INSTRUCTIONS FOR USE

VASCADE® Vascular Closure System (VCS)

5F and 6/7F (Arterial and Venous)

MD

CAUTION – Device is restricted to sale to 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 after an endovascular procedure. The system consists of a sterile disposable Vascular Closure Catheter which houses a resorbable Collagen Patch and a sterile Clip (refer to Figure 1).

The system is designed to deliver a resorbable Collagen Patch extra-vascularly at the vessel puncture site to aid in achieving haemostasis. 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 vessel site before the release of the patch. A second distal marker band locates the distal tip of the VASCADE Disc. In addition, the Disc is echogenic. The following versions of the VASCADE VCS exist:

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

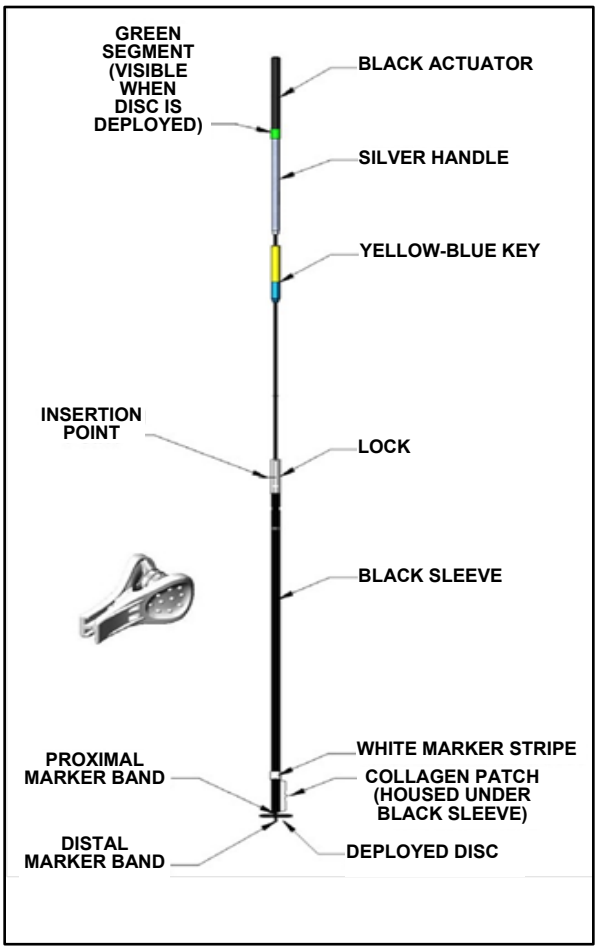


Figure 1. VASCADE VCS

Indications For Use

The VASCADE Vascular Closure System (VCS) is indicated for femoral arterial or venous access site closure while reducing time to haemostasis and ambulation compared to manual compression 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 compared to manual compression in patients who have undergone diagnostic endovascular procedures using a 5F, 6F or 7F procedural sheath.

Contraindications

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

Note:

- Clinicians are responsible for informing patients in advance of the procedure that the collagen in the implant is derived from animal tissue.
- The materials used in the device do not contain or consist of carcinogenic, mutagenic or reprotoxic (CMR) substances or endocrine disruptors.

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

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 Card to be given to the patient.
    - One (1) Patient Implant Leaflet with instructions on how to fill in the Patient Implant Card.
- One (1) printed Instructions for Use.

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.
- Do not reuse or re-sterilise. VASCADE is intended to be used once only for a single patient. Product reuse or re-sterilisation 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.
- Check for the absence of vessel tortuosity or side branches within 3-4 cm from the distal opening of the sheath and that the end of the sheath is not resting against the vessel wall. This is to prevent vascular injury during Catheter placement. If necessary, retract the sheath slightly to a non-tortuous location, making sure not to lose vascular access.
- DO NOT RELEASE the Collagen Patch if any part of the White Marker Stripe is showing (e.g. tissue tract is too short), as this may increase the risk of infection if the collagen protrudes from the skin.
- Do not deploy the extravascular Collagen Patch if there is a suspicion that the Disc is not seated against the intimal aspect of the vessel puncture site to avoid releasing the patch in the vessel. Partial or complete obstruction of blood flow may result. This step requires image guidance.

PRECAUTIONS

- VASCADE should only be used by a trained, licensed physician or healthcare professional.
  - Note: The training referred to here is previous training in vascular access and catheter placement and use. VASCADE does not require formal training beyond reading the Instructions for Use.
- Do not use in vessels with suspected intraluminal thrombus, haematoma, pseudoaneurysm or arteriovenous (AV) fistula. These conditions may interfere with the proper use and performance of the device.
- Do not use at the following access sites as the bleeding risk may increase:
  - Access site with suspected back wall stick.
  - Access site noted to be side stick.
  - Access site is “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).
- During access, be careful that the tissue tract is not pushed laterally or medially before accessing the vessel. This is to avoid misalignment of the tissue tract and the Collagen Patch relative to the vessel puncture site once the device is removed from the vessel, which may prolong time to haemostasis.
- Do not use if intra-procedural bleeding around the introducer sheath is noted, including haematoma formation (sign of possible multiple wall stick). This may suggest problems with the access site.
- 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.
- Do not soak the VASCADE Catheter in saline. This may result in Catheter pull-through during the sleeve retraction step. Momentarily insert only the Catheter tip in saline solution immediately before use to avoid over-hydration of the patch.
- Do not advance VASCADE into the patient if resistance is felt due to risk of vascular injury.
- Do NOT continue to pull on the Black Actuator once it is locked in place, as this may damage the device.
- Compressing the access site during removal of the sheath may hinder the Disc from tracking back to the vessel puncture site and cause Disc deformation. This may hinder achieving temporary haemostasis.
- Applying too much upward tension on the Black Actuator may cause Disc to pull out of vessel. Should this occur, convert to Institution’s Manual Compression Protocol.
- Not achieving temporary haemostasis may be an indication that the Disc is not against the vessel wall. Releasing the Collagen Patch may result in all or a portion of the Patch to be deployed in the vessel.
- VASCADE should be stored at room temperature (15° – 25°C), otherwise proper device performance may be affected.

Special Patient Populations

NOTE: The safety and effectiveness of the device have not been evaluated in the following patients:

- Less than 18 years of age.
- Pregnant and/or lactating women.
- Pre-existing immunodeficiency disorder and/or chronic use of systemic steroids.
- Known significant coagulation defect/bleeding disorders such as thrombocytopenia (platelet count < 100,000/mm^3), thrombasthenia, haemophilia, von Willebrand's disease or anaemia (haemoglobin < 10 g/dL and haematocrit < 30%).
- Previous vascular grafts or surgery at the target vessel access site.
- Symptomatic ipsilateral lower extremity ischaemia.
- Fluoroscopically visible calcium or atherosclerotic disease within 1 cm of the puncture site.
- Femoral vessel lumen less than 6 mm in diameter.
- Length of tissue tract (distance between the anterior vessel wall and skin) estimated to be less than 2.5 cm.
- INR ≥ 1.8 if the patient received warfarin.
- Fibrinogen level < 150 mg/dL if the patient received a fibrinolytic agent.
- Extreme morbid obesity (BMI > 45 kg/m^2) 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 the competent authority of the Member State in which the user and/or patient is established.

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
- Arteriovenous fistula
- Bleeding from the puncture site
- Bruising at the puncture site
- Death
- Deep vein thrombosis
- Device failure/malfunction
- Oedema
- Embolism (thrombus, air, calcific debris, device)
- Haematoma
- Infection
- Inflammatory response
- Intimal tear/dissection
- Laceration of the vessel wall
- Lower extremity ischaemia
- Oozing from the puncture site
- Perforation of the vessel wall
- Peripheral nerve injury
- Pseudoaneurysm
- Pulmonary embolism
- Puncture site pain
- Retroperitoneal bleeding
- Superficial vein thrombosis
- Vascular injury
- Vasospasm (arterial only)
- Vasovagal response
- Vessel occlusion
- Vessel thrombus
- Wound dehiscence

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 haemostasis and ambulation vs. Manual Compression (MC) after diagnostic or interventional endovascular procedures (cardiac or peripheral vascular catheterisation) performed through 6F or 7F introducer sheaths.
Design*	Prospective, randomised (2:1), controlled, multi-centre 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 or 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 prolonged hospitalisation. • 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, haematoma, 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 randomised and treated VASCADE patients at five (5) sites before hospital discharge.
**415 out of 420 randomised subjects (98.8%) completed a 30-day follow-up. Of the five (5) subjects who did not complete the study, three (3) were prematurely randomised 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 randomised and immediately withdrawn from the study due to final eligibility. All three (3**)** were randomised 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 ischaemia 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 hospitalisation	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 haemostasis	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 haematoma > 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
Localised 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 Haemostasis (TTH):** elapsed time between device removal (i.e. device removal for VASCADE and sheath removal for MC) and the first observed and confirmed haemostasis.
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 6.1 metres without evidence of re-bleeding from the femoral access sites).
	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: Achievement of final haemostasis using any method and freedom from major vascular complications for 30 days.
	Device Success (DS): Successful deployment of the delivery system, delivery of the collagen patch and achievement of haemostasis with VASCADE alone or with adjunctive compression.

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

Table 7: RESPECT Primary and Secondary Effectiveness Endpoints

	Diagnostic (N=211)			**Interventional (N=209)**			**Total (N=420)**		
	VASCADE (N=137)	**MC (N=74)**	***P* value***	**VASCADE (N=141)**	**MC (N=68)**	***P* value***	**VASCADE (N=278)**	**MC (N=142)**	***P* value***
TTH (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	
TTA (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	
TTDE (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	
TTD (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 8 summarise 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%

Procedure Success Rate was 100% for VASCADE and MC (Table 10).

Table 10: RESPECT Secondary Effectiveness Results, 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	VASCADE	275	275	100%	99%	100%
	Manual Compression	142	142	100%	97%	100%

*95% Exact Binomial Confidence Interval.

Device Success for all VASCADE subjects was 96% (Table 11).

Table 11: RESPECT Secondary Effectiveness Results, Device Success

Procedure	**Number of Subjects**	**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.

**Six (6) instances of failure to follow written Instructions for Use were not considered successes. Excluding these six instances, Device Success rates were 96% (Diagnostic), 99% (Interventional) and 98% (Total).

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-randomised, 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 catheterisation with a 5F introducer sheath.
Follow-up	30±7 days.
Study Population	30 subjects undergoing diagnostic procedures (cardiac or peripheral vascular catheterisation).
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 ischaemia threatening the viability of the limb	0	0.0%
Access site infection requiring intravenous antibiotics and/or prolonged hospitalisation	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 haemostasis	0	0.0%
Access site haematoma > 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%
Localised 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%

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 Haemostasis; TTA: Time to Ambulation; TTDE: Time to Discharge Eligibility; TTD: Time to Discharge.

VASCADE 5F Engineering Analysis

VASCADE 5F has a proportionally smaller Collagen Patch than the VASCADE 6/7F VCS device. Both devices have adequate tissue tract space-filling capability. Verification and validation testing was completed for both devices.

Conclusions of the Clinical Studies

The RESPECT study results demonstrated that patients treated with VASCADE VCS who have undergone diagnostic or interventional cardiac or peripheral endovascular procedures using a 6F or 7F introducer sheath have statistically and clinically significant decreased times to haemostasis and ambulation and reduced time to discharge eligibility for diagnostic procedures compared to patients treated with MC. Further, results showed that VASCADE VCS treated patients were non-inferior to MC-treated patients concerning major access site-related complications.

A confirmatory clinical study and engineering analysis demonstrated that the VASCADE 5F VCS is safe and effective for its intended purpose.

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 in vascular access and catheter placement and use. VASCADE does not require formal training beyond reading the Instructions for Use.
- Do not use in vessels with suspected intraluminal thrombus, haematoma, pseudoaneurysm or arteriovenous (AV) fistula. These conditions may interfere with the proper use and performance of the device.
- Do not use at the following access sites as the bleeding risk may increase:
    - Access site with suspected back wall stick.
    - Access site noted to be side stick.
    - Access site is “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).
- 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.
- VASCADE should be stored at room temperature (15° – 25°C), otherwise proper device performance may be affected.

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. Access is gained at the beginning of the index procedure for initial procedural sheath placement. Image-guided access is recommended to limit potential access site issues, such as multiple sticks, backwall stick, high stick, side stick, through-and-through or unintentionally nicking a nearby vein or artery. During access, where more than one hole is unintentionally made in a vessel or more than one vessel is perforated at a single access site, a closure device should not be used as it may result in a haematoma. For high stick, retroperitoneal bleeding may result.
2. Evaluate patient body build or use ultrasound to provide reasonable assurance that the tissue tract is greater than 2.5 cm.

Prior to Closure

3. Confirm a single wall common femoral vessel puncture site.
4. Record an anterior oblique fluoroscopic image with contrast or an ultrasound image (optional) so that the vessel puncture site location can be subsequently compared to the position of the radiopaque marker (or echogenic disc) just before Collagen Patch release. Reference Step 1 Part B for imaging steps during closure.
5. Verify sheath compatibility (e.g. length) and swap for a different sheath if necessary. Reference Technical Specifications.

⚠ **CAUTION**

During access, be careful that the tissue tract is not pushed laterally or medially before accessing the vessel. This is to avoid misalignment of the tissue tract and the Collagen Patch relative to the vessel puncture site once the device is removed from the vessel, which may prolong time to haemostasis.

Prep-B: Unpack the Device

1. Inspect the package for damage (breaks, tears, open seals, water damage, etc.).
2. Check that the expiry date has not passed.
3. Check that the correct product and size is used.
4. Remove the tray from the foil pouch using standard sterile technique (see Aseptic Presentation below).
5. Remove the Catheter and Clip from the tray.

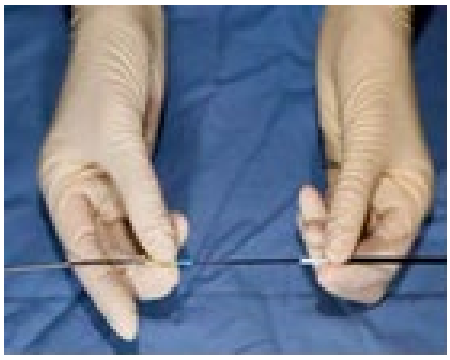
Aseptic Presentation

1. Place near the sterile field. Check that the scrubbed person to whom the product is passed is ready to receive it with a clear space in the field.
2. All sterile packages have a designated side to open from. Locate this side and slowly peel the package open.
3. Open the package with arms extended to avoid accidental contact with the product or sterile field. The secondary packaging is not considered sterile and must not touch the edges of the primary packaging. Create a large enough opening in the package to remove the primary packaging without touching the non-sterile areas.
4. Present the product to the scrubbed person.
5. Discard packaging following facility protocol.

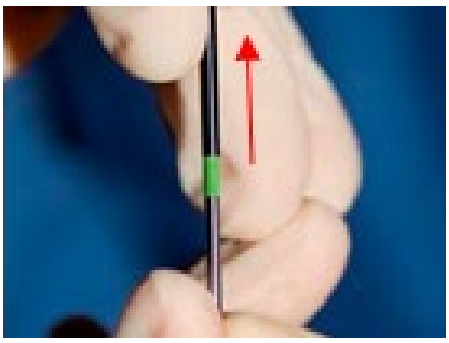
⚠ **WARNINGS**

- Do not reuse or re-sterilise. VASCADE is intended to be used once only for a single patient. Product reuse or re-sterilisation 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



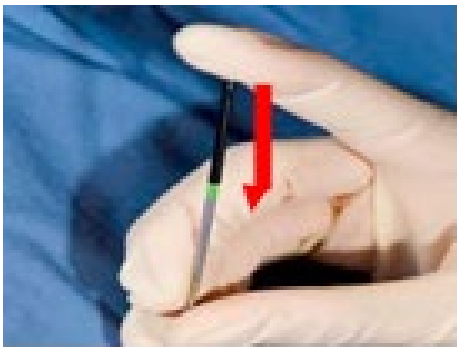
Perform the following inspection to prevent premature Collagen exposure:
1. Black Sleeve is locked in position.
2. Collagen Patch is not exposed.
3. Key is not engaged in the Lock and the Key is located at the proximal end of the device.



Check the Disc function:
1. Firmly hold the Silver Handle.
2. Pull back the Black Actuator until it locks in place.
3. The Green Segment will be visible.

Check the Disc shape:
1. Circular appearance.
2. Symmetrical appearance.
3. Intact membrane.

If there are any device defects, do not use the device. Report and return to the manufacturer.



Collapse the Disc by pressing the Black Actuator tip. Device is ready for use.

Prep-D: Prepare the Sheath

1. Verify that the sheath is not positioned in a tortuous vessel (i.e. by examining the sheath placement images obtained earlier).
2. If required, retract the sheath slightly to a non-tortuous location and verify the sheath is still positioned within the vessel.
3. Flush the sheath with sterile saline solution.

⚠ **WARNING**

Check for the absence of vessel tortuosity or side branches within 3-4 cm from the distal opening of the sheath and that the end of the sheath is not resting against the vessel wall. This is to prevent vascular injury during Catheter placement. If necessary, retract the sheath slightly to a non-tortuous location, making sure not to lose vascular access.

⚠ **CAUTION**

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

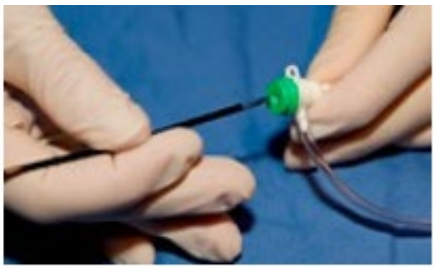
STEP 1 PART A: Exchange Sheath for VASCADE and Achieve Temporary Haemostasis

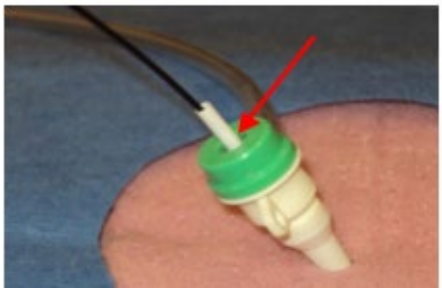
Step 1.1: Dip Device Tip in Saline

Briefly dip the device tip in saline up to the White Marker Stripe and quickly remove.

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

Step 1.2: Insert VASCADE

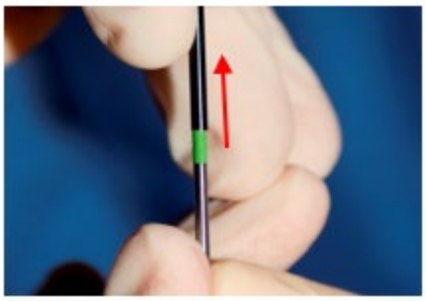


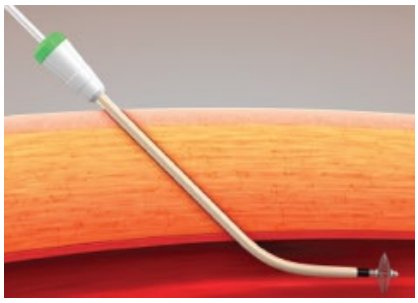


1. With the Disc collapsed, gently insert VASCADE into the introducer sheath hub until Lock is midway into the hub. Use short strokes to insert the device. About 0.5-inch (13 mm) of the Lock should remain exposed.
2. Verify that the Lock is NOT fully inserted into the sheath.

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

Step 1.3: Deploy the Disc



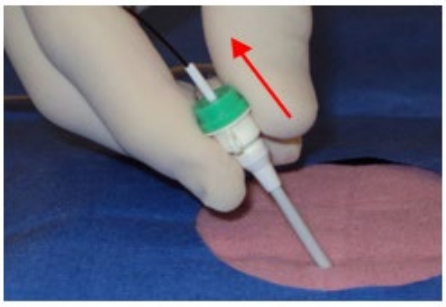


Deploy the Disc by firmly holding the Silver Handle and pulling back the Black Actuator until it locks in place.

NOTE
The Green Segment should be visible. If the Disc is not correctly deployed, the Black Actuator will slide back to its original position and the Green Segment will disappear (in VASCADE 5F approximately 1 mm of the Green Segment remains visible when disc is collapsed). Repeat the step to deploy the Disc as needed.

⚠ **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

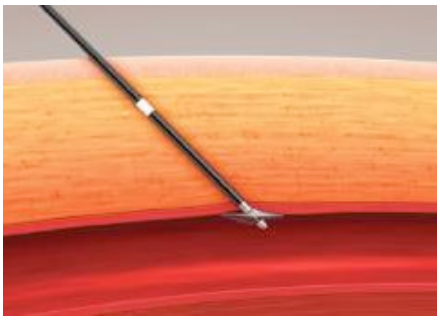


1. Gently remove sheath without applying any compression at the access site and without holding the VASCADE Catheter.
2. As the sheath slides over the VASCADE Catheter, grasp the Catheter close to the Lock as it exits the sheath.
3. Continue sliding the sheath over VASCADE and discard sheath.

⚠ **CAUTION**

Compressing the access site during removal of the sheath may hinder the Disc from tracking back to the vessel puncture site and cause Disc deformation. This may hinder achieving temporary haemostasis.

Step 1.5: Achieve Temporary Haemostasis



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

In the case of a failed access site where manual compression is needed, refer to the Switching to Manual Compression (MC) instructions (below).

NOTES

1. If the White Marker Stripe is visible above the skin, then the length of the tissue tract may not be long enough for the Collagen Patch.
2. If any portion of the White Marker Stripe is showing, switch to MC (below).

⚠ **WARNING**

DO NOT RELEASE the Collagen Patch if any part of the White Marker Stripe is showing (e.g. tissue tract is too short), as this may increase the risk of infection if the collagen protrudes from the skin.

⚠ **CAUTION**

- Applying too much upward tension on the Black Actuator may cause Disc to pull out of vessel. Should this occur, convert to Institution's Manual Compression Protocol.
- Not achieving temporary haemostasis may be an indication that the Disc is not against the vessel wall. Releasing the Collagen Patch may result in all or a portion of the Patch to be deployed in the vessel.

<u>As Needed: Switching to Manual Compression (MC)</u>

MC Assist

Use the VASCADE Disc with the Clip to Maintain Temporary Haemostasis While ACT Normalises (e.g. for anti-coagulated patients):

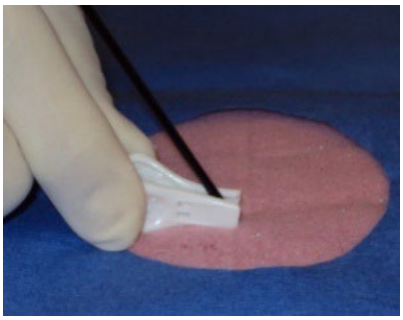
1. Apply the Clip (see Step 3.1) to the VASCADE Catheter to maintain temporary haemostasis.
2. Leave the device in place until the Activated Clotting Time (ACT) value normalises.
3. Collapse the Disc and remove VASCADE.
4. Achieve final haemostasis by applying MC per institutional protocol.

Alternative Option (e.g. for non-anti-coagulated patients):

1. Collapse the Disc and remove VASCADE.
2. Apply manual compression (MC) per institutional protocol.

STEP 1 PART B: Verify Disc Placement with Imaging

Step 1.6: Continue to Apply Upward Tension on the Catheter



Continue to apply gentle tension by placing the Clip on the Black Sleeve at skin level or holding gentle tension on the Black Actuator.

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

1. TO PREVENT INTRAVASCULAR COLLAGEN DEPLOYMENT, use imaging to verify Disc placement.
2. Confirm the position of the Disc (Catheter's proximal radiopaque marker for fluoroscopy, echogenic Disc for ultrasound).
3. This Disc should be positioned against the intimal surface of the vessel wall. Verify using imaging:
   - See below for an example of a fluoroscopic image demonstrating proper position of Disc. The proximal radiopaque marker should be at the vessel puncture site. This can be verified by comparing the marker's location to the vessel puncture site documented through fluoroscopic image recorded after introducer sheath placement. The Collagen Patch is immediately proximal to this proximal Marker Band. The Distal Marker Band locates the distal end of the Disc.
   - See below for an example of an ultrasound image demonstrating proper position of the echogenic Disc.

⚠ **WARNING**

Do not deploy the extravascular Collagen Patch if there is a suspicion that the Disc is not seated against the intimal aspect of the vessel puncture site to avoid releasing the patch in the vessel. Partial or complete obstruction of blood flow may result. This step requires image guidance.

⚠ **CAUTION**

Applying too much upward tension on the Black Actuator may cause Disc to pull out of vessel. Should this occur, convert to Institution's Manual Compression Protocol.

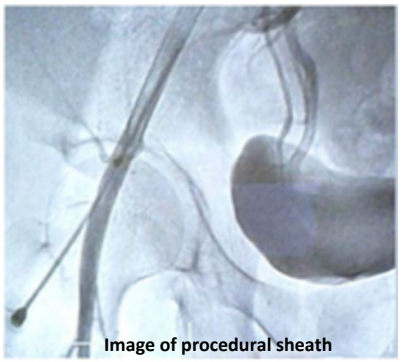


Image of procedural sheath

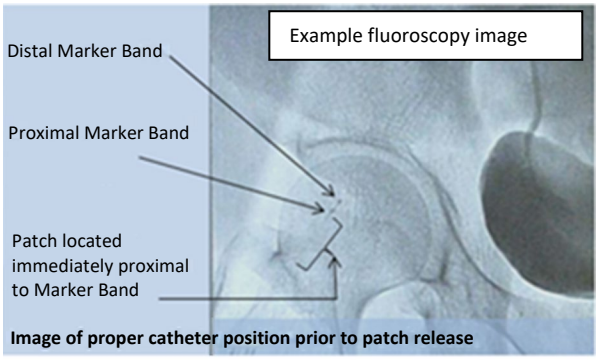
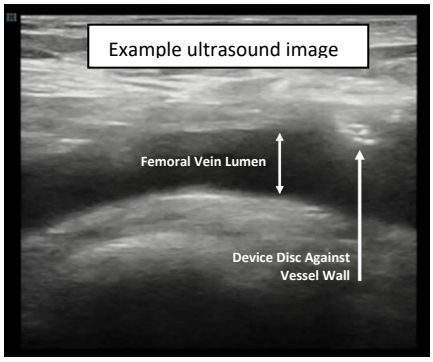
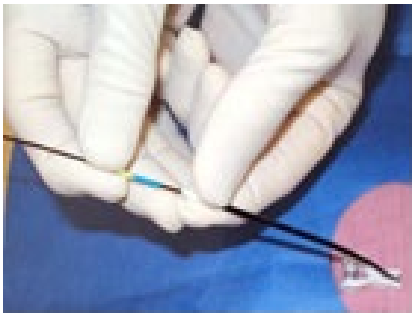


Image of proper catheter position prior to patch release

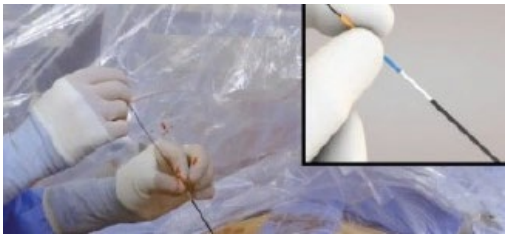


STEP 2: Deploy Collagen

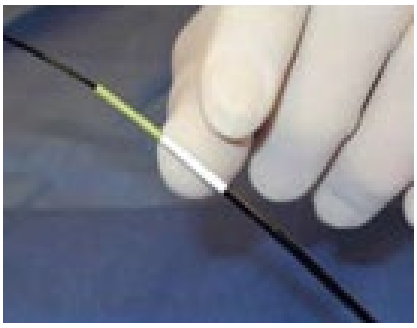
Step 2.1: Unlock the Black Sleeve

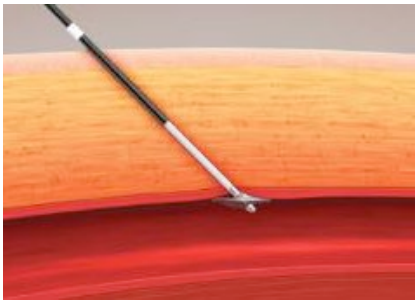


While continuing to apply gentle tension (through the Clip or by maintaining tension on the Black Actuator), slide the Key into the Lock. The blue segment should no longer be visible.



Step 2.2: Retract the Black Sleeve to Expose the Collagen



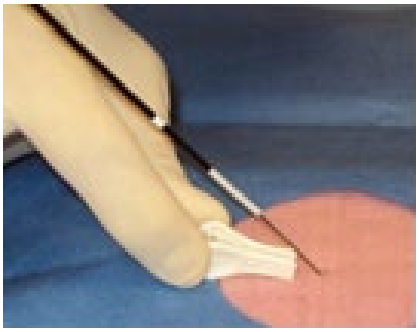


1. If the Clip is on, apply gentle upward tension on the Black Actuator, and remove the Clip.
2. While continuing to apply gentle tension on the Black Actuator, grasp the Lock with the other hand, and apply gentle upward tension on the Lock toward the Silver Handle. The Black Sleeve will move freely after some initial resistance. A second resistance point may be felt after the sleeve is moved approximately 1.6 cm (0.6 in).
3. Fully retract the Black Sleeve proximally to the Silver Handle. This exposes the Collagen Patch. The Green Tube is visible.

NOTES

1. If the Black Sleeve does not retract easily, confirm the blue end of the Key is fully engaged in the Lock.
2. If the Collagen Patch is removed during sleeve retraction, continue procedure by converting to MC (see “Converting to Manual Compression (MC)”).

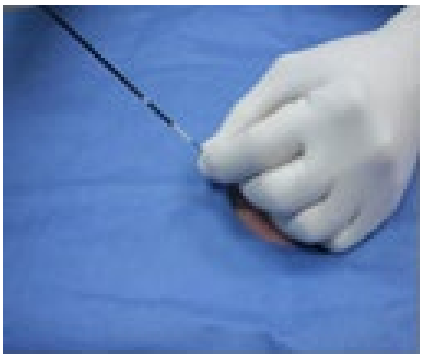
Step 2.3: Wait for Collagen Hydration



1. Apply the Clip on the Catheter using minimal tension or apply gentle upward tension on the Black Actuator to keep the disc up against the intima.
2. Allow approximately 30 seconds for collagen hydration (patch swell period) before stripping the collagen.

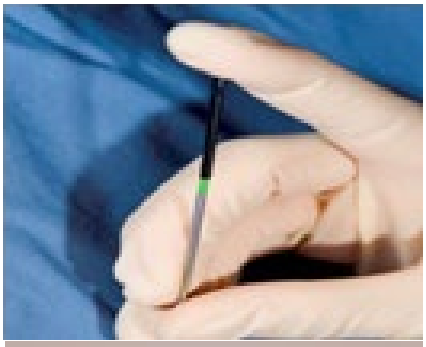
STEP 3: Achieve Final Haemostasis

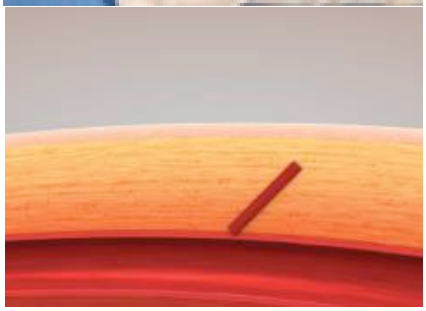
Step 3.1: Prepare to Strip Collagen



1. Remove the Clip.
2. Grasp the Green Tube between the thumb and the index finger.

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





Option 1: Move the Green Tube, Device Stationary

1. Advance the Green Tube down the tissue tract while maintaining gentle back tension on the device to keep the Disc positioned against the vessel wall. Slide the Green Tube back and forth 2-3 times to ensure release of Collagen Patch. Leave the Green Tube in the forward position.
2. Relax tension on device and collapse the Disc (see below).
3. Apply compression over the vessel puncture site and remove the device.*
4. Apply compression until final haemostasis is confirmed.

Option 2: 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. Grasp the Green Tube and hold stationary with respect to the body.
2. Collapse the Disc (see below).
3. Retract device until resistance is met. Let go of the Green Tube.
4. Apply compression over the vessel puncture site and remove the device.*
5. Apply compression until final haemostasis is confirmed.

*This action slides the collapsed Disc by the hydrated Collagen Patch without displacing the Collagen Patch.

Collapse the Disc:

1. With slack in the Catheter, press the Black Actuator tip.
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.

Step 3.3: Confirm Final Haemostasis

1. Apply compression as needed until final haemostasis is achieved.
2. Observe the access site for final haemostasis per institution protocol.
3. Apply sterile dressing to site per institution protocol.

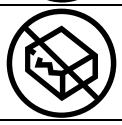
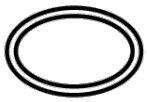
Step 3.4: In Recovery and Discharge

1. Maintain bed rest and periodically check site per institutional protocol pre and post ambulation.
2. If tissue tract oozing is present, apply compression.
3. Give the patient the completed Patient Implant Card prior to discharge.

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 waste.

Graphic Symbols on Packaging

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	ISO 15223-1	5.1.1 / Manufacturer	Medical device manufacturer.
	ISO 15223-1	5.1.3 / Date of Manufacture & 5.1.11 / Country of Manufacture	Indicates the date when the medical device was manufactured / to identify the country of manufacture of products (MX = Mexico).
	ISO 15223-1	5.1.2 / Authorised representative in the European Community	Authorised representative in the European Community.
	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	5.1.8 / Importer	Entity importing the medical device into the locale.
	ISO 15223-1	5.1.10 / Model number	Model number or type number of a product.
	ISO 15223-1	5.2.4 / Sterilised by irradiation	Medical device that has been sterilised by irradiation.
	ISO 15223-1	5.2.6 / Do not re-sterilise	Medical device that is not to be re-sterilised.
	ISO 15223-1	5.2.8 / Do not use if packaging is damaged	Medical device that should not be used if the packaging 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 reuse	Medical device intended for one use or for use on a single patient during a single procedure.
	ISO 15223-1	5.4.3 / Read instructions for use or 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.

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	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.
	N/A	Prescription Device	Device is restricted to sale to or on the order of a physician.
	N/A	Package quantity	Quantity of systems in package.
	EU MDR	The requirements for accreditation and market surveillance relating to the marketing of products / CE Mark with Notified Body Reference ####	Signifies European conformity (CE) mark. Indicates conformity of products where the Notified Body performed conformity assessment. Notified Body reference # is displayed.

*Standards and Regulations:
ISO 15223-1: Medical devices – Symbols to be used with information to be supplied by the manufacturer.
EU MDR: Regulation (EU) 2017/745, Medical Device Regulation

Patient card and leaflet symbols are defined in the leaflet.

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EC REP

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Limited Warranty

Cardiva Medical, Inc. warrants that each VASCADE Vascular Closure System is free from defects in workmanship and material under normal use and service and provided it is used prior to the stated expiry date. Cardiva Medical, Inc. will not be liable for any incidental, special or consequential loss, damage or expense directly or indirectly derived from the use of its product. Liability under this warranty is limited to refund or replacement of any device that has been found by Cardiva Medical, Inc. to be defective at the time of shipment. Damage to the device through misuse, alteration, improper storage or improper handling shall void this limited warranty. The remedies set forth in this warranty and limitation shall be the exclusive remedy available to any person. No employee, agent or distributor of Cardiva Medical, Inc. has any authority to alter or amend this limited warranty or assume or bind Cardiva Medical, Inc. to any additional liability or responsibility with respect to this device. There is no express or implied warranty, including any implied warranty of merchantability or fitness for a particular purpose, on the Cardiva Medical, Inc. product(s) described herein.

Summary of Safety and Clinical Performance (SSCP)

The SSCP is available in the European Database on Medical Devices (EUDAMED: https://ec.europa.eu/tools/eudamed).