CARDIVA MEDICAL, INC.

VASCADE® Vascular Closure System (VASCADE VCS)

INSTRUCTIONS FOR USE
5F and 6/7F

MD

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

DESCRIPTION

The VASCADE Vascular Closure System (VCS) is intended to seal the femoral arterial or femoral venous access site at the completion of an endovascular procedure. The system consists of a sterile disposable Vascular Closure Catheter which houses a resorbable Collagen Patch, and the VASCADE Clip (refer to Figure 1).

The system is designed to deliver a resorbable Collagen Patch, extra-vascularly, at the arteriotomy or venotomy site to aid in achieving hemostasis. The patch expands as a result of rehydration in the presence of blood in the tissue tract to provide an extravascular seal. A radiopaque proximal marker band on the Catheter provides means to verify placement of the patch in the tissue tract adjacent to the femoral arteriotomy or venotomy site prior to the release of the patch. A second distal marker band locates the distal tip of the VASCADE Disc. There are two versions of products in the VASCADE product family:

- For use in 5F 12cm[1] introducer sheaths
- For use in 6F or 7F 12cm[1] introducer sheaths.

INDICATIONS FOR USE

The VASCADE™ Vascular Closure System (VCS) is indicated for femoral arterial or femoral venous access site closure while reducing times to hemostasis and ambulation in patients who have undergone diagnostic or interventional endovascular procedures using a 5F, 6F, or 7F procedural sheath. The VASCADE VCS is also indicated to reduce time to discharge eligibility when used for femoral arterial closure in patients who have undergone diagnostic endovascular procedures using a 5F, 6F, or 7F procedural sheath.

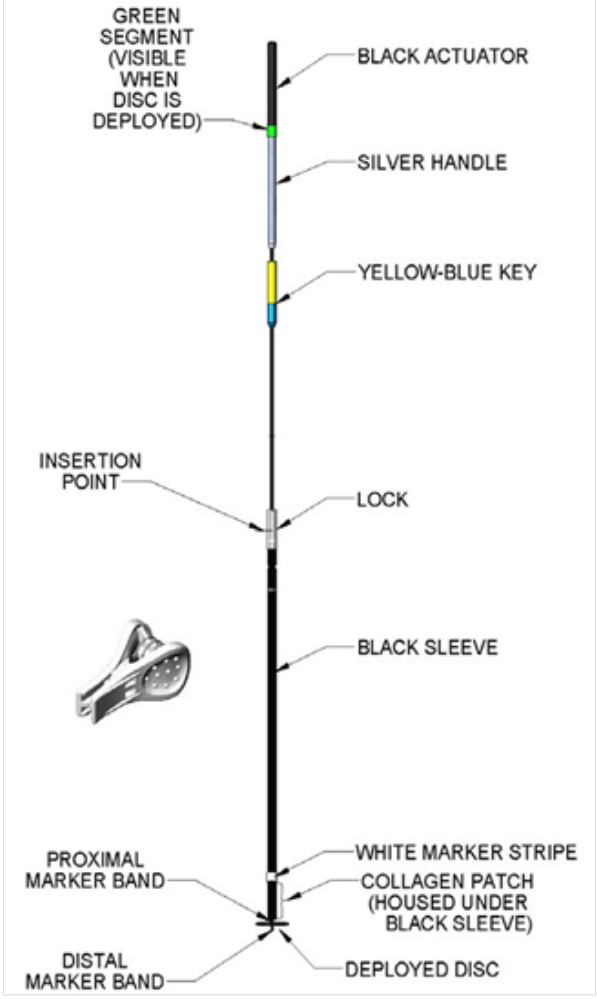


Fig. 1 – VASCADE Vascular Closure System (VCS)

CONTRAINDICATIONS

The VASCADE VCS should not be used in patients with a known allergy to bovine derivatives.

[1] Overall length of the sheath (including the hub) needs to be less than 15cm.

INTENDED PURPOSE

VASCADE Family devices are intended for the percutaneous closure of femoral vessel access sites in patients who have undergone catheter-based procedures.

PATIENT TARGET GROUP

The VASCADE VCS is intended for patients who require femoral arterial or venous access site closure and have undergone diagnostic or interventional endovascular procedures using a 5F, 6F or 7F procedural sheath. The VASCADE VCS is also indicated in patients who have undergone diagnostic endovascular procedures using a 5F, 6F or 7F procedural sheath and require femoral arterial closure.

INTENDED USER

Physicians and technicians with experience accessing femoral vessels via introducer sheaths.

CLINICAL BENEFITS

Clinical benefits are rapid closure of vascular access sites, which may increase comfort after the procedure and allow patients to start walking again sooner.

TECHNICAL SPECIFICATIONS

Device	Model	Sheath Size Inner Diameter (ID)	Sheath Length	Disc Diameter	Collagen Patch* Length	Collagen Dry Weight	Device Working Length	Device Max OD (with Collapsed disc)
VASCADE 5F VCS	700-500DX	5F	Up to 12 cm	6.5 mm	15 mm	8.5 mg ± 2 mg	15 cm	1.80 mm
VASCADE 6/7F VCS	700-580I	6-7F	Up to 12 cm	6.5 mm	15 mm	12 mg ± 3 mg	15 cm	2.1 mm

*The Collagen Patch is made of Type I Bovine Collagen delivered in a compressed form. The collagen implant is a biological material compatible with Magnetic Resonance Imaging (MRI).

CONTENTS OF PACKAGE

Each shelf carton contains at minimum:

- Multiple single-use devices (quantity per labelling)
- Each single-use sterile device is supplied with:
    - One (1) Sterile Clip
    - One (1) Patient Implant Information Guide.
- One (1) printed Instructions for Use.

SAFETY MESSAGES

WARNINGS

- Do not reuse or re-sterilize. The VASCADE VCS is intended to be used once only for a single patient. Product reuse or re-sterilization, may result in transmission of infectious or blood borne diseases and/or death.
- Do not use if components or packaging appear to be damaged or defective or if any portion of the packaging has been previously opened. Damaged or opened packages may compromise product functionality.
- Do not use if product is beyond the expiration date. Product performance has not been established beyond the labeled shelf life.
- Do not deploy the VASCADE Disc in a stent. Do not pull the deployed VASCADE Disc through a stent. Damage to the product may occur.
- Do not use VASCADE if access is through a previously placed permanent closure device such as a metal clip and/or permanent suture. Interference between the two closure devices may result.
- Do not deploy the Collagen Patch if there is a suspicion that the VASCADE Vascular Closure Disc is not seated against the intimal aspect of the arteriotomy or venotomy site. Partial or complete obstruction of blood flow may result.
- Do not deploy a second collagen patch at the same access site within 30 days. The previously implanted collagen patch may be inadvertently introduced into the femoral vessel.
- Grip the Lock to retract Black Sleeve. Do not grip the device distal to the Lock as this may result in operator injury which could lead to possible infection.

PRECAUTIONS

- The VASCADE VCS should only be used by a trained licensed physician or healthcare professional.
    - Note the training referred to here is previous training for accessing vessels, and positioning and using catheters. The VASCADE VCS device does not require formal training beyond review of the content provided in this IFU
- Do not use in access sites where there is suspicion of a “backwall” stick. Increased bleeding risk may occur.
- Do not use if arteriotomy or venotomy is noted to be a “side stick.” Bleeding risk may increase.
- Do not use if arteriotomy or venotomy site is noted to be “high,” above the Inguinal Ligament (cephalad to lower half of the femoral head or the inferior epigastric artery origin from the external iliac artery/ inferior epigastric vein entry into the external iliac vein). This may increase the risk of bleeding.
- Do not use in an artery with suspected intraluminal thrombus, hematoma, pseudoaneurysm, or arteriovenous fistula. These conditions may complicate proper device use and performance.
- Do not use if intra-procedural bleeding around the introducer sheath is noted including hematoma formation (sign of possible multiple wall stick). This may suggest problems with the access site.
- Do not use in a procedural sheath > 12cm in length (or >15cm in overall length) or with a diameter other than 5F for VASCADE 5F, or 6F or 7F for VASCADE 6/7F. This may complicate Disc deployment.

SPECIAL PATIENT POPULATIONS

NOTE: The safety and effectiveness of VASCADE VCS have not been evaluated in the following patients who are/have:

- Less than 18 years of age;
- Pregnant and/or lactating women;
- Pre-existing immunodeficiency disorder and/or chronic use of systemic steroids;
- Known significant coagulopathy/bleeding disorder such as thrombocytopenia (platelet count <100,000/mm^3), thrombasthenia, hemophilia, von Willebrand's disease or anemia (Hemoglobin <10g/dL, Hematocrit <30%);
- Previous vascular grafts or surgery at the target vessel access site;
- Symptomatic ipsilateral lower extremity ischemia;
- Fluoroscopically visible calcium or atherosclerotic disease within 1 cm of the puncture site;
- Femoral artery or vein lumen less than 6 mm;
- Length of the tissue tract, the distance between the anterior arterial or venous wall and skin, is estimated to be less than 2.5cm;
- INR ≥1.8 if patient received warfarin;
- Fibrinogen level < 150 mg/dl if patient received fibrinolytic agent;
- Extreme morbid obesity (BMI > 45 kg/m2) or underweight (BMI < 20 kg/m^2);
- Uncontrolled hypertension (BP > 180/110);

Serious Incident Reporting

A notice from the user and/or patient that any serious incident has occurred in relation to the device should be reported to the manufacturer and FDA.

Adverse Events

Complications may occur and may be related to the endovascular procedure or the vascular closure. They include, but are not limited to:

- Allergic response
- Vessel occlusion
- Vessel thrombus
- Arterio-venous fistula
- Bleeding from the puncture site
- Oozing from the puncture site
- Bruising at the puncture site
- Death
- Device failure/malfunction
- Edema
- Embolization (of thrombus, air, calcific debris, or device)
- Pulmonary Embolism
- Hematoma
- Infection
- Inflammatory response
- Intimal tear / dissection
- Laceration of the vessel wall
- Lower extremity ischemia
- Perforation of the vessel wall
- Peripheral nerve injury
- Pseudoaneurysm
- Retroperitoneal bleeding
- Deep vein thrombosis
- Superficial vein thrombosis
- Vascular injury
- Vasovagal response
- Vasospasm
- Puncture site pain

Clinical Studies

The safety and efficacy of the VASCADE VCS was evaluated in the following clinical studies to support the approved indications for use: the RESPECT Trial (VASCADE 6/7F) and the VASCADE 5F Confirmatory Trial (VASCADE 5F). The design and results of each study are provided below.

VASCADE 6/7F VCS – RESPECT Clinical Trial

Study Design and Baseline

Table 1: RESPECT Study Design

RESPECT Trial	
Objective	Evaluate safety and effectiveness of VASCADE 6/7F VCS to seal common femoral arterial access sites and reduce times to hemostasis and ambulation vs. Manual Compression (MC) after diagnostic or interventional endovascular procedures (cardiac or peripheral vascular catheterization) performed through 6F or 7F introducer sheaths.
Design*	Prospective, randomized (2:1), controlled, multi-center clinical trial conducted at 20 sites in the USA and one site in Australia.
Inclusion Criteria	• 18 to 80 years of age. • Able and willing to sign an Informed Consent Form. • Eligible candidates for an elective, non-emergency diagnostic or interventional endovascular procedure via the common femoral artery using a 6F or 7F introducer sheath who were also eligible for post-procedure manual compression. • Able and willing to complete a 30-day ± 7 days follow-up evaluation.
Exclusion Criteria	• Clinically significant peripheral vascular disease. • Bleeding disorder • Ipsilateral femoral arteriotomy within the previous 30 days. • Planned endovascular procedure within the next 30 days • Previous vascular grafts at target access site • Extreme morbid obesity (BMI > 45 kg/m^2) or underweight (BMI < 20 kg/m^2). • Known allergy/adverse reaction to bovine derivatives. • Planned extended hospitalization. • Administration of low molecular weight heparin (LMWH) within 8 hours of the procedure. • Femoral artery diameter less than 6 mm at access site. • Multi arterial sticks. • Received unfractionated heparin with an Activated Clotting Time (ACT) greater than 300 seconds in the absence of a glycoprotein (GP) IIb/IIIa inhibitor or greater than 250 seconds in the presence of a glycoprotein IIb/IIIa inhibitor. • Intra-procedural bleeding around sheath or suspected intraluminal thrombus, hematoma, pseudoaneurysm or AV fistula. • Uncontrolled hypertension. • Length of tissue tract estimated to be less than 2.5 cm.
Follow-up**	30±7 days.

*An ultrasound sub-study recorded images of the access site of 100 consecutively randomized and treated VASCADE patients at five (5) sites before hospital discharge.
**415 out of 420 randomized subjects (98.8%) completed a 30-day follow-up. Of the five (5) subjects who did not complete the study, three (3) were prematurely randomized and immediately withdrawn from the study due to ineligibility, one (1) was lost to follow-up and one (1) withdrew consent to participate before the 30-day follow-up.

Table 2: RESPECT Study Population

	VASCADE*	MC	All Subjects
Total**	**278**	**142**	**420**
Diagnostic	137	74	211
Interventional	141***	68	209

Table 3: RESPECT Baseline Characteristics

Baseline Characteristics	All Subjects (N=420)
Age (years), mean	62
BMI (kg/m^2), mean	30
Female (%)	29%

*Three (3) subjects were prematurely randomized and immediately withdrawn from the study due to final eligibility. All three (3**)** were randomized to the VASCADE group and no VASCADE device was introduced. The three (3) are included in the totals above. | **The study also included 69 VASCADE roll-in cases, consisting of 45 diagnostic and 24 interventional patients. | ***Seventy-seven percent (77%) of the VASCADE interventional subjects received bivalirudin, 27% received heparin, 60% received clopidogrel and 8% received GP IIb/IIIa inhibitors.

Table 4: RESPECT Activated Clotting Time (ACT) For Patients Receiving Unfractionated Heparin

	Diagnostic (N=9)		Interventional (N=84)	
	VASCADE (N=5)	MC (N=4)	VASCADE (N=57)	MC (N=27)
ACT*	221.0 ± 68.7	171.8 ± 16.8	289.5 ± 136.9	289.0 ± 100.7

*Values are expressed as mean ± standard deviation.

Safety Results

The primary and secondary safety endpoints were the rates of access site-related major and minor complications through follow-up (Table 5). Results showed that VASCADE VCS subjects were non-inferior to MC-treated subjects with regard to major access site-related complications.

Table 5: RESPECT Reported Major and Minor Complications

Access Site Complications at 30 Days by Event	Diagnostic (N=210)					Interventional (N=207)					Total (N=417)				
	VASCADE (N=136)		MC (N=74)		*P* value*	VASCADE (N=139)		MC (N=68)		*P* value*	VASCADE (N=275)		MC (N=142)		*P* value*
Any Major Access Site Complication	**0**	**0.0%**	**0**	**0.0%**	**1.00**	**0**	**0.0%**	**0**	**0.0%**	**1.00**	**0**	**0.0%**	**0**	**0.0%**	**1.00**
Access site bleeding requiring transfusion	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
Vascular injury requiring repair	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
New ipsilateral lower extremity ischemia threatening the viability of the limb	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
Access site infection requiring intravenous antibiotics and/or prolonged hospitalization	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
New onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
Permanent access site-related nerve injury (> 30 days)	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00	0	0.0%	0	0.0%	1.00
Any Minor Access Site Complication	**2**	**1.5%**	**2**	**2.7%**	**0.61**	**1**	**0.7%**	**8**	**11.8%**	**0.001**	**3**	**1.1%**	**10**	**7.0%**	**0.002**
Access site bleeding requiring > 30 minutes to achieve hemostasis	0	0%	2	2.7%	0.12	1	0.7%	8	11.8%	0.001	1	0.4%	10	7.0%	0.0001
Access site hematoma > 6 cm	1	0.7%	0	0%	1.00	0	0%	0	0%	1.00	1	0.4%	0	0%	1.00
Delayed bleeding from the access site (following hospital discharge)	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00
Ipsilateral lower extremity arterial embolism	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00
Ipsilateral deep vein thrombosis**	3	2.2%	0	0%	N/A	1	0.7%	0	0%	N/A	4	1.5%	0	0%	N/A
Access site-related vessel laceration	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00
Access site wound dehiscence	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00
Localized access site infection treated with intramuscular or oral antibiotics	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00
Arteriovenous fistula not requiring treatment**	0	0%	0	0%	N/A	1	0.7%	0	0%	N/A	1	0.4%	0	0%	N/A
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection**	0	0%	0	0%	N/A	1	0.7%	0	0%	N/A	1	0.4%	0	0%	N/A
Pseudoaneurysm not requiring treatment**	1	0.7%	0	0%	N/A	3	2.2%	0	0%	N/A	4	1.5%	0	0%	N/A
New-onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	1	0.7%	0	0%	1.00	0	0%	0	0%	1.00	1	0.4%	0	0%	1.00
Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0%	0	0%	1.00	0	0%	0	0%	1.00	0	0%	0	0%	1.00

*Two-sided Fisher's exact test.

**Due to different complication-detecting methods between study arms (100 VASCADE patients and no other study patients underwent a femoral ultrasound in an ultrasound sub-study), rates of pseudoaneurysm requiring or not requiring treatment, arteriovenous fistula not requiring treatment and ipsilateral deep vein thrombosis (which were detected by ultrasound) are presented but not compared between arms, nor are they included in the computation of the VASCADE overall minor complication rate (top row).

Effectiveness Results

Table 6: Effectiveness Endpoint Definitions

Primary Effectiveness Endpoint	**Time to Hemostasis (TTH):** elapsed time between device removal (i.e. device removal for VASCADE and sheath removal for MC) and the first observed and confirmed arterial hemostasis (no or minimal subcutaneous oozing and the absence of expanding or developing hematoma).
Secondary Effectiveness Endpoints	**Time to Ambulation (TTA):** elapsed time between removal of the device (i.e. removal of the device for VASCADE and removal of the sheath for MC) and when ambulation was achieved (patient standing and walking at least 20 feet without rebleeding).
	Time to Discharge Eligibility (TTDE): elapsed time between removal of the device (i.e. removal of the device for VASCADE and removal of the sheath for MC) and when the patient was eligible for hospital discharge based on an assessment of the access site.
	Time to Discharge (TTD): elapsed time between final removal of the device (i.e. removal of the device for VASCADE and removal of the sheath for MC) and hospital discharge.
	Procedure Success: Attainment of final hemostasis using any method and freedom from major vascular complications through 30 days.
	Device Success (DS): Ability to deploy the delivery system, deliver the collagen, and achieve hemostasis with the VASCADE Vascular Closure System alone or with adjunctive compression.

TTH, TTA, TTDE and TTD results are provided in Table 7. Results demonstrated statistically significant decreased times to hemostasis and ambulation for subjects treated with VASCADE compared with MC.

Table 7: Primary and Secondary Effectiveness

	Diagnostic (N=211)			Interventional (N=209)			Total (N=420)		
	VASCADE (N=137)	Manual Compression (N=74)	p-value*	VASCADE (N=141)	Manual Compression (N=68)	p-value*	VASCADE (N=278)	Manual Compression (N=142)	p-value*
Time to Hemostasis (minutes)									
N	136	74		139	68		275	142	
Mean	4.0	18.2	< 0.0001	5.5	24.9	< 0.0001	4.8	21.4	< 0.0001
Std Deviation	4.2	8.1		6.3	15.1		5.4	12.4	
Median	2.6	18.5	< 0.0001	3.3	20.5	< 0.0001	3.0	20.0	< 0.0001
Min	0.6	4.3		0.8	0.0		0.6	0.0	
Max	24.7	64.6		31.6	97.0		31.6	97.0	
Time to Ambulation (hours)									
N	136	74		139	68		275	142	
Mean	2.6	4.6	< 0.0001	5.0	7.2	0.003	3.8	5.8	< 0.0001
Std Deviation	2.0	1.6		6.7	3.7		5.1	3.1	
Median	2.2	4.4	< 0.0001	4.1	6.4	< 0.0001	3.2	5.2	< 0.0001
Min	1.0	1.7		2.2	2.5		1.0	1.7	
Max	20.1	11.0		78.0	22.8		78.0	22.8	
Time to Discharge Eligibility (hours)									
N	136	74		138	68		274	142	
Mean	3.1	5.0		6.6	8.2		4.8	6.5	
Std Deviation	2.1	1.6		8.4	4.0		6.4	3.3	
Median	2.6	4.8		4.6	7.0		3.6	5.7	
Min	1.4	2.2		2.6	3.0		1.4	2.2	
Max	20.5	11.3		78.4	23.2		78.4	23.2	
Time to Hospital Discharge (hours)									
N	136	74		139	68		275	142	
Mean	12.0	7.3		24.5	20.8		18.3	13.7	
Std Deviation	45.4	7.3		16.2	6.7		34.5	9.8	
Median	3.4	5.3		23.4	19.9		17.2	13.9	
Min	1.7	2.4		3.4	4.9		1.7	2.4	
Max	432.9	55.6		147.6	45.7		432.9	55.6	

*p-value from t-test for comparing means and Wilcoxon's test for comparing medians

Table 8 and Table 9 summarize the cumulative data for TTH, TTA, TTDE and TTD, respectively.

Table 8: RESPECT Cumulative TTH & TTA - All Subjects

TTH					TTA				
Time point	**VASCADE (N=278)**		**MC (N=142)**		**Time point**	**VASCADE (N=278)**		**MC (N=142)**	
N	275		142		N	275		142	
≤ 1 minute	8	3%	1	1%	≤ 1 hour	0	0%	0	0%
≤ 2 minutes	51	19%	1	1%	≤ 2 hours	22	8%	1	1%
≤ 3 minutes	136	49%	1	1%	≤ 3 hours	122	44%	12	8%
≤ 4 minutes	195	71%	1	1%	≤ 4 hours	179	65%	31	22%
≤ 5 minutes	221	80%	5	4%	≤ 5 hours	255	93%	68	48%
≤ 10 minutes	246	89%	16	11%	≤ 10 hours	268	97%	131	92%
≤ 20 minutes	263	96%	85	60%	≤ 15 hours	270	98%	138	97%
≤ 30 minutes	274	100%	132	93%					

Table 9: RESPECT Cumulative TTDE & TTD - All Subjects

Time point	**TTDE**				**TTD**			
	VASCADE (N=278)		**MC (N=142)**		**VASCADE (N=278)**		**MC (N=142)**	
N	274		142		275		142	
≤ 2 hours	10	4%	0	0%	1	0%	0	0%
≤ 4 hours	152	55%	20	14%	86	31%	12	8%
≤ 6 hours	247	90%	79	56%	123	45%	50	35%
≤ 8 hours	257	94%	117	82%	131	48%	66	46%
≤ 12 hours	262	96%	131	92%	134	49%	69	49%
≤ 24 hours	270	99%	142	100%	207	75%	129	91%
≤ 48 hours	272	99%	142	100%	265	96%	141	99%

Table 10 summarizes the secondary effectiveness endpoint of Procedure Success. The Procedure Success Rate was 100% for VASCADE and Manual Compression.

Table 10: Secondary Effectiveness, Procedure Success

Procedure	**Treatment Assignment**	**Number of Patients**	**Number of Successes**	**Success Rate**	**95% Confidence Interval***	
Diagnostic	VASCADE	136	136	100%	97%	100%
	Manual Compression	74	74	100%	95%	100%
Interventional	VASCADE	139	139	100%	97%	100%
	Manual Compression	68	68	100%	95%	100%
Total	Cardiva VCS	275	275	100%	99%	100%
	Manual Compression	142	142	100%	97%	100%

*95% Exact Binomial Confidence Interval

Table 11 summarizes the results of Device Success. The overall Device Success Rate for the total patients was 96%.

Table 11: Secondary Effectiveness, Device Success

Procedure	Number of Patients**	Number of Successes	Success Rate	95% Confidence Interval*	
Diagnostic	136	128	94%	88.7%	97.4%
Interventional	139	135	97%	92.8%	99.2%

*95% Exact Binomial Confidence Interval

** Includes 6 instances of failure to follow written Instructions for Use. Excluding these 6 instances, Device success rates are 96% (Diagnostic), 99% (Interventional) and 98% (Total)

Evaluation of VASCADE 5F VCS

VASCADE 5F VCS – Clinical Trial (Confirmatory)

Study Design and Baseline

Table 12: VASCADE 5F VCS Study Design

VASCADE 5F Confirmatory Trial	
Objective	Evaluate the safety and effectiveness of VASCADE 5F VCS (5F)*.
Design	Prospective, non-randomized, non-blinded, single treatment trial conducted in one (1) site in Australia.
Inclusion/Exclusion Criteria**	Identical to those of the RESPECT study (VASCADE 6/7F VCS) except that patients underwent catheterization with a 5F introducer sheath.
Follow-up	30±7 days.
Study Population	30 subjects undergoing diagnostic procedures (cardiac or peripheral vascular catheterization procedures via the femoral artery approach when using a standard 5F introducer sheath).
Safety and Effectiveness Endpoints	Identical to those of the RESPECT Trial (VASCADE 6/7F VCS).

*The 5F device is a scaled down version of the slightly larger 6/7F VCS.

**Patient baseline demographic characteristics at baseline such as gender, age and BMI were comparable to those of the RESPECT study population.

Safety Results

Table 13: VASCADE 5F VCS Major and Minor Complications Reported

Major Access Site Complications	5F (N=30)	
Any major access site complication	**1**	**3.3%**
Access site re-bleeding requiring transfusion	1*	3.3%
Vascular injury requiring repair	0	0.0%
New ipsilateral lower extremity ischemia threatening the viability of the limb	0	0.0%
Access site infection requiring intravenous antibiotics and/or prolonged hospitalization	0	0.0%
New-onset access site-related neuropathy in the ipsilateral lower extremity requiring surgical repair	0	0.0%
Permanent access site-related nerve injury (> 30 days)	0	0.0%
Any Minor Access Site Complication	**1**	**3.3%**
Access site bleeding requiring > 30 minutes to achieve hemostasis	0	0.0%
Access site hematoma > 6 cm	0	0.0%
Delayed bleeding from the access site (following hospital discharge)	0	0.0%
Ipsilateral lower extremity arterial embolism	0	0.0%
Ipsilateral deep vein thrombosis	0	0.0%
Access site-related vessel laceration	0	0.0%
Access site wound dehiscence	0	0.0%
Localized access site infection treated with intramuscular or oral antibiotics	0	0.0%
Arteriovenous fistula not requiring treatment	0	0.0%
Pseudoaneurysm requiring thrombin injection or fibrin adhesive injection	0	0.0%
Pseudoaneurysm not requiring treatment	0	0.0%
New onset access site-related neuropathy in the ipsilateral lower extremity not requiring surgical repair	1*	3.3%
Ipsilateral pedal pulse diminished by two grades or transiently lost	0	0.0%

*One occurrence only.

Effectiveness Results

Table 14: VASCADE 5F VCS TTH, TTA, TTDE and TTD Effectiveness Endpoints

	5F (N=30)			
	TTH (minutes)	**TTA (hours)**	**TTDE (hours)**	**TTD (hours)**
N	30	30	30	30
Mean	3.0	4.1	5.6	11.9
Std Deviation	2.4	5.9	9.0	16.0
Median	2.3	2.3	3.1	3.5
Min	0.2	1.5	2.0	2.0
Max	11.8	25.9	46.9	73.0

TTH: Time to Hemostasis; TTA: Time to Ambulation; TTDE: Time to Discharge Eligibility; TTD: Time to Discharge.

VASCADE 5F Engineering Analysis

Engineering analysis for the scaled down VASCADE 5F VCS included Collagen Patch size calculations resulting in a proportionally smaller Collagen Patch as compared with the VASCADE 6/7F VCS device. These analyses confirmed equivalent tissue-tract space-filling capability between the 5F and 6/7F versions of the VASCADE device. In addition, fundamentally the same verification and validation testing was completed for the 5F VASCADE VCS device as was completed for the 6/7F VASCADE VCS device.

Conclusions of the Clinical Studies

The results from the RESPECT clinical trial demonstrate that patients who have undergone diagnostic or interventional cardiac or peripheral vascular endovascular procedures using a 6F or 7F introducer sheath and were treated with VASCADE VCS have statistically and clinically significant decreased times to hemostasis and ambulation for diagnostic and interventional procedures, and statistically and clinically significant decreased time to discharge eligibility for diagnostic procedures, when compared to patients treated with manual compression. In addition, the trial demonstrated that patients treated with the VASCADE VCS were noninferior to patients treated with manual compression with respect to major access site-related complications.

A confirmatory clinical study and engineering analysis demonstrated that the VASCADE 5F VCS is equivalent to the VASCADE 6/7F VCS in design and performance.

General Use Instructions

⚠ WARNINGS

- Do not use VASCADE if access is through a previously placed permanent closure device such as a metal clip and/or permanent suture. Interference between the two closure devices may result.
- Do not deploy a second collagen patch at the same access site within 30 days. The previously implanted collagen patch may be inadvertently introduced into the femoral vessel.
- Do not deploy the VASCADE Disc in a stent. Do not pull the deployed VASCADE Disc through a stent. Damage to the product may occur.

⚠ CAUTIONS

- VASCADE should only be used by a trained, licensed physician or healthcare professional.
    - Note the training referred to here is previous training for accessing vessels, and positioning and using catheters. The VASCADE VCS device does not require formal training beyond review of the content provided in this IFU.
- Do not use in an artery with suspected intraluminal thrombus, hematoma, pseudoaneurysm or arteriovenous fistula. These conditions may complicate proper device use and performance.
- Do not use in access sites where there is suspicion of a “backwall” stick. Increased bleeding risk may occur.
- Do not use if arteriotomy or venotomy is noted to be a “side stick.” Bleeding risk may increase.
- Do not use if arteriotomy or venotomy site is noted to be “high,” above the Inguinal Ligament (cephalad to lower half of the femoral head or the inferior epigastric artery origin from the external iliac artery/ inferior epigastric vein entry into the external iliac vein). This may increase the risk of bleeding.
- Do not use in a procedural sheath > 12 cm in length (or > 15 cm in overall length) or with a diameter other than 5F for VASCADE 5F, or 6F or 7F for VASCADE 6/7F. This may complicate Disc deployment.

NOTES

- See Figure 1 for an image of the device.
- Use the device only as described in the Technical Specifications (see Page 2).

PREPARATION STEPS: Patient Access Considerations and Device Preparation

Prep-A: Patient Access Considerations and Preparation for Closure

Access

1. At the time of initial introducer sheath placement, patient body habitus should be evaluated to provide reasonable assurance that the distance between the femoral arteriotomy or femoral venotomy and the skin surface is greater than 2.5cm.

Prior to Closure

2. After introducer sheath placement, an anterior oblique fluoroscopic image with contrast or an ultrasound image may be digitally recorded and stored, so that the arteriotomy or venotomy site location can be compared to the position of the radiopaque marker just prior to Collagen Patch release.
3. The radiopaque marker is located immediately distal to the Collagen Patch.
4. A single wall, common femoral arteriotomy or venotomy should also be confirmed at this time.

⚠ **CAUTION**

During access care should be taken so that the tissue tract is not pushed laterally or medially prior to accessing the vessel. This is to avoid misalignment of the tissue tract and the Collagen Patch relative to the arteriotomy or venotomy site once the device is removed from the vessel which may result in prolonged time to hemostasis.

Prep-B: Unpack the Device

1. Inspect the package for damage (breaks, tears, open seals, water damage, etc.).
2. Verify that the expiration date has not passed.
3. Check that the correct product and size is used. Use the Cardiva VASCADE VCS only as described in Technical Specifications (page 2).
4. Using standard sterile technique (See Aseptic Presentation below), remove the tray containing the VASCADE VCS Catheter and Clip from the foil pouch.
5. Carefully remove VASCADE VCS Catheter and Clip from the tray.

Aseptic Presentation

- Inspect the product packaging. Observe for any breaks, holes, or openings that would compromise the integrity and sterility of the product.
- Read the label. Check the expiration date and verify correct product/size is used.
- Position near the sterile field. Be sure the scrubbed person receiving the product is prepared and ready to receive it with a clear space in the field.
  - All packaging for sterile products has a designated side to open from. Locate this side and slowly peel the package open.
  - Open the packaging with arms extended to avoid accidental contact with the product or the sterile field. Be sure the secondary sterile packaging containing the product does not come in contact with the edges of the external packaging as they are not considered sterile. Create a large enough opening in the package to remove the interior packaging containing the product without touching the non-sterile areas.
- Present the product to the scrubbed person.
- Discard packaging following facility protocol

⚠ **WARNINGS**

- Do not reuse or re-sterilize. The VASCADE VCS is intended to be used once only for a single patient. Product reuse or re-sterilization, may result in transmission of infectious or blood borne diseases and/or death.
- Do not use if components or packaging appear to be damaged or defective or if any portion of the packaging has been previously opened. Damaged or opened packages may compromise product functionality.
- Do not use if product is beyond the expiration date. Product performance has not been established beyond the shelf life on the label.

Prep-C: Inspect the Device

Fig. 2 – Verify Yellow-Blue Key is not engaged in the Lock and Black Sleeve is locked in position

1. Examine the device by first verifying that the Black Sleeve is locked in position and the Collagen Patch is not exposed.
2. Also verify that the Yellow-Blue Key **(Figure 2)** is not engaged in the Lock (the Lock is located at the proximal aspect of the Black Sleeve), and the Yellow-Blue Key is located at the proximal end of the Catheter Shaft.

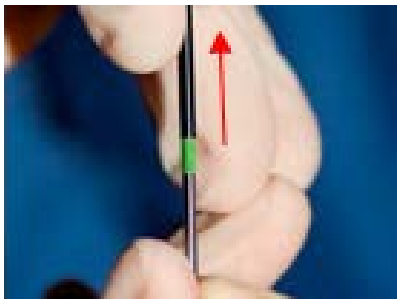


Fig. 3 – Pull back on Black Actuator Tip to deploy the Disc

3. Inspect the Catheter further by examining the deployed VASCADE Disc.
    a. To deploy the Disc, hold the Silver Handle firmly and pull back on the Black Actuator until it locks in place.
    b. When the Disc is locked in the deployed position, the Green Segment will become visible as shown in Figure 3.

Fig. 4 – Deployed & Collapsed Disc

4. Examine the Disc, which should appear circular and symmetrical with an intact membrane.
    a. **Figure 4** shows the deployed and collapsed Disc.

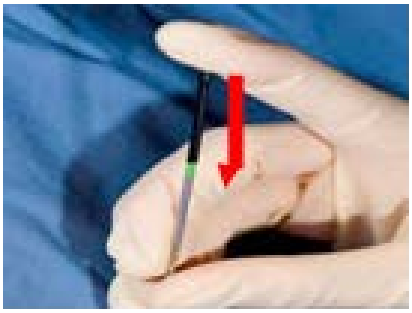


Fig. 5 – Collapse Disc by pressing Black Actuator Tip like a ballpoint pen

5. After examination, collapse the Disc by pressing the Black Actuator tip down **(Figure 5)**. The tip of the VASCADE VCS Catheter should return to its original profile.

Prep-D: Prepare the Sheath

1. Verify that the sheath is not positioned in a tortuous vessel.
2. If required, retract the sheath slightly to a non-tortuous location. Verify that the sheath is still positioned within the artery or vein.
3. Flush the sheath with sterile saline solution prior to insertion of the device.

⚠ **WARNING**

Verify there is no vessel tortuosity or side branches within 3-4 cm from the distal opening of the sheath and the end of the sheath is not resting against the vessel wall. This is to prevent any vascular injury as a result of advancing the catheter. If required, retract the sheath slightly to a non-tortuous location, being careful not to lose vessel access.

⚠ **CAUTION**

Do not use if intra-procedural bleeding around the introducer sheath is noted including hematoma formation (sign of possible multiple wall stick). This may suggest problems with the access site.

STEP 1 PART A: Exchange Sheath for VASCADE and Achieve Temporary Hemostasis

Step 1.1: Dip Device Tip in Saline

Prior to insertion of device in the introducer sheath, momentarily insert the tip of the VCS Catheter in saline solution up to the White Marker Stripe and quickly remove.

⚠ **CAUTION**
Do not soak the VASCADE VCS Catheter in saline. Momentarily insert only the Catheter tip in saline solution immediately before use to avoid over-hydration of the patch, which may result in Catheter pull through during the sleeve retraction step.

Step 1.2: Insert VASCADE

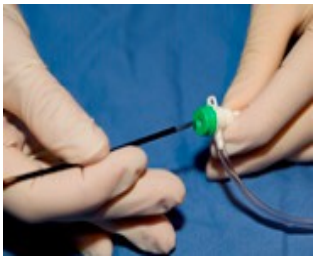


Fig. 6 – Insert device into hub of introducer sheath

1. Gently insert the VASCADE VCS Catheter (with Disc collapsed) into the introducer sheath hub as shown in **Figure 6**.

⚠ **CAUTION**
Do not advance VASCADE VCS Catheter into the patient if resistance is felt due to risk of vascular damage.

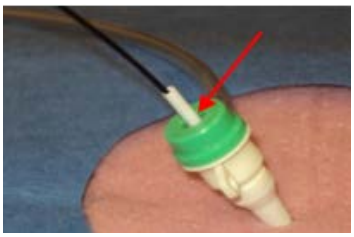


Fig. 7 – Insert device half way of the Lock

2. Insert the VASCADE VCS Catheter such that approximately half of the Lock is visible. Make certain that the Lock is NOT fully inserted into the sheath. See **Figure 7** for correct placement.

Step 1.3: Deploy the Disc

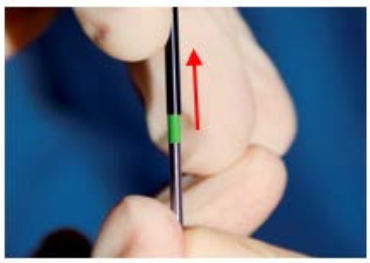


Fig. 8 – Pull back on Black Actuator Tip to deploy the Vascade Disc

Deploy the Disc by holding the Silver Handle and pulling back the Black Actuator until it locks in place as shown in **Figure 8.**

NOTE: When the Disc is properly deployed, the Green Segment will become visible distal to the Black Actuator. If the catheter is not properly locked in place, the Black Actuator will slide back to its original position and the Green Segment will disappear (in VASCADE 5F approximately 1mm of the Green Segment remains visible when Disc is collapsed) indicating that the Disc is not properly deployed. In this case repeat the step for deploying the Disc by pulling the Black Actuator more firmly until it locks in place.

⚠ **CAUTION**
Do **not** continue to pull on the Black Actuator once it is locked in place as this may damage the device.

Step 1.4: Remove the Sheath

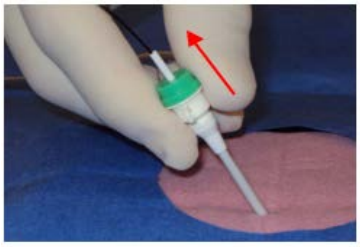


Fig. 9 – Grasp hub of sheath and remove over catheter

1. Gently remove sheath, without applying any compression at the access site or holding the VASCADE VCS Catheter**,** as shown in **Figure 9**.
2. As the sheath slides over the VASCADE VCS Catheter, grasp the Catheter proximal to the LOCK as it exits the distal end of the introducer sheath.
3. Continue sliding the sheath over the VASCADE VCS Catheter and discard sheath.

⚠ **CAUTION**
Compressing the access site during sheath removal may not allow the Disc to track back to the arteriotomy or venotomy and may cause Disc deformation. This may lead to inability to achieve temporary hemostasis.

Step 1.5: Achieve Temporary Hemostasis

Apply gentle tension on the Black Actuator until temporary hemostasis is achieved.

Note whether any portion of the White Marker Stripe, which is located near the distal aspect of the Black Sleeve, is visible above the skin. If it is, then the length of the tissue tract is less than 2.5 cm, indicating the tissue tract may not be long enough for the Collagen Patch.

NOTE: If any portion of the White Marker Stripe is showing and the collagen patch is not to be deployed continue the procedure as follows:

For diagnostic cases: The VASCADE VCS Catheter should be removed by collapsing the Disc and then manual compression can be applied per institutional protocol.

For anti-coagulated patients: The Clip may be applied to the VASCADE VCS Catheter on the skin surface as shown in **Figure 10** to maintain temporary hemostasis. The device may then stay in dwelling to allow time for the ACT level to normalize. The device can then be removed followed by application of manual compression per institutional protocol to achieve final hemostasis.

⚠ **WARNING**
If any portion of the White Marker Stripe is showing DO NOT RELEASE the Collagen Patch as this may increase the risk of infection.

STEP 1 PART B: Verify Disc Placement with Imaging

Step 1.6: Continue to Apply Upward Tension on the Catheter

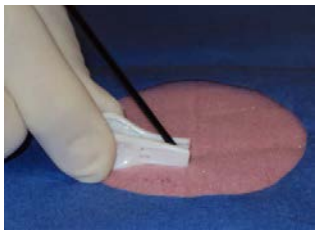


Fig. 10 – Apply Clip to Black Sleeve at skin level

Once temporary hemostasis is achieved, apply the Clip to the Black Sleeve at skin level as shown in **Figure 10.**

Step 1.7: Use Imaging to Verify Deployed Disc Placement Prior to Deploying Collagen

Verify that the deployed Disc is positioned against the intimal surface of the vessel at the arteriotomy or venotomy site, either by fluoroscopy (to verify the more proximal radiopaque marker is positioned against the arteriotomy or venotomy), or by ultrasound.

- The marker should be at the arteriotomy or venotomy site which can be verified by comparing its location with the location of the arteriotomy or venotomy documented at the time of the introducer sheath insertion.
- The Collagen Patch is immediately proximal to this Marker Band.
- The Distal Marker Band locates the distal end of the Disc.

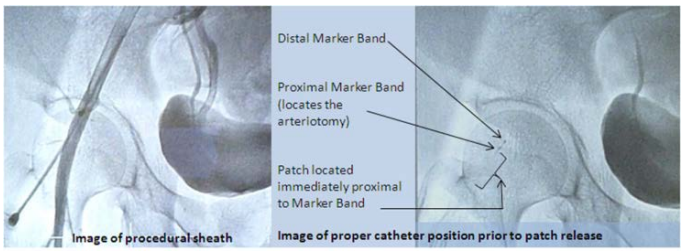


Fig. 11 – Fluoroscopic image demonstrating proper position of Disc against the intima

⚠CAUTION

Applying too much upward tension on the Black Actuator may cause Disc to pull out of vessel. Should this occur, convert to your **institution's manual compression protocol.**

⚠ WARNING

It is important to ensure that the Disc is in contact with the intimal aspect of the arteriotomy or venotomy before deploying the extra- vascular Collagen Patch to avoid releasing the Collagen Patch in the vessel**. This is indicated by having temporary hemostasis and further verified by either fluoroscopy (Figure 11a) or ultrasound imaging (Figure 11b)**.

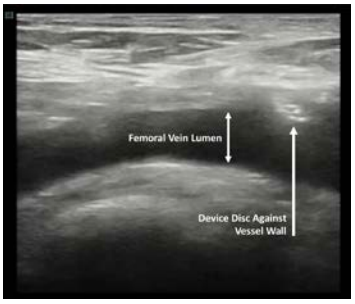


Fig. 11b – Ultrasound image demonstrating proper position of Disc

STEP 2: Deploy Collagen

Step 2.1: Unlock the Black Sleeve

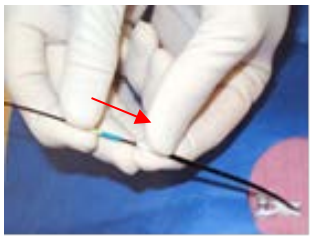


Fig. 12 – Unlock the Black Sleeve by sliding Yellow-Blue Key into the Lock

Once the Disc location is verified, expose the extra-vascular resorbable Collagen Patch by unlocking the Black Sleeve. This is done by grasping the Lock with the left hand, between the thumb and the index finger, and grasping the Yellow-Blue Key with the right hand and then sliding the Yellow-Blue Key into the Lock until no blue color is visible, as shown in **Figure 12**.

Step 2.2: Retract the Black Sleeve to Expose the Collagen

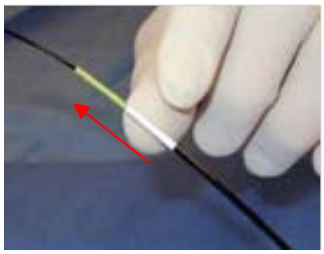


Fig. 13 – Retract the Black Sleeve by grasping the Lock and applying gentle upward tension toward the Silver Handle

1. Once the Sleeve is unlocked and while still holding on to the Lock, remove the Clip with the right hand, and gently slide the Lock back along the angle of entry to retract the Black Sleeve as shown in Figure 13. The Black Sleeve will move freely after some initial resistance. A second resistance point may be felt after the sleeve is moved approximately 1.6 cm (0.6 inch).
2. Proceed to fully retract the Black Sleeve proximally to the Silver Handle. This action exposes the Collagen Patch extra-vascularly, which will swell at the arteriotomy or venotomy site.

⚠ WARNING

Grip the Lock to retract Black Sleeve. Do not grip the device distal to the Lock as this may result in operator injury which could lead to possible infection.

NOTE: If the Black Sleeve does not retract easily, recheck that the blue end of the Yellow-Blue Key is fully engaged in the Lock.

NOTE: If the Collagen Patch is removed during sleeve retraction, for non-anti-coagulated patients, collapse the Disc, remove the Catheter and apply manual compression, per institutional protocol. If the patient is anti-coagulated, the Clip may be applied to the VASCADE VCS Catheter on the skin surface to maintain temporary hemostasis. The device may then stay in dwelling in order to allow time for the ACT level to normalize. The device can then be removed followed by application of manual compression to achieve final hemostasis.

Step 2.3: Wait for Collagen Hydration

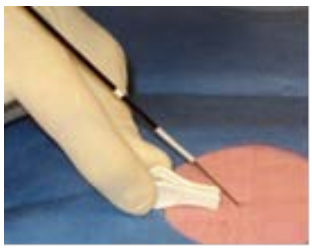


Fig. 14 – Reapply Clip during the Collagen Patch swell period

1. The Collagen Patch may be allowed to swell for up to 30 seconds prior to removal of the VASCADE VCS Catheter.
2. The Clip should be reapplied during the Collagen Patch swell period with minimal tension on the Catheter (Figure 14).

STEP 3: Achieve Final Hemostasis

Step 3.1: Prepare to Strip Collagen

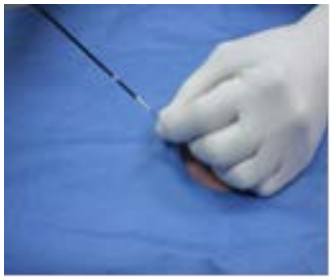


Fig. 15 – Grasp Green Tube prior to collapsing the Disc

1. AFTER 15-30 seconds of patch swell time and PRIOR TO collapsing the Disk, remove the Clip.
2. Rest the palm of the hand on the patient and grasp the green tube between the thumb and the index finger as shown in **Figure 15.**

Step 3.2: Strip Collagen Using the Green Tube, Then Remove Device

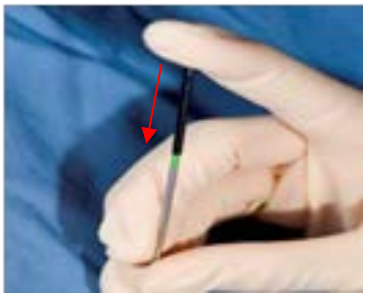


Fig. 16 – Collapse the Disc by pressing on the Black Actuator Tip

Option 1: Move the Device while keeping the Green Tube Stationary (e.g., where the Green Tube is not sufficiently visible to easily move it, such as in patients with deeper tissue tracts)

1. Collapse the Disc (See below).
2. While keeping the green tube stationary pull back the VASCADE VCS Catheter proximally. The Catheter Handle will move approximately 1.5cm while the green portion of the catheter remains stationary. This action slides the collapsed catheter Disc by the Collagen Patch while maintaining the position of the Collagen Patch.
3. Once this initial movement has occurred, let go of the Green Tube.
4. Gentle manual compression may be applied at the arteriotomy or venotomy site.
5. Remove the VASCADE VCS Catheter, and apply manual compression.

Option 2: Move the Green Tube, Device Stationary

1. Push the green tube in the proximal direction approximately 1.5 cm while gently pulling back on the VASCADE VCS Catheter to maintain Disc position against artery or vein wall.
2. The green tube may be slid back and forth 2-3 times in order to assure release of the Collagen patch from device.
3. Upon completion of this step, apply proximal compression, collapse the Disc (See below).
4. Gentle manual compression may be applied at the arteriotomy or venotomy site.
5. Remove the VASCADE VCS Catheter, and apply manual compression.

Collapse the Disc:

1. With slack in the catheter, collapse the Disc by pressing on the Black Actuator Tip as shown in **Figure 16**.
2. 6/7F Device: The Green Segment should not be visible.
3. 5F Device: Only a small portion (~1 mm) of the Green Segment may be visible.

NOTE: Prior to the VASCADE VCS Catheter removal confirm that the Disc is completely collapsed by verifying that the Green Segment is no longer visible for 6/7F device and only a small portion approximately 1mm is visible for the 5F device. Care should be taken not to compress directly over the catheter during the removal step of the device so that the catheter can be easily removed and without displacement of Collagen Patch.

Step 3.3: Confirm Final Hemostasis

1. Observe for vessel hemostasis.
2. Manual compression can be used to decrease or stop any tract ooze until full hemostasis is achieved.
3. Apply sterile dressing to site per institution protocol.

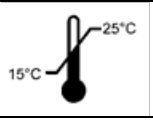
Step 3.4: In Recovery and Discharge

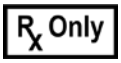
1. Maintain bed rest and periodically check site until patient is ready to ambulate.
2. Complete information on Patient Implant Card and provide to the patient.

Step 3.5: Dispose of Device

After use, dispose of the contaminated device and/or packaging materials using standard hospital procedures and universally accepted practices for bio-hazardous wastes.

GRAPHICAL SYMBOLS ON THE VASCADE VCS PACKAGING

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	ISO 15223-1	5.1.1 / Manufacturer	Medical device manufacturer
	ISO 15223-1	5.1.4 / Use-By Date	Date after which the medical device is not to be used.
	ISO 15223-1	5.1.5 / Batch Code	Manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1	5.1.6 / Catalogue number	Manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1	5.1.10 / Model Number	Model number or type number of a product.
	ISO 15223-1	5.2.4 / Sterilized using irradiation	Medical device that has been sterilized using irradiation.
	ISO 15223-1	5.2.6 / Do not resterilize	Medical device that is not to be re-sterilized.
	ISO 15223-1	5.2.8 / Do not use if package is damaged	Medical device that should not be used if the package has been damaged or opened.
	ISO 15223-1	5.2.12 / Double sterile barrier system	Indicates two sterile barrier systems
	ISO 15223-1	5.3.4 / Keep dry	Medical device that needs to be protected from moisture.
	ISO 15223-1	5.3.7 / Temperature limit	Temperature limits to which the medical device can be safely exposed.
	ISO 15223-1	5.4.2 / Do not re-use	Medical device that is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1	5.4.3 / Consult instructions for use or consult Electronic instructions for use	Need for the user to consult the instructions for use.
	ISO 15223-1	5.4.4 / Caution	Caution is necessary when operating the device or control close to where the symbol is placed or the current situation needs operator awareness or operator action in order to avoid undesirable consequences.
	ISO 15223-1	5.4.5 / Contains or presence of natural rubber latex B.2 / Negation Symbol	Indicates that there is no presence of natural rubber or dry natural rubber latex as a material of construction within the medical device or the packaging of a medical device.
	ISO 15223-1	5.4.8 / Contains biological material of animal origin	Indicates a medical device that contains biological tissue, cells, or their derivatives, of animal origin.
	ISO 15223-1	5.7.7 / Medical device	The item is a medical device.

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	21 CFR 801.109	Prescription Device	Product is a medical device and Federal Law (USA) restricts this device to sale by or on the order of a physician
	N/A	Package quantity	Quantity of systems in package

**Standards and Regulations:*
ISO 15223-1: *Medical devices-Symbols to be used with information to be supplied by the manufacturer*
US FDA Title 21 CFR 801.109*: Prescription Devices*

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