mm) diameter floppy tip coronary guidewire, 175 cm minimum length

The Articulating Sheath tip, Proximal Sheath tip, Proximal Filter hoop, Distal Filter hoop and Distal Filter tip are radiopaque to enable visualization during use. See Figure 1 and Figure 2.

Package contains one (1) Sentinel System

INDICATIONS FOR USE

The Sentinel Cerebral Protection System is indicated for use as an embolic protection device to capture and remove thrombus/debris while performing transcatheter aortic valve replacement procedures. The diameters of the arteries at the site of filter placement should be between 9 – 15 mm for the brachiocephalic and 6.5 – 10 mm in the left common carotid.

CONTRAINDICATIONS

- Do not use in patients for whom anticoagulant and antiplatelet therapy is contraindicated.
- Do not use in patients with a known hypersensitivity to nickel-titanium.
- Do not use in vessels with excessive tortuosity.
- Do not use in patients with uncorrected bleeding disorders.
- Do not use in patients with compromised blood flow to the right upper extremity.
- Do not use in patients who have arterial stenosis >70% in either the left common carotid artery or the brachiocephalic artery.
- Do not use in patients whose brachiocephalic or left carotid artery reveals significant stenosis, ectasia, dissection, or aneurysm at the aortic ostium or within 3 cm of the aortic ostium.

WARNINGS

- Carefully read all instructions and labeling prior to use. Observe all warnings, cautions, and precautions noted throughout these instructions. Failure to do so may result in complications.
- Refer to the instructions for use supplied with any interventional devices to be used in conjunction with the Sentinel System for their intended uses, sizing, warnings, and precautions.

- The safety and effectiveness of the Sentinel System have not been demonstrated with transcatheter aortic valves other than the SAPIEN XT, SAPIEN 3, CoreValve®, and CoreValve® Evolut R®.
- The appropriate antiplatelet/anticoagulation therapy should be administered pre- and post-procedure in accordance with standard medical practice.
- Prior to use, the packaging and product should be inspected for signs of damage. Never use a damaged product or product from a damaged package.
- Never advance or withdraw the Sentinel System without proper fluoroscopic guidance or against resistance until the cause is determined. Advancing with such resistance may lead to embolization of debris, and vessel and/or device damage.
- It is recommended that the patency of the right radial or brachial artery be assessed prior to the introduction of the Sentinel System.
- It is recommended that the patient be tested for occlusion of the radial or brachial artery prior to device introduction.
- Do not use the device in left radial or left brachial access.
- Do not use the Sentinel System to deliver any type of fluid to the patient e.g. contrast media, heparinized saline, etc. due to risk of air embolization and compromise to device performance.
- Minimize movement of the Sentinel System after initial placement and stabilize the patient's right arm by their side. Excessive movement of filters may lead to embolization of debris, vessel and/or device damage.
- Do not deploy the filters within a previously repaired artery, an artery that has been used for dialysis purposes, or an AV fistula.
- Observe the Sentinel System under fluoroscopy and monitor the patient to verify the filters have not become occluded with debris resulting in slow or no flow. The filters should be recovered if they become occluded or if flow is compromised (See Procedural Use – Retrieval).
- Indwell time of the Sentinel System is not to exceed 90 minutes as occlusion could occur, resulting in slow or no flow.
- Failure to adequately close off the Flush Ports (Front Handle, Rear Handle) may result in air embolism.
- Do not undersize or oversize the filters in relation to the selected vessel diameter. This may result in inadequate vessel wall apposition or incomplete deployment of the filters. (Refer to Sizing Guide, Table 1).
- Do not apply excessive force to the Sentinel System. This may lead to distal embolization of debris, and vessel and/or device damage.

PRECAUTIONS

- Do not forcefully bend or reshape the Articulating Sheath of the Sentinel System. This may cause device damage.
- A guidewire with excessive stiffness may alter the shape of the Articulating Sheath curve and make cannulation of the left common carotid difficult.
- Use of a guidewire with an intermediate coil may result in compromised guidewire movement.
- Improper bending of the Sentinel System may damage the catheter.
- Do not re-sterilize or reuse on another vessel or patient.

ADVERSE EVENTS

Possible adverse events associated with Sentinel System use and application procedure include, but are not limited to, the following:

- | | |
|---|--|
| • Access site complications | • Gastrointestinal (GI) bleed |
| • Angina | • Hematoma |
| • Aortic dissection | • Ischemia (coronary, limb, carotid) |
| • Arrhythmia | • Infection (local or systemic) |
| • Arteriovenous fistula | • Myocardial Infarction (MI) |
| • Atelectasis | • Nerve injury |
| • Bleeding, operative or post-operative | • Pericardial effusion |
| • Cardiac Tamponade | • Pneumonia |
| • Cardiogenic Shock | • Pulmonary edema |
| • Conduction system injury | • Pulmonary embolism |
| • Congestive Heart Failure (CHF) | • Respiratory failure |
| • Death | • Respiratory insufficiency |
| • Endocarditis | • Stroke |
| • Embolism, including air | • Vessel injury (e.g., dissection, rupture, perforation, pseudoaneurysm) |

Adverse events experienced during clinical studies are presented in the Clinical Study Overview section.

HOW SUPPLIED

- Do not use if package is opened or damaged.
- Do not use if labeling is incomplete or illegible

STORAGE

- Store in cool, dry and dark place.
- Use the device prior to the Expiration Date noted on the box and pouch.

PHYSICIAN TRAINING

The Sentinel System should only be used by physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with endovascular procedures.

INSTRUCTIONS FOR USE

Preparing the Sentinel System for Use

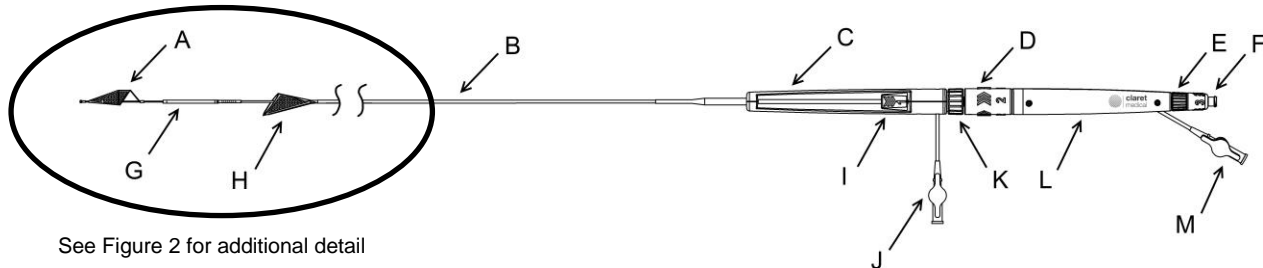
1. Administer anticoagulation medications and monitor activated clotting time per standard institutional guidelines. Anticoagulant therapy sufficient to maintain an Activated Clotting Time of at least 250 seconds for the duration of the procedure is recommended.
2. Perform an angiogram and/or Computed Tomography (CT) of the aortic arch per TAVR standard of care, it is also recommended that vessels above the arch be assessed.
3. Identify the location within the vessels where the filters will be deployed to ensure appropriate vessel sizing.

WARNING: Do not use the filters in vessels outside the indicated target vessel diameter ranges. This may result in inadequate vessel wall apposition, incomplete deployment of the filters, and/or vessel damage.

4. Ensure the introducer sheath size will accommodate the Sentinel System.
5. Using sterile techniques remove the Sentinel System from the packaging and place the system in a sterile work area.

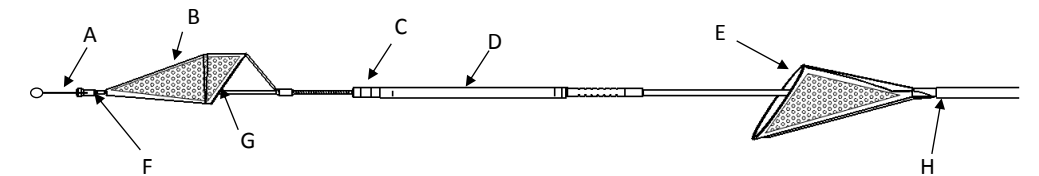
CAUTION: Do not use the product if the packaging sterile barriers have been damaged or compromised.

WARNING: Inspect the device for any damage. Never use a damaged product or product from a damaged package.



- | | | | |
|--------------------------|-----------------------------|-------------------------------|--------------------------|
| A Distal Filter | E Rear Handle Lock | I Proximal Filter Slider (#1) | M Rear Handle Flush Port |
| B Proximal Sheath | F Distal Filter Slider (#3) | J Front Handle Flush Port | |
| C Front Handle | G Articulating Sheath | K Front Handle Lock | |
| D Articulation Knob (#2) | H Proximal Filter | L Rear Handle | |

Figure 1: Sentinel Cerebral Protection System



- | | | |
|---|-----------------------------------|-------------------------------------|
| A Stylet | D Articulating Sheath | G Radiopaque Distal Filter Hoop |
| B Distal Filter | E Radiopaque Proximal Filter Hoop | H Proximal Sheath Radiopaque Marker |
| C Radiopaque Articulating Sheath Tip Marker | F Radiopaque Distal Filter Tip | |

Figure 2: Sentinel Cerebral Protection System – Distal Section

Flushing the Sentinel System

CAUTION: Do not prepare the Sentinel System or sheath the Proximal and Distal Filters until immediately prior to use.

Note: The device handle has two handle locks: Rear Handle Lock and the Front Handle Lock. Refer to Figure 1. Closing these locks facilitates flushing, prevents back-bleeding, and prevents motion of the device handle components and Distal Filter. The locks should be temporarily opened to facilitate movement of the handle components as required.

Note: The primary controls used to deploy the device, the Proximal Filter Slider (#1), the Articulation Knob (#2), and the Distal Filter Slider (#3), are all marked with the number "1", "2" and "3" indicating the order in which they are used. In this document, these names will be shown with the control number appended to the name.

1. Remove the packaging stylet from the distal guidewire lumen and discard.
2. Ensure that both the Front Handle Lock and the Rear Handle Lock are tightened.
3. Flush through the Flush Port in the Distal Filter Slider (#3) with heparinized saline until all air is removed and fluid passes from Distal Filter Tip guidewire lumen. See Figure 1.
4. Flush through the Rear Handle Flush Port (M) with heparinized saline until all air is removed and fluid passes from the tip of the Articulating Sheath. See Figure 1. Ensure that the Rear Handle Flush Port stopcock is closed following flushing.
5. Flush through the Front Handle Flush Port (J) with heparinized saline until all air is removed and fluid passes from the tip of the Proximal Sheath. See Figure 1. Ensure that the Front Handle Flush Port stopcock is closed following flushing.
6. Submerge the distal end of the device in heparinized saline, and loosen the Rear Handle Lock (L). With the distal tip submerged, slowly retract the Distal Filter by pulling back on the Distal Filter Slider (#3) until the filter is fully collapsed into the Articulating Sheath (D). The submerged filter may be agitated during sheathing in order to facilitate removal of bubbles. Tighten the Rear Handle Lock (L).

Note: Flushing and sheathing of the Distal Filter may be repeated to ensure all air has been removed from the system.

CAUTION: Do not over-retract the Distal Filter as damage may occur.

7. Ensure the Articulating Sheath is fully advanced until the Articulation Knob (#2) is in contact with the Front Handle Lock to ensure it does not interfere with sheathing the Proximal Filter. Tighten the Front Handle Lock. While submerged, sheath the Proximal Filter by slowly advancing the Proximal Filter Slider (#1) relative to the Front Handle until the Proximal Filter is fully sheathed. The submerged filter may be agitated during sheathing in order to facilitate removal of bubbles. See Figure 1 and Figure 8.
Note: Flushing and sheathing of the Proximal Filter may be repeated to ensure all air has been removed from the system.
8. While submerged, again flush through the Front Handle Flush Port with heparinized saline until all air is removed and fluid passes from the tip of the Proximal Sheath. See Figure 1. Ensure that the flush port stopcock is closed following flushing.

WARNING: Do not use a Sentinel System that has not been properly flushed. Failure to prepare and flush the device before use may introduce air and result in patient injury.

Note: Tighten both the Rear and Front Handle Locks prior to delivering device to prevent inadvertent movement.

Note: Use a minimum of 10cc of heparinized saline to flush through the Front Handle Flush Port to ensure all air has been removed from the system.

Note: Refer to the instructions for use supplied with any interventional devices to be used in conjunction with the Sentinel System for their intended uses, sizing, warnings, and precautions.

Procedural Use - Delivery and Deployment

WARNING: Do not use a Sentinel System that has not been properly flushed. Failure to prep and flush the device before use may introduce air and patient injury may result.

WARNING: To prevent damage to the System and/or harm to the patient, never advance, manipulate, or withdraw the Sentinel System without proper fluoroscopic guidance.

WARNING: The Sentinel System is not to be used to deliver any type of fluid to the patient e.g. contrast media, heparinized saline, etc.

1. Using standard interventional technique, place a 6 French introducer sheath into the radial or brachial artery of the patient's right arm after properly checking for patency of the artery before insertion of the Sentinel System.
2. Backload a floppy tip 0.014" coronary guidewire into the Distal Filter Tip located at the distal end of the Sentinel System until the guidewire tip is located just inside the distal tip of the Sentinel catheter.
 - o DO NOT use, a guidewire with excessive stiffness that may alter the shape of the Articulating Sheath curve and make cannulation of the left common carotid difficult.
 - o DO NOT use a guidewire with an intermediate coil as this may result in compromised guidewire movement.
3. Introduce the Sentinel System into the introducer sheath.
4. In the patient's right arm, advance the guidewire relative to the Sentinel System until the distal tip of the guidewire is a minimum of 10 cm beyond the distal tip of the Sentinel System using fluoroscopic guidance.
5. Advance the Sentinel System and the guidewire together using standard interventional technique until the Proximal Filter is in the intended target location in the brachiocephalic artery with the Articulating Sheath section of the catheter extending down the ascending aorta. Should the catheter tip extend down the descending aorta, pull the system back and rotate to advance down the ascending aorta.

WARNING: Do not advance the Sentinel System without a guidewire extending distally past the tip of the catheter a minimum of 10 cm.

WARNING: Do not use excessive force on the Sentinel System while introducing or advancing through the introducer sheath or blood vessels. Excessive force may cause damage to the device and/or patient harm.

Note: The Articulating Sheath will protrude into the aorta during proximal filter deployment.

6. Deploy the Proximal Filter by holding the Front Handle in a fixed position and slowly retracting the Proximal Filter Slider (#1) fully.

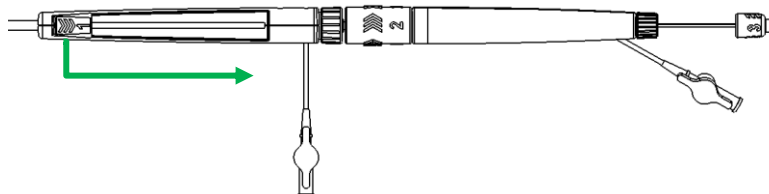


Figure 3: Proximal Filter Deployment

7. Confirm proper Proximal Filter position using fluoroscopy. The Proximal Filter should be positioned in the brachiocephalic artery to prevent any debris from reaching the right carotid artery. See Figure 3 and Figure 4.
8. If the proximal filter position is not optimal, the filter may be retrieved and repositioned up to two times. This may be done by holding the Front Handle in a stationary position and advancing the Proximal Filter Slider (#1) until the Proximal Filter is re-sheathed. The Proximal Filter may then be repositioned by advancing or retracting the catheter until optimal positioning is achieved. Finally, the Proximal Filter is redeployed by retracting the Proximal Filter Slider (#1) while holding the Front Handle in a fixed position.

CAUTION: Repositioning, if required, should only occur during initial placement and the proximal filter should be re-sheathed prior to re-positioning.

9. Confirm filter-to-vessel wall apposition using fluoroscopy, and ensure that the Proximal Filter and Proximal Sheath do not move after placement.
10. Withdraw the guidewire until the tip is located just within the distal tip of Sentinel catheter.
11. Loosen the Front Handle Lock to facilitate positioning of the Articulating Sheath.
12. Position the Articulating Sheath by manipulating the Rear Handle relative to the Front Handle in order to position the catheter tip. Rotate the Articulation Knob (#2) on the Rear Handle in the direction of the arrows in order to deflect the tip of the Articulating Sheath as necessary toward the left common carotid artery ostium.

CAUTION: Do not move the Front Handle, and thus the Proximal Filter, while manipulating the Rear Handle.

13. Advance the 0.014" guidewire beyond the distal tip of the Articulating Sheath in order to place the guidewire in the left common carotid artery.

CAUTION: Do not to advance the guidewire more than 5 cm into the left common carotid artery.

14. Position the Articulating Sheath so that the curvature matches the Brachiocephalic Artery – Aorta – Left Common Carotid Artery junction and is pulled up to the carina between the two vessels, see Figure 5.

Note: Ensure that the Articulating Sheath is well apposed to the carina, and does not protrude into the aortic space. See Figure 5 for correct positioning and Figure 7 for incorrect positioning.

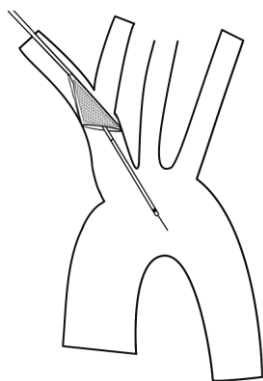


Figure 4

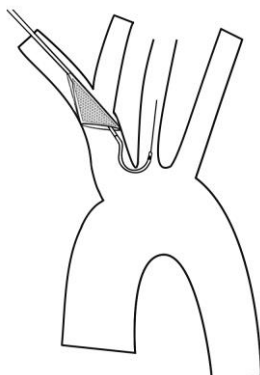


Figure 5

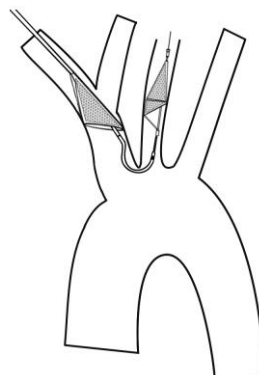


Figure 6

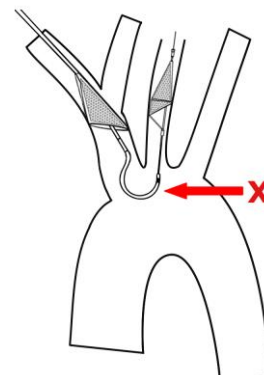


Figure 7

15. Secure the position of the Articulating Sheath by tightening the Front Handle Lock.
16. Loosen the Rear Handle Lock and advance the Distal Filter under fluoroscopy by pushing the Distal Filter Slider (#3) forward until the Distal Filter frame is fully expanded and apposed to the vessel wall. The Distal Filter should be positioned just beyond the Articulating Sheath tip and movement should be minimized once it is fully expanded in the vessel. See Figure 6.

WARNING: Minimize movement of the Sentinel System after filter deployment. Excessive movement may lead to embolization of debris, and vessel and/or device damage.

17. If the distal filter position is not optimal, the filter may be retrieved and repositioned up to two times. This may be done by gently withdrawing the Distal Filter Slider (#3) relative to the Rear Handle until the radiopaque Distal Filter Tip is flush with the Radiopaque Articulating Sheath Tip Marker as visualized on fluoroscopy, indicating that the Distal Filter is re-sheathed. The Distal Filter may then be repositioned with the Articulating Sheath and Handle manipulations until optimal positioning is achieved. Finally, the Distal Filter is redeployed by pushing the Distal Filter Slider (#3) forward until the Distal Filter frame is fully expanded and apposed to the vessel wall. See Figure 6.
18. Confirm filter-to-vessel wall apposition of the distal filter using fluoroscopy. See Figure 6.
19. Tighten the Rear Handle Lock. See Figure 1.

CAUTION: Verify that the Front Handle Lock and the Rear Handle Lock are tight and secure before any subsequent procedures.

CAUTION: Repositioning, if required, should only occur during initial placement and the distal filter should be re-sheathed prior to re-positioning.

20. Cover the exposed portion of the Sentinel System with a drape to prevent movement during subsequent endovascular procedures.

CAUTION: Care must be taken NOT to kink the exposed catheter.

WARNING: If gross movement of either the Proximal or Distal Filter is noted, check to ensure filters remain apposed to the vessel walls by fluoroscopy.

WARNING: If the arterial flow is believed to be compromised (slow / no flow), the filters should be re-sheathed and retrieved. See Retrieval below.

Procedural Use – Retrieval

WARNING: Do not pull excessively on the Sentinel System to avoid filter membrane tears, filter hoop detachment, system damage or patient harm during use.

WARNING: Never advance or withdraw the Sentinel System without proper fluoroscopic guidance.

WARNING: Never withdraw or move an intravascular device against any resistance until the resistance cause is determined. Advancing or retracting with resistance may lead to embolization of debris, and vessel and / or device damage.

1. Loosen the Rear Handle Lock. See Figure 1.
2. Gently withdraw the Distal Filter Slider (#3) relative to the Rear Handle until the radiopaque Distal Filter Tip is flush with the Radiopaque Articulating Sheath Tip Marker as visualized on fluoroscopy. Tighten the Rear Handle Lock.

WARNING: Exercise caution when using the partial enclosure recovery method. If resistance is felt during catheter withdrawal, advance the Distal Filter and Articulating Sheath together distally and withdraw the Distal Filter more fully into the Articulating Sheath before re-attempting withdrawal of the catheter.

3. Loosen the Front Handle Lock and withdraw the Articulating Sheath tip from the left common carotid artery by manipulating, straightening, rotating, and advancing or withdrawing the Rear Handle and rotating the Articulation Knob (#2) until the Articulating Sheath tip is straight and is within the aorta.
4. Advance the Articulating Sheath completely by advancing the Rear Handle until the Articulation Knob (#2) contacts the Front Handle Lock to prevent interference with the Proximal Sheath or Proximal Filter during Proximal Filter retrieval. Tighten the Front Handle Lock. See Figure Figure 8.

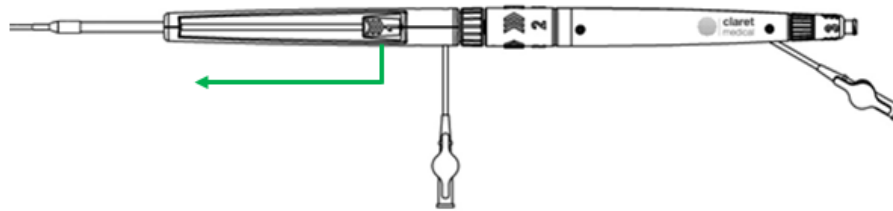


Figure 8: Sentinel Distal Filter Deployment

5. Re-sheath the Proximal Filter by holding the Front Handle in a stationary position and slowly advancing the Proximal Filter Slider (#1) until the Proximal Sheath Radiopaque Marker meets the Articulating Sheath as visualized on fluoroscopy. See Figure 8. Minimize retracting or advancing the Front Handle during this step. Vessel damage may occur or debris may be lost should the Proximal Filter be moved when in the deployed state.
6. Advance the guidewire prior to withdrawal of the Sentinel System. Withdraw the catheter system while using fluoroscopy.

Note: If there is any resistance to removing the Sentinel System from the introducer, remove the introducer and the Sentinel System together.

CAUTION: Do not re-sterilize or reuse this device.

Note: After use, dispose of product and packaging in accordance with hospital, administrative, and/or local government policy. In the event of a product complaint or malfunction the device should be returned to Claret Medical.

SENTINEL CLINICAL STUDY SUMMARY

Cerebral Protection in Transcatheter Aortic Valve Replacement, The SENTINEL Study

Purpose: To assess the safety and effectiveness of the Claret Medical Sentinel Cerebral Protection System used for embolic protection during Transcatheter Aortic Valve Replacement (TAVR) compared to TAVR standard of care (without cerebral protection).

Design: The SENTINEL Study was a prospective, single blind, multi-center, randomized study using the Sentinel® Cerebral Protection System in patients with severe symptomatic calcified native aortic valve stenosis indicated for TAVR. A total of three hundred and sixty-three (363) patients at nineteen (19) centers in the United States and Germany were randomized across three arms (Safety, Test, and Control) in a 1:1:1 fashion. Subjects who met the commercially approved indications for TAVR and complied with the study inclusion/exclusion criteria were enrolled.

Subjects randomized to the Safety, Test and Control Arms underwent the following regimen:

- 1) Safety Arm: TAVR + the Sentinel System. Subjects enrolled in this arm of the study underwent safety follow up post procedure, 30 and 90 days post procedure. Safety Arm subjects did not undergo MRI or neurocognitive assessments.
- 2) Test Arm: TAVR + the Sentinel System. Subjects enrolled in this arm of the study underwent safety follow up post-procedure, 30 and 90 days; effectiveness with Magnetic Resonance Imaging (MRI) follow up at 2-7 days, and 30 days; and neurocognitive evaluation at 2-7, 30 and 90 days post-procedure.
- 3) Control Arm: TAVR only. Subjects enrolled into this arm of the study underwent safety follow up at post-procedure, 30 and 90 days; effectiveness with MRI follow up at 2-7 days and 30 days; and neurocognitive evaluation at 2-7, 30 and 90 days post-procedure.

A Clinical Events Committee (CEC) remained blinded throughout the trial and adjudicated all MACCE event endpoints. Independent blinded MRI and neurocognitive corelabs analyzed all the MRI and neurocognitive endpoint data.

Primary Endpoints:

- 1) **Safety:** The primary safety endpoint was the occurrence of all Major Adverse Cardiac and Cerebrovascular Events (MACCE) at 30 days compared to a historical performance goal, with MACCE defined as all death, all stroke, and all Class 3 Acute Kidney Injury (AKI). The primary safety endpoint analysis was based on the combination of the Safety and Test Arms.
- 2) **Effectiveness:** The primary effectiveness endpoint was total new lesion volume in protected territories (i.e. regions of the brain perfused by the Brachiocephalic and Left Common Carotid arteries) at 2-7 days post procedure as assessed by diffusion weighted MRI (DW-MRI). Two assessments were designed to evaluate DW-MRI infarct lesion volume between patients with and without protection. The first hypothesis-driven criterion was to show that there was a statistically significant reduction in median total new DW-MRI lesion volume in protected territories for patients with protection with the Sentinel System compared to those without protection (Criterion #1). The second criterion was intended to show that there was an observed reduction of at least 30% in median new lesion volume (Criterion #2) in protected territories in the Test Arm comparing to the Control Arm.

Secondary Endpoints: Secondary endpoints consisted of the following:

- 1) **Safety:** In-hospital MACCE (Safety + Test); MACCE rate at 30 days (Test vs Control); Major vascular complications during the index procedure and within 30 days of the index procedure (Safety + Test); Incidence of serious adverse events within 30 days (Safety + Test vs Control)
- 2) **Effectiveness (Test vs Control):** 2-7 day median number of new lesions in protected territories; 2-7 day median total new lesion volume in all territories; 2-7 days median number of new lesions in all territories; change in neurocognitive battery z-score from baseline to 30 days; 30 day median new lesion volume in protected territories; 30 day median number of new lesions in protected and all territories; 2-7 day maximum new lesion volume in protected and all territories; 2-7 day maximum new lesion number in protected and all territories; 30 day maximum new lesion number in protected and all territories; Captured debris histopathology (Test Arm only); Correlation of 2-7 day MRI lesion volume with changes in neurocognitive battery composite z-score at 90 days, 30 days, and 2-7 days; Correlation of 30 day MRI lesion volume with changes in neurocognitive battery composite z-score at 90 days and 30 days; 30 day new lesion volume in all territories; Change in neurocognitive battery composite z-score from baseline to 2-7 days and to 90 days; Acute delivery and retrieval success; Change in neurocognitive domain scores from baseline to 2-7 days, 30 days, and 90 days

Eligibility Criteria Summary: The study population consisted of male and female patients, at least 18 years of age.

Key inclusion criteria included the following:

- Symptomatic severe aortic stenosis eligible for treatment with a US commercially approved TAVR system
- Acceptable aortic arch anatomy and vessel diameters without significant stenosis

Key exclusion criteria included the following:

- Anatomic:
 - Right extremity vasculature not suitable
 - Brachiocephalic, left carotid or aortic arch not suitable
- Clinical:
 - Cerebrovascular accident or transient ischemic attack within six months
 - Neurological disease with persistent deficits
 - Carotid disease requiring treatment within six weeks
 - Contraindications to MRI
 - Renal insufficiency
 - Severe LV dysfunction
 - Balloon valvuloplasty within 30 days

Accountability: Patients were exited from the study upon completing the final protocol required 90-day follow-up visit. In some cases, patients prematurely exited or withdrew from the study for, including but not limited to, the following reasons:

- Not eligible for treatment (including patients who may have signed Informed Consent and been randomized).
- Patient death.
- Voluntary withdrawal – the patient voluntarily chose not to participate further in the study.
- Lost to follow-up (LTFU) – the patient was more than 14 days late to a study visit and three documented attempts to contact the patient were unsuccessful. A patient who missed a study visit but attended a subsequent visit was no longer considered lost to follow-up. A missed visit was considered a protocol deviation and the deviation was documented and reported.
- Physician decision – In the physician’s opinion, it was not in the best interest of the patient to continue study participation.
- Patient was determined to be ineligible during the procedure per the angiographic inclusion criteria or experienced a clinical event that put the patient at risk.

The tables below summarize patients who exited the study at 30 days (primary safety endpoint) and at 90 days (study completion). Note: Some subjects received a 30-day follow-up visit prior to study exit and are reflected in the overall safety follow-up rates.

Table 3: Study Exit Summary (30 Days)

	Safety Arm	Test Arm	Control Arm	Total Randomized
Voluntary Withdrawal	2.4%	2.5%	5.9%	3.6%
Lost to Follow-Up	1.7%	0.8%	1.7%	1.4%
Physician’s Decision	0.00%	0.8%	0.8%	0.5%
Death	1.6%	0.8%	1.7%	1.4%
Other	0.8%	0.8%	0.8%	0.8%
Overall “exited” Patients	6.5%	5.7%	10.9%	7.7%
Overall LTFU patients not evaluable for 30d MACCE				1.1% (4/363)

One patient had a stroke and exited at day 29 and was evaluable for 30d MACCE

One patient died at day 19 and was evaluable for 30d MACCE

Table 4: Study Exit Summary (90 days)

	Safety Arm	Test Arm	Control Arm	Total Randomized
Completion of Study as Planned	84.6%	79.3%	71.4%	78.5%
Voluntary Withdrawal	3.3%	3.3%	9.2%	5.2%
Lost to Follow-Up	5.7%	7.4%	9.2%	7.4%
Physician's Decision	0.0%	1.7%	2.5%	1.4%
Death	4.1%	5.0%	4.2%	4.4%
Other	2.4%	3.3%	3.4%	3.0%
Overall	100%	100%	100%	100%

Among 244 subjects assigned to receiving the Sentinel System, 13 subjects were not treated with Sentinel System (3 no TAVR, 6 inadequate vascular access, 3 late screen failure, 1 treated as Control). Acute delivery and retrieval success (i.e. both filters successfully deployed) was achieved in 94.4% (218/231) of patients treated with the Sentinel System and Procedural Success (at least one filter deployed) was achieved in 99.6% (230/231) of the treated patients.

The SENTINEL study also allowed for up to 5 roll-in patients at each investigational site. In total, 65 roll-in subjects were treated in SENTINEL with follow-up results similar to those observed in the randomized treatment arm.

Demographics: The total population consisted of 428 patients. Of these, 65 were training phase non-randomized "Roll-In" subjects that utilized the Sentinel System during TAVR. Information on the randomized (n=363) patients is provided in Table 5 below.

Table 5: Patient Demographics

Attribute	Safety Arm (N=123)	Test Arm (N=121)	Control Arm (N=119)
Age (mean, yrs)	82	82	83
Female (%)	55	52	49
STS PROM Score (mean, %)	6.2	6.4	7.5
Previous stroke (%)	8	4	5
Previous TIA (%)	8	7	7
Diabetes (%)	27	41	38
h/o atrial fibrillation (%)	30	35	30
Heavily calcified aorta (%)	3	2	3
h/o CAD (%)	54	50	56
h/o PVD (%)	16	14	15
NYHA III/IV (%)	83	85	82
Valve area (cm ²)	0.7 ± 0.18	0.7 ± 0.17	0.7 ± 0.20
Mean aortic valve gradient (mmHg)	42 ± 15	44 ± 15	41 ± 14

Adverse Events: The adverse events presented in Table 6 and Table 7 were observed in SENTINEL through 30 days and 90 days, respectively. All events were adjudicated by an independent Clinical Events Committee (CEC).

Table 6: Adverse Events Through 30 Days

Event Type	(Safety + Test Arms) N=244		Control Arm N=119	
	Total Events	Subjects w/Event(s)	Total Events	Subjects w/Event(s)
Acute kidney injury	7	2.9% (7)	5	2.5% (3)
Vascular complication	21	8.6% (21)	9	7.6% (9)
TAVR Access Site	20	8.2% (20)	9	7.6% (9)
Radial Artery	0	0% (0)	N/A	N/A
Brachial Artery	1	0.4% (1)	N/A	N/A
Stroke	13	5.3% (13)	10	8.4% (10)
Disabling	2	0.8% (2)	1	0.8% (1)
Non-disabling	11	4.5% (11)	9	7.6% (9)
Transient Ischemic Attack (TIA)	1	0.4% (1)	0	0.0% (0)
Death	3	1.2% (3)	2	1.7% (2)

Note: AKI includes Class 1, 2, and 3

Table 7: Adverse Events Through 90 Days

Event Type	(Safety + Test Arms) N=244		Control Arm N=119	
	Total Events	Subjects w/Event(s)	Total Events	Subjects w/Event(s)
Acute kidney injury	7	2.9% (7)	5	2.5% (3)
Vascular complication	21	8.6% (21)	9	7.6% (9)
TAVR Access Site	20	8.2% (20)	9	7.6% (9)
Radial Artery	0	0% (0)	N/A	N/A
Brachial Artery	1	0.4% (1)	N/A	N/A
Stroke	13	5.3% (13)	12	9.2% (11)
Disabling	2	0.8% (2)	3	2.5% (3)
Non-disabling	11	4.5% (11)	9	7.6% (9)
Transient Ischemic Attack (TIA)	1	0.4% (1)	1	0.8% (1)
Death	11	4.5% (11)	4	3.4% (4)

Note: AKI includes Class 1, 2, and 3

Results: The principle safety and effectiveness results from patients in the SENTINEL study are provided below. The primary safety analysis was based on all patients as randomized to the Safety and Test Arms, referred to as Intention to Treat (ITT) population. The primary safety endpoint included imputation for missing clinical outcomes data using the logistic regression method. The imputation model included baseline characteristics including age, sex, BMI, history of diabetes, atrial fibrillation, stroke with permanent deficit, and geography.

Primary Safety Endpoint: The primary safety endpoint of the SENTINEL trial was met with a p-value of <.0001 in both ITT populations (with and without imputation), see Table 8. The primary safety endpoint analysis was based on a one-sided binomial test, compared to an a priori performance goal (PG) threshold of 18.3% for determination of non-inferiority. The point estimate for the historical performance goal was derived from published FDA documents as well as the published literature.

Table 8: Primary Safety Endpoint (Non-Inferiority) – 30-Day Adjudicated MACCE Rate

	Total Events	Subjects w/Event(s)	Performance Goal	Upper 95% Confidence Interval ¹	P-value ¹
ITT, with imputation ⁴	NA ²	18/244 (7.4%)	18.3% ³	10.7%	<.0001
ITT	17	17/234 (7.3%)	18.3%	10.7%	<.0001

Note: MACCE, Major Adverse Cardiac and Cerebrovascular Events, are defined as All Death, All Stroke, and Acute Kidney Injury (Class 3) at 30 days compared to a historical performance goal.

¹Upper confidence interval and p-value based on exact one-sided test for alternative hypothesis: rate < PG with 0.05 alpha level

²Binary outcome based on imputation analysis, number of events does not apply

³Performance Goal of 18.3% was used for testing non-inferiority

⁴Imputation for missing data

Primary Effectiveness Endpoint: The primary effectiveness endpoint analysis (Criterion 1 and 2) was based on the ITT population comparing the Test Arm and Control Arm. The primary effectiveness endpoint included imputation for missing clinical outcomes data using the predictive mean matching method based on blinded, aggregate, SENTINEL data.

The primary effectiveness endpoint based on ITT was not found to be statically significant with a p-value 0.33 (Table 9). Criterion 2 was met and the observed treatment effect of 42% in protected territories was > 30% target (Table 10).

The evaluation of effectiveness in SENTINEL consisted of multiple neuroimaging, histopathology, histomorphometry and neurocognitive endpoint analyses. Results for all analyses are provided below; additional information on key outcomes from each of these four areas is also provided.

Table 9: Primary Effectiveness Criterion 1 - Median 2-7 Day DW-MRI Total New Lesion Volume (Protected Territories)

	Test Arm median (IQR), n, min, max	Control Arm median (IQR), n, min, max	Observed Treatment Difference (Test - Control)	p-value ¹
ITT with Imputation, mm3	109.1 (36.9, 379.7), n=121, 0 min, 5175.9 max	174 (39.6, 469.3), n=119, 0 min, 24300 max	-64.9	0.24
ITT, mm3	102.8 (36.9, 423.2), n=91, 0 min, 5175.9 max	178 (34.3, 482.5), n=98, 0 min, 24300 max	-75.1	0.33

¹Based on two-sided Wilcoxon test

Table 10: Primary Effectiveness Criterion 2 - 30% Reduction in 2-7 Day DW-MRI Median Total Lesion Volume (Protected Territories)

	Test Arm median (IQR), n, min, max	Control Arm median (IQR), n, min, max	Target	Observed % Reduction (Test-Control)/Control
ITT, mm3	102.8 (36.9, 423.2), n=91, 0 min, 5175.9 max	178 (34.3, 482.5), n=98, 0 min, 24300 max	30%	42.2

Key Secondary Safety Endpoints: A breakdown of the MACCE components compared to the concurrent Control Arm is provided in Table 11.

Table 11: 30-Day MACCE and Component Rates

	(Safety + Test Arms) % patients with event (n patients with event/N patients) [exact 95% CI]	Control Arm % patients with event (n patients with event/N patients) [exact 95% CI]
ITT		
Any MACCE	7.3% (17/234) [4.3%,11.4%]	9.9% (11/111) [5.1%,17.0%]
Death	1.3% (3/234) [0.3%,3.7%]	1.8% (2/111) [0.2%,6.4%]
Stroke	5.6% (13/231) [3.0%,9.4%]	9.1% (10/110) [4.4%,16.1%]
Disabling	0.9% (2/231) [0.1%,3.1%]	0.9% (1/109) [0.0%,5.0%]
Non-disabling	4.8% (11/231) [2.4%,8.4%]	8.2% (9/110) [3.8%,15.0%]
AKI (Class 3)	0.4% (1/231) [0.0%,2.4%]	0% (0/110) [0.0%,3.3%]

Secondary Safety Analyses are provided below (ITT population).

- **In-Hospital MACCE:** Numerically lower between the Safety + Test Arms [5.7% (14/244)] versus the Control Arm [8.4% (10/119)]. The observed stroke rate in the Safety + Test Arms (4.9%) versus the Control Arm (8.4%) resulted in a 41.7% relative reduction.
- **30-Day MACCE (Test Arm vs Control Arm):** 6.0% (7/117) and stroke rate of 4.3% (5/116) in the Test Arm were numerically lower than the Control Arm, [9.9% (11/111) and 9.1% (10/110) respectively].
- **Major vascular complications (Index procedure and within 30 days):** Incidence of adjudicated major vascular events were low during the index procedure with no radial or brachial events during the procedure, and only one brachial event (0.4%) within 30 days of the index procedure.
- **Serious Adverse Events (30 days):** Site reported serious adverse events were similar between the Safety + Test Arms and the Control Arm. The events did not exceed rates reported from contemporary TAVR studies, with 42.6% (104/244) being reported for the Safety + Test Arms and 42.9% (51/119) for the Control Arm.

Safety was evaluated out to 90 days for all patients. Similar to the 30-Day MACCE rate, 90-Day MACCE was numerically lower between the Safety Cohort [11.3% (24/213)] and Control Arm [12.9% (12/93)]. Specifically, strokes were numerically lower between the Safety + Test Arms [6.4% (13/202)] and the Control Arm [12.0% (11/92)].

Key Secondary Effectiveness Endpoints:

The table below compares results observed in the regions of the brain protected by the Sentinel System and the entire brain (all territories).

Table 12: Protected and All Territories 2-7 Day Median Total New Lesion Volume

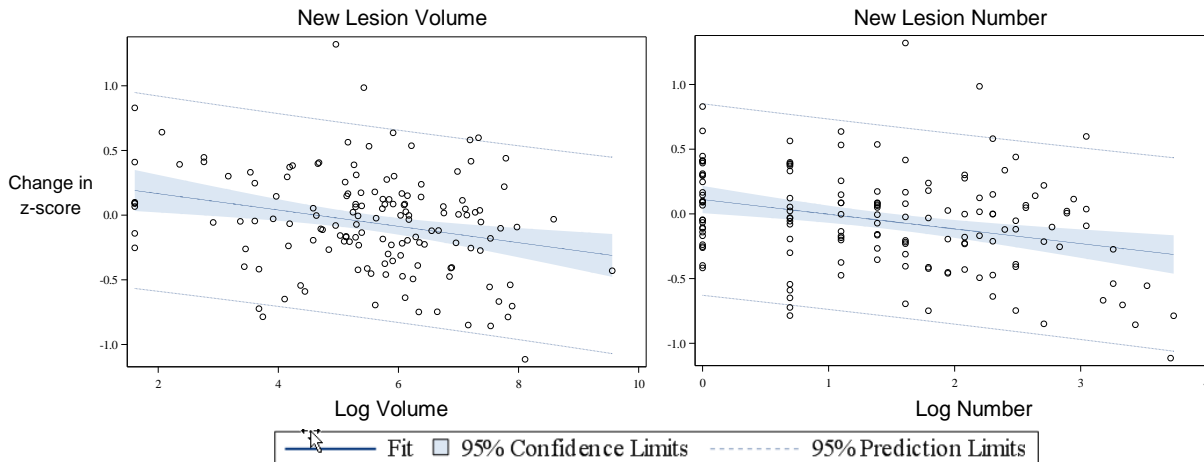
	Protected Territories			All Territories		
	Test Arm median (IQR), n, min, max	Control Arm median (IQR), n, min, max	Observed Treatment Difference (Test – Control) (mm ³)	Test Arm median (IQR), n, min, max	Control Arm median (IQR), n, min, max	Observed Treatment Difference (Test – Control) (mm ³)
ITT with Imputation, mm ³	109.1 (36.9, 379.7), n=121 0 min, 5175.9 max	174 (39.6, 469.3), n=119 0 min, 24300 max	-64.9	247.2 (97.6, 572.2), n=121 0 min, 14179 max	311.1 (110.7, 848.4), n=119 0 min, 24300 max	-63.9
ITT, mm ³	102.8 (36.9, 423.2), n=91 0 min, 5175.9 max	178 (34.3, 482.5), n=98 0 min, 24300 max	-75.1	294 (69.2, 786.4), n=91 0 min, 14179 max	309.8 (105.5, 859.6), n=98 0 min, 24300 max	-15.8

A neurocognitive test battery of composite z-scores from baseline to follow-up between the Test and Control Arms was performed at 30 days, no difference in the mean change in z-score between the Test Arm and the Control Arm were observed, possibly due to 82% of the population having been below the age adjusted norm (i.e. floor effect). The composite z-score is an overall cognition score that is the average of the z-scores from each of the five cognitive domains assessed: attention, executive function, processing speed, verbal memory and visual memory. A relative negative z-score indicates worsening neurocognition while a relative positive z-score indicates an improvement in neurocognition. In SENTINEL, the range of changes in z-score from baseline to 30 days was -1.45 to 1.39 and was not statistically significant between the test and control arms (reference Table 13 for the mean change in z-score).

Table 13: Change in Composite Z-Score (Baseline - 30 Days)

	Test Arm Mean ± SD, n	Control Arm Mean ± SD, n
ITT	-0.09 ± 0.44, 93	-0.03 ± 0.37, 92

A key finding in SENTINEL was the correlation of neurocognitive decline at 30 days with DW-MRI New Lesions Volume and Number (log transformed) at 2-7 days post procedure in All Territories ($r = -0.27$, 95% confidence interval of -0.42 to -0.11 ; $r = -0.30$, 95% confidence interval of -0.44 to -0.15 , respectively). A z-score of zero is average, the figures below demonstrate that increases in lesion volume and number correlate to a decrease in composite z-score, e.g. a decrease in neurocognitive function.

**Figure 9: Change in Composite Z-Score (Baseline - 30 Days) Correlated to New Lesion Volume & Number in All Territories**

Remaining Secondary Endpoint Results: Results for prospectively defined secondary endpoints not discussed above as performed on the ITT population are included below:

- **2-7 Day Median Number of New Lesions (Protected Territories):** The number of new lesions was numerically lower in the Test Arm (2) versus the Control Arm (3).
- **2-7 Day Median Number of New Lesions (All Territories):** The number of new lesions was numerically lower in the Test Arm (3) versus the Control Arm (5) but was not statistically significant.
- **Difference in Neurocognitive Battery Composite Z-Score from Baseline to 30 Days:** The difference in composite z-score was not statistically different between the Test Arm and Control Arm.
- **30-Day Median Total New Lesion Volume (Protected Territories):** The total new lesion volume at 30 days was zero for both the Test Arm and Control Arm and was not significant.
- **30-Day Median Number of New Lesions (Protected & All Territories):** The number of new lesions at 30 days was zero for both the Test Arm and Control Arm in both protected and all territories and was not significant.
- **2-7 Day Maximum and Median New Lesion Volume (Protected & All Territories):** None of the results from this evaluation were found to be statistically significant.
- **30-Day Maximum and Median New Lesion Volume (Protected & All Territories):** None of the results from this evaluation were found to be statistically significant.
- **Correlation of 2-7 Day Lesion Volume to 2-7 Day and 90 Day Z-Score:** The correlations were not found to be statistically significant at these time points.
- **Correlation of 30-Day Lesion Volume to 30 Day and 90 Day Z-Score:** The correlations were not found to be statistically significant at these time points.
- **30-Day Median Total New Lesion Volume (All Territories):** The total new lesion volume at 30 days was zero for both the Test Arm and Control Arm and was not significant.
- **Difference in Neurocognitive Battery Composite Z-Score from Baseline to 2-7 Days & 90-Days:** The difference in composite z-score was not statistically different between the Test Arm and Control Arm at either time point.
- **Acute Delivery and Retrieval Success:** Acute delivery and retrieval success was achieved in 94.4% (218/231) of patients (both filters deployed). At least on filter was deployed in 99.6% of patients.
- **Change in Individual Neurocognitive Domain Scores:** No statistically significant changes were observed in any of the domain analyses.

Key Post Hoc Analyses: As the Sentinel System is a temporary accessory device, a post hoc analysis of the SENTINEL data evaluating strokes at the time points most applicable to device usage (i.e. peri-procedural, ≤ 72 hours) was performed. The percentage of strokes ≤ 72 hours in the Safety + Test Arms (3.0%) were compared to the percentage of strokes ≤ 72 hours in the Control Arm (8.2%). The results of this analysis demonstrated a relative reduction of 63% in stroke rates in favor of the Sentinel System, reference Figure 10 below.

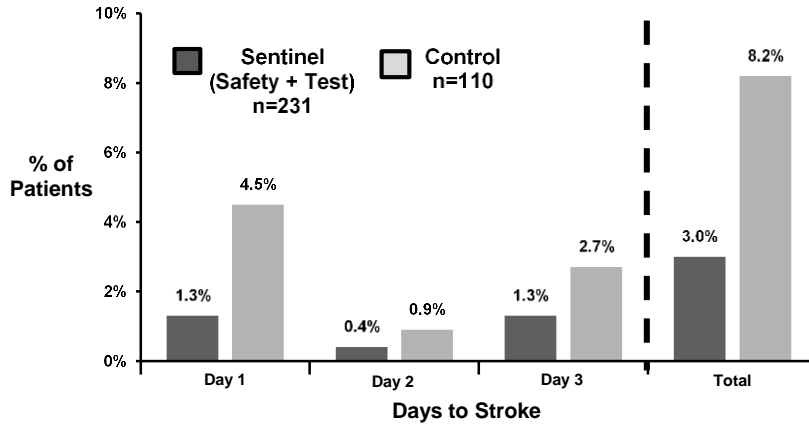


Figure 10: Peri-Procedural Stroke Rate Results

A key secondary finding in SENTINEL was from the quantitative histopathological analysis of TAVR procedure related embolic material (Test Arm only). It demonstrated that debris was captured in 99% of TAVR patients regardless of valve type (see figure below) and that 1 in 4 patients had an average of 25 particles $\geq 0.5\text{mm}$ in size (all patients broken down into quartiles based upon debris size captured).

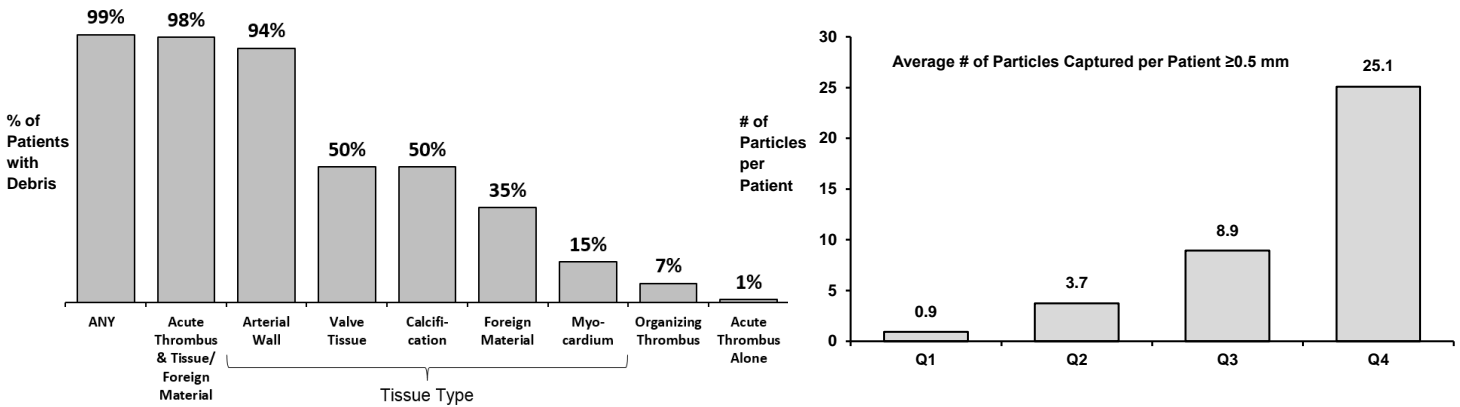


Figure 11: Histopathology Results

Conclusions: The SENTINEL trial demonstrated that there is reasonable assurance of safety for the Sentinel System, and that it effectively captures debris. Sentinel System deployment was achieved in 94.4% of patients and 100% of devices were successfully retrieved with only one vascular injury (0.4%). The primary safety endpoint was met and 30-day MACCE events in patients treated with the Sentinel device were less than the prespecified performance goal of 18.3% with a p-value $<.0001$. A post hoc analysis showed a 63% relative reduction in peri-procedural stroke rates in favor of the Sentinel System (3.0% vs 8.2%).

The effectiveness success criterion #1 was not met and a statistically significant reduction in DW-MRI lesions post-TAVR was not seen; however, effectiveness success criterion #2 was met by showing a 42% observed treatment effect in DW-MRI median lesion volume reduction in protected territories in favor of the Test Arm.

Histopathological and histomorphological analyses showed that a wide range of embolic material/debris was captured in 99% of patients regardless of valve type and that 1 in 4 patients had 25 particles $\geq 0.5\text{mm}$ in size. The study also demonstrated a correlation between volumetric ($r=-0.27$) and numeric ($r=-0.30$) lesion burden in all territories of the brain and neurocognitive deterioration in patients.

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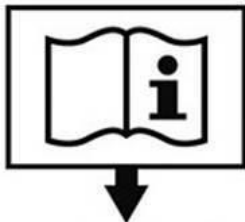
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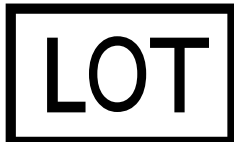
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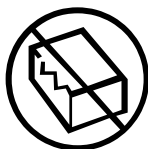
Single use



Sterile by Radiation Sterilization



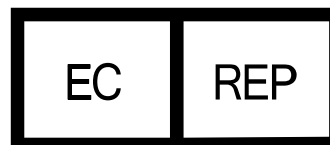
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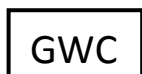
Do not use if packaging is damaged



Do not re-sterilize



Keep dry



Recommended guidewire



Recommended introducer



Non-pyrogenic

U.S Patent Nos. 8,372,108; 8,876,796; 9,055,997; 9,326,843; 9,345,565, and 9,017,364. Other U.S. and Foreign patents pending.