USA

Celt ACD® PLUS

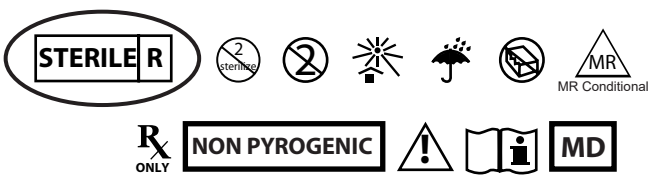
Vascular Closure Device

INSTRUCTIONS FOR USE

READ ALL INSTRUCTIONS, WARNINGS, CAUTIONS AND SAFETY INFORMATION CAREFULLY PRIOR TO USE.

CAUTION:
Federal Law restricts this device to sale by or on the order of a physician (or allied healthcare professionals, authorized by, or under the direction of such physician) who is trained in diagnostic and/or interventional catheterization procedures.

Prior to use, the operators must review the Instructions for Use and be familiar with the deployment techniques associated with the use of this device.



Vasorum Ltd
Trinitas House, 2012 Orchard Avenue,
Citywest Campus, Dublin 24, Ireland
Tel: +353 1 4035460

SECTION A – DESCRIPTION

The **Celt ACD® PLUS** Vascular Closure Device is a single use puncture site closure device which is radiopaque and if required can be visualized under fluoroscopic control during all phases of deployment. It is designed to close a femoral artery puncture site following either a diagnostic or interventional catheterization procedure. The device is manufactured as either a 5F, 6F or 7F delivery system, with a pre-mounted implant on its tip. During deployment, the delivery system is activated and delivers a small biocompatible stainless steel (316LVM) implant (see Contraindications Section D) into the arterial wall thereby closing the puncture site and effecting hemostasis.

SECTION B – COMPONENTS

The consists of the following:

1. A delivery system.
2. Pre-attached implant.

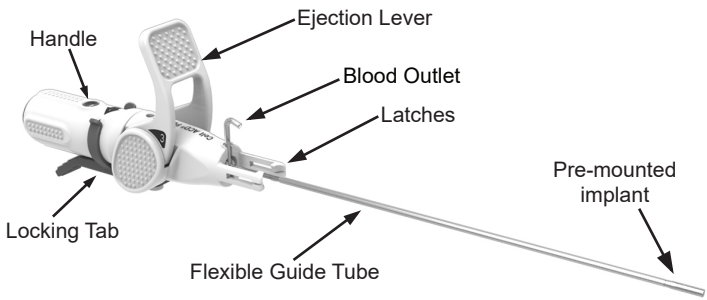


Fig. 1

SECTION C – INDICATION FOR USE

The **Celt ACD® PLUS** Vascular Closure Device is indicated for the percutaneous closure of common femoral artery puncture sites while reducing time-to-hemostasis in patients who have undergone diagnostic or interventional intra-arterial catheterization procedures where either **5F**, **6F** or **7F** introducer sheaths have been used.

CAUTION:
The device is intended for use with a pre-existing introducer sheath. The device should only be used with sheaths that have a maximum overall length not greater than that shown in Table 1 and an internal lumen diameter which is not less than that shown in Table 1.

It is essential that the device correctly fits the intended introducer sheath.

SHEATH SIZE	MAX OVERALL LENGTH	MIN LUMEN DIAMETER
5F	15CM	1.7MM
6F	15CM	2.1MM
7F	15CM	2.4MM

TABLE 1

SECTION D – CONTRAINDICATIONS

The **Celt ACD® PLUS** Vascular Closure Device is contraindicated in patients with a known allergy to 316LVM stainless steel.

SECTION E- WARNINGS

1. Do not use if package is damaged or any portion of the package has been previously opened.
2. Do not use if the label is missing or not indicating that the device is sterile.
3. Do not use any of the components if they appear damaged or defective in any way.
4. Do not reuse or resterilize. The **Celt ACD® PLUS** Vascular Closure Device is for SINGLE USE ONLY.
5. Do not use in patients if there is any indication that puncture has been made above the inguinal ligament. Puncture above the inguinal ligament may result in retroperitoneal bleeding.
6. Do not use in patients with a stent situated ≤ 1 cm from the puncture site that would interfere with placement of the device implant.

SECTION F – PRECAUTIONS

1. The **Celt ACD® PLUS** Vascular Closure Device is intended for use by healthcare professionals and personnel possessing adequate instruction in the use of the device and in intravascular catheter procedures.
2. A single wall puncture technique must be used to ensure that puncture of the posterior wall of the artery does not occur.
3. Aseptic sterile techniques should be observed at all times when using the **Celt ACD® PLUS** Vascular Closure Device.
4. Exercise care during device handling to reduce the possibility of accidental damage to the **Celt ACD® PLUS** Vascular Closure Device.
5. In the event of persistent bleeding from the femoral access site after use of the **Celt ACD® PLUS** Vascular Closure Device, use standard manual or mechanical compression techniques.
6. Disposal of contaminated devices, components, and packaging materials should follow universal precautions for bio-hazardous waste.
7. The safety and effectiveness of the **Celt ACD® PLUS** Vascular Closure Device has not been evaluated in the following patients:

    - Patients with a femoral artery lumen diameter less than 5 mm for 5F and 6F sheaths and less than 6mm for 7F sheath size.
    - Patients with evidence of systemic bacterial or cutaneous infection, including groin infection.
    - Patients suffering with definitive or potential coagulopathy or platelet count < 100,000/µl.
    - Patients in which introducer sheaths smaller than 5F or greater than 7F have been used.
    - Patients where the puncture site is via a vascular graft.
    - Patients in whom there is any indication that puncture has been made in the profunda femoris artery.
    - Patients with a very superficial artery where the depth from skin to the artery surface at the access site is less than 4 mm.

SECTION G – POTENTIAL COMPLICATIONS

1. Bruising, oozing or bleeding at the puncture site.
2. Hematoma or Ecchymosis.
3. Pain, discomfort or transitory local irritation and inflammation at the puncture site.
4. Access-site related nerve injury, vascular spasm, local pulse deficits, ischaemia or access-site wound dehiscence.
5. Infection at the procedure site.
6. Failure of the device to deploy correctly in the artery.
7. Vaso-vagal response.

Other events that could possibly occur, but are considered extremely unlikely include:

8. Occlusive intraluminal thrombus and/or emboli formation at the **Celt ACD® PLUS** Vascular Closure Device implant site.
9. Partial or complete occlusion of the arterial lumen.
10. Damage of the arterial wall including stenosis/narrowing.
11. Swelling of the treated limb.
12. Embolization (device, thrombus, tissue, air or calcific debris).
13. Pseudoaneurysm, arterial or deep vein thrombosis or arteriovenous fistula.
14. Corrective intervention, including transfusion and/or surgery, due to any of the above complications.

SECTION H – SPECIAL PATIENT POPULATIONS

The safety and effectiveness of the **Celt ACD® PLUS** Vascular Closure Device has not been established in the following patient populations:

1. Patients that have any amputation from an access site limb.
2. Patients that have undergone a percutaneous procedure using a vascular closure device for hemostasis within the previous 30 days or using manual/mechanical pressure for hemostasis within the prior 30 days in the same leg.
3. Patients with a systolic blood pressure reading below 90 mmHg.
4. Severe, acute non-cardiac systemic disease or terminal illness with a life expectancy of less than one year.
5. Use of systemic thrombolytic agents within 24 hours prior to or during the catheterization procedure which cause the concentration of fibrinogen to be < 100 mg/dl or if post-thrombolytic fibrinogen (in case of thrombolysis within 24 hours or intra-procedural) cannot be measured.
6. Patients with severe claudication, iliac or femoral artery diameter stenosis greater that 50%, or previous bypass surgery or stent placement in the vicinity of the access site.
7. If a palpable hematoma is observed during the procedure.
8. Patients with an active hematoma, arteriovenous fistula, or pseudoaneurysm.
9. Morbidly obese patients (Body Mass Index > 35 kg/m2).
10. Patient is known or suspected to be pregnant or lactating.
11. Patients in whom there has been an antegrade puncture.
12. Patients in whom there has been difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial wall puncture.
13. Patients who have undergone prior or recent use of an intra-aortic balloon pump through the arterial access site.
14. Patients with uncontrolled hypertension (BP ≥ 180/110 mmHg) at time of vascular closure.
15. Patients with acute ST-elevation myocardial infarction ≤ 48 hours before catheterization.
16. Patients who are unable to ambulate at baseline.
17. Patients known to require an extended hospitalization (e.g., patient is undergoing cardiac surgery).

SECTION I – ADVERSE EVENTS

The **Celt ACD® PLUS** Vascular Closure Device was evaluated in a pivotal, multi-center, randomized, two-arm controlled trial which was conducted across four international sites, two in the United States and two in Europe. A total of 207 patients undergoing interventional catheterization procedures were recruited with 148 randomized to the **Celt ACD® PLUS** group and 59 to the manual compression group (ratio 2.5:1). The adverse events reported during the trial were categorized as either major or minor complications. The primary safety end-point was the combined rate of major complications within 30 + 7 days following the interventional procedure. The secondary safety end-point was the combined rate of minor complications within 30 + 7 days following the interventional procedure. Clincal data collected on the **Celt ACD® device is directly applicable to the Celt ACD® PLUS**

A. Reported Major Complications

The major complications reported are shown in Table 2. All three complications were categorized as 'Other'. The major complication reported in the **Celt ACD®** group was embolization of the **Celt ACD®** implant in the right leg following proper functioning of the delivery system. The event was most likely a result of inadequate proximal wing positioning outside the artery at the puncture site secondary to the device not being pulled back sufficiently prior to opening the proximal wings of the implant. The embolized implant was successfully retrieved radiologically with a snare with access through the left femoral artery and was deposited in the subcutaneous tissue outside the left femoral artery access site. The major complications in the manual compression group were; one patient reporting syncope during the follow-up period and one patient suffering brain stem ischemia.

There was a lower major complication rate with the **Celt ACD®** compared to the manual compression group and the upper limit of the 95% confidence interval was within the 4% non-inferiority margin.

#	MAJOR COMPLICATION	CELT ACD (N=148)	MANUAL COMPRESSION (N=59)	TOTAL (N=207)
1	Vascular repair or the need for vascular repair (via surgery, ultrasound -guided compression, transcatheter embolization, or stent-graft).	0	0	0
2	Retroperitoneal bleeding.	0	0	0
3	Access-site-related infection requiring intravenous antibiotics and/or extended hospitalization.	0	0	0
4	Permanent access site-related nerve injury.	0	0	0
5	Surgery for access site-related nerve injury.	0	0	0
6	Access site related bleeding requiring transfusion.	0	0	0
7	Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram.	0	0	0
8	Any complication requiring surgery, vascular repair, or transfusion is a major complication and not a minor complication.	0	0	0
9	**Other**	0	0	0
	Syncope during the follow-up period.	0	1	1
	Brain Stem Ischemia.	0	1	1
	Device embolization from the femoral artery access point.	1	0	1
TOTAL-MAJOR COMPLICATIONS N (%)		1 (0.68%)	2 (3.39%)	3 (1.45%)
DIFFERENCE IN MAJOR COMPLICATION RATE (95% CI)		-2.71% (-7.09%, 1.66%)$		
p-value&		0.0013		

$ Farrington-Manning 95% confidence limits; & Farrington-Manning method (test for margin of 4%, z=3.01)

Table 2: Major complications as reported by the Clinical investigation sites (N)

B. Reported Minor Complications

Overall in the study, there was a total of 12 minor complications reported with seven in the **Celt ACD®** group and five in the manual compression group. The reported minor complications are shown in Table 3. Of the seven minor complications reported in the **Celt ACD®** group, three were related to access site bleeding which required more than 30 minutes to achieve hemostasis. One was related to an access site hematoma of greater than 6 cm and another to ecchymosis of greater than 5 cm. Another patient reported pain in the right groin which was resolved at follow-up. Another reported right sided weakness and confusion which were not device related.

#	MINOR COMPLICATION	CELT ACD (N=148)	MANUAL COMPRESSION (N=59)	TOTAL (N=207)
1	Access site hematoma ≥ 6 cm.	1	3	4
2	Ecchymosis > 5 mm.	1	1	2
3	Locally induced vasovagal episode requiring therapy.	0	0	0
4	Pseudoaneurysm, documented by ultrasound that does not require intervention.	0	0	0
5	Arteriovenous (AV) fistula documented by ultrasound that does not require intervention.	0	0	0
6	Access site-related bleeding requiring > 30 minutes to re-achieve hemostasis.	3	0	3
7	Late access site-related bleeding (i.e. following hospital discharge)	0	0	0
8	Transient loss of ipsilateral lower extremity pulse.	0	0	0
9	Ipsilateral deep vein thrombosis.	0	0	0
10	Transient access site-related nerve injury.	0	0	0
11	Access site-related vessel laceration (not requiring surgical repair or intervention).	0	0	0
12	Access site wound dehiscence.	0	0	1
13	Localised access site infection treated with intramuscular or oral antibiotics.	0	0	0
14	Pseudoaneurysm treated with ultrasound-guided thrombin injections or ultrasound-guided fibrin adhesive injection.	0	0	0
15	Ipsilateral lower extremity arterial emboli.	0	0	0
16	**Other**	0	0	0
	Pain to the right groin.	1	0	1
	Confusion; Right side weakness.	1	0	1
	Decreased power to the right leg.	0	1	1
TOTALt-MINOR COMPLICATIONS N (%)		7 (4.73%)	5 (8.47%)	12 (5.8%)
DIFFERENCE IN MINOR COMPLICATION RATE (95% CI)		-3.74% (-10.43%, 2.94%)$		
p-value&		0.012		

$ Farrington-Manning 95% confidence limits; & Farrington-Manning method (test for margin of 4%, z=2.27).

Table 3: Minor complications as reported by the clinical investigation sites (N)

In the manual compression group the five minor complications were reported across four patients. Three patients were reported to have access site hematomas of greater than 6 cm and one reported ecchymosis of greater than 5 cm. One patient reported decreased power to the right leg patient which had resolved at follow-up.

There was a lower minor complication rate with the **Celt ACD®** compared to the manual compression group and the upper limit of the 95% confidence interval was within the 4% non-inferiority margin.

C. Doppler Ultrasound (DUS) Study

To provide a further assessment of safety of **Celt ACD®** a DUS-based quantitative and qualitative analysis of the Common Femoral Artery (CFA) was carried out in a sub-study. The sub-study was designed to determine if there were any changes in the vessel and blood flow related to **Celt ACD®** implantation. This was assessed by comparing vessels in which **Celt ACD®** was deployed to vessels in which manual compression was used to achieve hemostasis. Patient selection was on a first come basis and all of the ultrasounds were done at one of the study sites in Germany. In the sub-study data from a total of 35 patients was available for analysis. These were a sub-set of the patients recruited in the Pivotal Trial. Using 2 Dimensional grey scale and color-Doppler ultrasound (Siemens Sanoline G40 and GE Healthcare Vivid 7) a DUS evaluation of the inguinal region of the CFA from 1 cm proximal to 1 cm distal of the arterial puncture site was carried out.

Quantitative Analysis

The continuous variables of CFA diameter (cm) and Peak Systolic Velocity (PSV) (cm-sec) were measured and analyzed. Both pre- and post-procedure vessel internal diameter data were available for a total of 35 patients recruited into the study (**Celt ACD®** n=25, Manual Compression n=10). The median diameter (and inter-quartile range) at the puncture site pre- and post-procedure is shown in Table 4, along with the difference in pre- and post-procedure measures, between the manual compression and **Celt ACD®** randomized groups. As the data were non-normal, a Mann Whitney test was applied and no statistically significant difference was found between the randomized groups for change in internal diameter of the common femoral artery.

	Celt ACD (n=25)	Manual Compression (n=10)	p-value
Pre-diameter (cm) at puncture site	**8.45** (7.85, 9.45)	**8.90** (8.7, 9.7)	
Post-diameter (cm) at puncture site	**9.15** (7.2, 10.0)	**9.63** (9.0, 9.85)	
Difference in diameter (cm; post- pre)	**1.20** (0.35,1.70)	**0.5** (-0.05, 0.8)	0.134$

$ Mann-Whitney U test between groups.

Table 4: Median (Inter-quartile range) CFA diameter pre- and post-procedure and difference in Celt ACD® and manual compression in ultrasound sub-study

The mean velocity of blood in the vessel (and 95% Confidence interval) at the puncture site pre- and post-procedure is shown in Table 5, along with the difference in pre- and post-procedure measures, between the manual compression and **Celt ACD®** randomized groups. There were 20 **Celt ACD®** group and 10 manual compression observations available for analysis. As the data were normally distributed, a Students t-test was applied and there was found to be no statistically significant difference between the randomized groups for change in velocity. In summary, the statistical analysis found no significant difference between the randomized groups in terms of the change in pre- and post-measurements of CFA diameter and PSV at the puncture site.

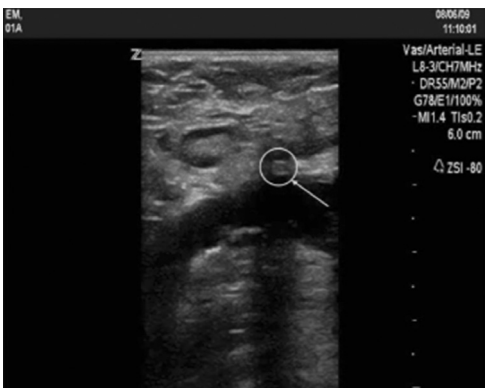
	CELT ACD (n=20)$	Manual compression (n=10)	p-value
Pre-velocity (cm/s) at puncture site	**109.25** (89.59, 128.91)	**110.0** (91.84, 128.16)	
Post-velocity (cm/s) at puncture site	**99.25** (79.61, 118.89)	**103.7** (84.30, 123.10)	
Difference in velocity (cm/s; post-pre) at puncture site	**-10** (-38.75, 18.75)	**-6.3** (-30.38, 17.78)	0.861#

t-test for difference between groups. $ 5 participants did not have velocity data at pre- and post-procedure.

Table 5: Mean (95% CI) Velocity pre- and post-procedure and difference in Celt ACD® and manual compression in ultrasound sub-study.

Qualitative Assessment

The qualitative assessment of the artery was made both before the procedure and 30 days after implantation of **Celt ACD®** or after use of manual compression to achieve hemostasis. There was no evidence of hematoma, pseudoaneurysm, or arteriovenous fistula observed in any patient in the ultrasound sub-study. No iatrogenic vascular injury was discovered in any patients in the study. All subjects in the sub-study demonstrated patency of the access site artery. There were no episodes of arterial thrombosis or clinically significant stenosis in this sub-study patient cohort. Peri-arterial inflammation was not identified in any of the images during the DUS study. Direct visualization of the **Celt ACD®** implant, while not a part of the protocol nor a focus of examination, was noted in many of the examinations, typically represented as a bright echogenic image in the CFA (common femoral artery). See Ultrasound Image A.



Ultrasound Image A: Ultrasound showing normal vessel lumen with **Celt ACD®** located in the vessel wall, indicted with the circle.

Conclusions from Ultrasound Sub-Study

The DUS data reported concludes that arterial blood flow is not interrupted by successful **Celt ACD®** closure of a femoral access site and that luminal patency is preserved in patients undergoing percutaneous interventional procedures when compared to manual compression. Imaging also demonstrates a lack of soft tissue reaction to the implant.

SECTION J – CLINICAL STUDY

Celt ACD® Pivotal Clinical Trial

Study Design

The **Celt ACD®** Vascular Closure Device was evaluated in a pivotal, multi-center, randomized, two-arm controlled trial which was conducted across four international sites, two in the United States and two in Europe. The control arm consisted of patients who were treated with manual compression. A total of 207 patients undergoing cardiac or peripheral vascular interventional catheterization procedures were recruited with 148 randomized to the **Celt ACD®** group and 59 to the manual compression group. The original randomization process (2:1 randomization) continued until 181 individuals had been randomized (122 to **Celt ACD®** and 59 to manual compression). Following discussion and approval by the FDA there was an alteration in the randomization process for the remaining 26 individuals who were not randomized but were directly allocated to the **Celt ACD®** group. This resulted in 148 patients in the **Celt ACD®** group and 59 patients in the manual compression group (2.5:1 ratio). Statistical power analysis showed that the alteration in the randomization process had no effect on the statistical power of the trial (power at 80%) given the small numbers involved in the reallocation and the fact that there were no dropouts (a 6% dropout rate was factored into the original sample size calculations). The study patients were followed for 30 ± 7 days after the catheterization procedure.

For a description of the safety endpoints, including major and minor complications, please see Section I.

Patient Assessment - Subject Selection and Exclusion Criteria
Patients undergoing interventional catheterization procedures requiring femoral artery access that were over 18 years of age and were able to give consent were eligible for the study. The inclusion and exclusion criteria included:

Inclusion Criteria:

1. Over 18 years of age.
2. Each patient, or his or her guardian or legal representative, is willing to give informed consent.
3. Clinically indicated for an intra-arterial procedure involving access through the common femoral artery and conducted through an access sheath size between 5F and 7F inclusive.

Exclusion Criteria:

1. Patients with known allergy to any of the materials used in the device.
2. Severe acute non-cardiac systemic disease or terminal illness with a life expectancy of less than one year.
3. Evidence of systemic bacterial or cutaneous infection, including groin infection.
4. Patients suffering with definitive or potential coagulopathy or platelet count < 100,000/µl.
5. Use of systemic thrombolytic agents within 24 hours prior to or during the catheterization procedure which cause the concentration of fibrinogen to be < 100 mg/dl or if post-thrombolytic fibrinogen (in case of thrombolysis within 24 hours or intra-procedural) cannot be measured.
6. Patients in whom an introducer sheath smaller than 5F or greater than 6F have been used.
7. Currently participating in another investigational device or drug study.
8. Patients with severe claudication, iliac or femoral artery diameter stenosis greater than 50% or previous bypass surgery or stent placement in the vicinity of the access site.
9. If puncture site is via a vascular graft.
10. If a palpable hematoma is observed during the procedure.
11. Patients in whom there is any indication that puncture has been made in the profunda femoris artery or superficial femoral artery, or adjacent to the bifurcation.
12. Patients with a common femoral artery lumen diameter of less than 5 mm for 5F and 6F sheaths.
13. Patients that have any amputation from an access site limb.
14. Patients that have undergone a percutaneous procedure using a vascular closure device for hemostasis within the previous 30 days or using manual/mechanical pressure for hemostasis within the prior 30 days in the same leg.
15. Patients with a systolic blood pressure reading below 90 mmHg.
16. Patients with an active hematoma, arteriovenous fistula, or pseudoaneurysm.
17. Patients with a very superficial artery where the depth from skin to the artery surface at the access site is less than 4 mm.
18. Morbidly obese patients (Body Mass Index > 35kg/m2).
19. Patients with a stent ≤ 1 cm of the puncture site that would interfere with placement of the device implant.
20. Patient is known or suspected to be pregnant, or is lactating.
21. Patients in whom there has been an antegrade puncture.
22. Patients in whom there has been difficulty in obtaining vascular access resulting in multiple arterial punctures and/or posterior arterial wall puncture.
23. Patients who have undergone prior or recent use of an intra-aortic balloon pump through the arterial access site.
24. Patients with uncontrolled hypertension (BP ≥ 180/110 mmHg) at time of vascular closure.
25. Patients with acute ST-elevation myocardial infarction ≤ 48 hours before catheterization procedure.

26. Patients with cardiogenic shock (hemodynamic instability requiring intravenous medication or mechanical support) experienced during or immediately post- catheterization.
27. Patients who are unable to ambulate at baseline.
28. Patients known to require an extended hospitalization (e.g., patient is undergoing cardiac surgery).
29. Patient has already participated in the trial.
30. Patient is unavailable for follow-up.

Demographic Data

Table 6 shows the baseline characteristics between the two randomized groups and the total.

There were no statistically significant differences observed for any of the baseline characteristics between the two groups. A higher number of male patients were enrolled in the trial, 77% male versus 23% female, which is a reflection of the general referral pattern for patients undergoing percutaneous interventional procedures at the investigation sites.

	CELT ACD (n=148)	Manual compression (n=59)	Total (n=207)	p-value
Age in years (mean, 95% CI) (SD, Range)	**66.75** (65.01, 68.49) (SD=10.8; 42, 92)	**67.44** (64.39, 70.49) (SD=11.7; 40, 92)	**66.95** (65.44, 68.45) (SD=11.0; 40, 92)	0.69#
Height in cm (mean, 95% CI) (SD, Range)	**172.9** (171.3, 174.5) (SD=9.56; 145, 197)	**171.7** (169.4, 173.9) (SD=7.82; 155,187)	**172.5** (171.1, 173.9) (SD=9.12; 145,197)	0.30#
Weight in kg (mean, 95% CI) (SD, Range)	**85.38** (79.76, 91.0) (SD=16.22; 40,154)	**82.78** (78.88, 86.68) (SD=14.83; 54.4,117)	**84.65** (80.48, 88.82) (SD=15.80; 40,154)	0.93#
BMI (kg/m2)1 (mean, 95% CI) (SD, Range)	**27.75** (27.00, 28.50) (SD=4.47; 14.2, 47.5)	**28.18** (26.97, 29.38) (SD=4.41; 19.5,40.9)	**27.87** (27.00, 28.50) (SD=4.45; 14.2,47.5)	0.55#
Male (N, %)	**112** (75.7%)	**47** (79.66%)	**159** (76.81%)	0.54~
Sheath size 6F, N (%) 7F, N (%)	**144** (97.3%) **4** (2.7%)	**57** (96.6%) **2** (3.4%)	**201** (97.1%) **6** (2.9%)	1.0$
Femoral artery site Right N (%) Left (%)	**142** (95.9%) **6** (4.1%)	**57** (96.6%) **2** (3.4%)	**199** (96.1%) **8** (3.9%)	1.0$
Type of cath-eterization Cardiac Peripheral	**144** (97.3%) **4** (2.7%)	**57** (96.6%) **2** (3.4%)	**201** (97.1%) **6** (2.9%)	1.0$
History of mild/ moderate PVD	**148** (100%)	**59** (100%)	**207** (100%)	n/a
Use of antiplatelet/ anticoagulant pre/ post procedure	**148** (100%)	**59** (100%)	**207** (100%)	n/a
Type anticoag-ulant: Bivalirudin Unfractionated heparin Warfarin	**35** (23.6%) **112** (75.7%) **1** (0.7%)	**18** (30.5%) **41** (69.5%) **0** (0%)	**53** (25.6%) **153** (73.9%) **1** (0.5%)	0.32@
Systolic blood pressure (pre) (mean, 95% CI) (SD, Range)	N=137 **141.4** (137.9,145.0) (SD=20.9; 94, 204)	N=55 **141.5** (135.3,147.8) (SD=23.1;105,203)	N=192 **141.45** (138.4, 144.5) (SD=21.5; 94,204	0.98#
Diastolic blood pressure (pre) (mean, 95% CI) (SD, Range)	N=137 **76.8** (74.9,78.8) (SD=11.6;46,111)	N=55 **76.0** (72.2.79.8) (SD=14.1;54,144)	N=192 **76.6** (74.8,78.4) (SD=12.4;46,144)	0.67#
Activated clot-ting time (ACT) in secs (mean, 95% CI) (SD, Range)	N=100 **249.6** (233.0,266.2) (SD=83.8;104,481)	N=36 **244.5** (212.8,276.2) (SD=93.7; 113,428)	N=136 **248.3** 233.6,262.9) (SD=86.2;104,481)	0.76#
Hypertensive	**113** (76.9%)&	**51** (86.4%)	**164** (79.6%)&	0.12~
Diabetes	**35** (23.7%)	**17** (28.8%)	**52** (25.1%)	0.44~

independent t-test; $ Fishers exact test; ~ Chi-square test;
@ Chi-square test without warfarin.
&missing on one individual; 1 n=10 participants had BMI>35.

Table 6: Baseline characteristics by randomized groups.

Data Analysis and Results

Primary Effectiveness Endpoint – Time-to-Hemostasis (TTH)

The primary effectiveness endpoint was time-to-hemostasis (TTH). Time-to-hemostasis was defined as the elapsed time between sheath removal and the time hemostasis is first observed. Hemostasis was defined as cessation of pulsatile bleeding in the absence of expanding or developing hematoma. Cutaneous or subcutaneous oozing that is readily treated by light compression methods sandbags, pressure dressing or light manual pressure was considered to comply with the definition of hemostasis.

The TTH data are shown in Table 7. Data on TTH were missing for 7 individuals from the manual compression group. The data were significantly skewed (non-normal), therefore, median and inter-quartile range (25th to 75th percentile) in addition to the mean (standard deviation SD) are presented, and the non-parametric Wilcoxon rank sum test and parametric t-test were both applied to compare the two randomized groups.

There was a considerably lower median TTH in the **Celt ACD®** group (0 mins) compared to manual compression (8.5 mins), which was highly statistically significant. There was also a statistically significant lower mean TTH in the **Celt ACD®** group (0.99 mins) compared to the manual compression arm (17.54 mins; Table 7).

Time-to-hemostasis (TTH, mins)	CELT ACD (n=148)	Manual compression (n=52) &	All patients (n=200) &	p-value
Mean (SD)	**0.99** (4.15)	**17.54** (54.55)	**5.29** (28.78)	0.034#
95% CI for mean TTH	(0.32, 1.67)	(2.35,32.73)	(1.28, 9.31)	
Median (mins)	**0**	**8.5**	**0**	< 0.0001$
Inter-quartile range (IQR)	(0, 0.33)	(0, 20)	(0, 2)	
Range (min, max)	(0, 44)	(0,398)	(0, 398)	

Continuous data presented in minutes.
Independent t-test with Satterthwaite method for unequal variances.
$Data were non-normal therefore the Wilcoxon rank sum test was used to test the null hypothesis.
&Seven subjects did not have time to hemostasis recorded in the manual compression group.

Table 7: Primary effectiveness end-point – time-to-hemostasis (TTH)

The TTH data were further analyzed by post-procedural time interval and these data are shown in Table 8. This analysis shows that 60% of patients in the **Celt ACD®** group had immediate hemostasis and that 95.9% had hemostasis in under 5 minutes and 98.6% under 10 min. The manual compression patients, unlike the **Celt ACD®** patients, did not have the sheath removed immediately at the end of the procedure. Analysis of information from patient notes (n=16) showed that the mean time between end of procedure and sheath removal was 2 hrs. 46 min. This was not factored into the statistical analysis of the data collected. In the manual compression group 28.8% had 'immediate' hemostasis and 65.3% achieved hemostasis in less than 10 minutes.

N (%) of patients achieving hemostasis within time interval		0 mins	0.1-5 mins	5.1-10 mins	10.1-15 mins	15.1-30 mins	30.1-60 mins	> 60 mins
	CELT ACD N=148	**89** (60.1)	**53** (35.8)	**4** (2.7)	**0**	**1** (0.7)	**1** (0.7)	**0**
	Manual compression N=52&	**15** (28.8)	**1** (1.9)	**18** (34.6)	**3** (5.8)	**14** (26.9)	**0** (0)	**1** (1.9)

&Seven subjects did not have time to hemostasis recorded in the manual compression group.

Table 8: TTH by post-procedural time interval for interventional ITT patients.

Secondary Effectiveness End-Points

The secondary effectiveness end-points were time-to-ambulation (TTA), time-to- dischargeability (TTD), procedure success and device success.

Time-to-Ambulation (TTA)

Time-to-ambulation was defined as the elapsed time between sheath removal and the time when the patient stands and walks 6m or approximately 20ft without re-bleeding. Patients were recommended to have their ambulatory status evaluated at a range of times, however ambulation was not required if contrary to the clinical judgment of the physician.

The time-to-ambulation (TTA) data for those with data available (n=145, 70%) are shown in Table 9a. Data on actual TTA were not available for 62 patients (30%) and most missing data were from the fourth center (n=58 missing TTA). There were no statistically significant differences in the mean or median TTA between the **Celt ACD®** and manual compression groups.

Time-to-ambulation (TTA in miutes)	CELT ACD (n=101)[&]	Manual compression (n=44)[&]	All patients (n=145)	p- value
Mean (SD)	**360.0** (418.4)	**406.4** (216.2)	**374.0** (368.7)	0.38[#]
95% CI for mean	(274.4,442.5)	(340.7,472.1)	(313.5,434.6)	
Median (mins)	**240**	**360**	**265.0**	0.49[$]
Inter-quartile range (IQR)	(170,360)	(252.5,512)	(180,447)	
Range (min, max)	(74,2644)	(30,895)	(30,2644)	

Continuous data presented in minutes.
Independent t-test with unequal variances assumed.
$ Data were non-normal therefore the Wilcoxon rank sum test is used to test the null hypothesis.
& Data not available on all subjects (only 68% of Celt ACD® and 74.6% of manual compression group had data available for analysis).

Table 9a: Time-to-ambulation (TTA) – Secondary effectiveness end-point.

Table 9b shows TTA categorized by post-procedural time interval. The data show that 73% of the **Celt ACD®** group and 48% of the manual compression group were ambulated within 6 hours.

		< 2 hrs	2-3.9 hrs	4-5.9 hrs	6-7.9 hrs	8-9.9 hrs	10-11.9 hrs	= ≥ 12 hrs
N (%) of patients ambulated within time interval	CELT ACD (n=101)[$]	2 (2.0)	47 (46.5)	25 (24.8)	11 (10.9)	6 (5.9)	1 (1.0)	9 (8.9)
	Manual compression (n=44)[$]	2 4.6)	6 (13.6)	13 29.5)	6 13.6)	8 (18.2)	3 (6.8)	6 (13.6)

$ Data not available on all subjects (only 48% of Celt ACD® and 49% of manual compression group had data available for analysis)

Table 9b: TTA by post-procedural time interval for interventional ITT patients.

Table 9c shows the results regarding whether the subject was fit for ambulation by < 6 hours or ≥ 6 hours, for which there were more complete data (n=197, 95.2%). For the **Celt ACD®** device group the majority of individuals (81%) were fit for ambulation within 6 hours, compared to 70.9% of the manual compression group. This difference was not statistically significant.

		< 6 hours	≥ 6 hours	p-value
N (%) of patients fit for ambulation within time interval	CELT ACD (n=142)[$]	**115** (81.0%)	**27** (19.0%)	P = 0.12[&]
	Manual compression (n=55)[$]	**39** (70.9%)	**16** (29.1%)	

$ Data not available on all subjects (n=6 not recorded for Celt ACD®and n=4 for manual compression (MC)); **differences between actual time and data presented here (n=2 and n=6 in CELT ACD and MC group respectively had actual time ≥ 6 hours, but were considered fit for ambulation within 6 hours; n=1 in MC group not recorded here but had TTA data; n=1 in CELT ACD group had TTA< 6 hours but considered not fit for ambulation).**
& Chi-square test applied (statistic=2.36)

Table 9c: Fit for ambulation by post-procedural time interval of 6 hours.

Time-to-Dischargeability (TTD)

Time-to-Dischargeability (TTD) was defined as the elapsed time between sheath removal and the time when the patient is medically able to be discharged based solely on the assessment of the access site as determined by the patient's physician.

The time-to-dischargeability was available for 100 (48.3%) patients, and the results for both randomized groups are shown in Table 10a. There were no statistically significant differences in the mean or median TTD between the **Celt ACD®** and manual compression groups.

Time-to-dischargeability (TTD in mins)	CELT ACD (n=71)[&]	Manual compression (n=29)[&]	All patients (n=100)	p- value
Mean (SD)	662.51 (511.7)	511.76 (350.2)	618.79 (473.8)	0.15[#]
95% CI for mean	(541.40, 783.61)	(378.55, 644.96)	(524, 712.81)	
Median (mins)	416	330	377	0.47[$]
Inter-quartile range (IQR)	(179,1196)	(240, 796)	(184.5, 1074)	
Range (min, max)	(6, 1402)	(34, 1140)	(6, 1402)	

Continuous data presented in minutes
Independent t-test with equal variances assumed
$ Data were non-normal therefore the Wilcoxon rank sum test is used to test the null hypothesis
& Data not available on all subjects (only 48% of Celt ACD® and 49% of manual compression group had data available for analysis)

Table 10a. Secondary effectiveness end-point – time-to-dis chargeability (TTD).

Table 10b shows TTD categorized by post-procedural time interval. For the **Celt ACD®** group approximately 52% of subjects (n=37) were eligible for discharge within 12 hours. For the manual compression group 69% (n=20) were eligible for discharge within 12 hours.

N (%) of patients eligible for discharge within time interval	Interval (hrs)	< 2 hrs	2-3.9 hrs	4-5.9 hrs	6-7.9 hrs	8-9.9 hrs	10-11.9 hrs	= ≥ 12 hrs
	Celt ACD (n=71)[$]	**4** (5.6)	**27** (38.0)	**4** (5.6)	**1** (1.4)	**1** (1.4)	**0**	**34** (47.9)
	Manual compression (n=29)[$]	**3** (10.3)	**4** (13.8)	**8** (27.6)	**0**	**2** (6.9)	**3** (10.3)	**9** (31.0)

$ Data not available on all subjects (only 48% of Celt ACD® and 49% of manual compression group had data available for analysis)

Table 10b: TTD by post-procedural time interval for interventional ITT patients.

Procedure and Device Success

Procedure Success (PS) was defined as the attainment of hemostasis using any method with no major complications during the follow-up period. Device Success (DS) was defined as the successful deployment of the **Celt ACD®** device with the attainment of hemostasis. The procedure and device success rates for the **Celt ACD®** group and the manual compression group are shown in Table 11.

The rate of procedure success was similar in both groups at 99.3% (147/148) in the **Celt ACD®** group and 98.1% (51/52) in the manual compression group. The difference in procedure success rate between the two groups was not statistically significant.

The device success was 99.3% (147/148) due to one **Celt ACD®** device implant deploying correctly but not being properly positioned in the femoral artery puncture site, resulting in the embolization of the device. This was the sole major complication in the **Celt ACD®** group in the trial.

	Celt ACD n=148)	Manual compression (n= 52)&	All patients (n=200)	Difference (95% CI)	p-value
Procedure Success	**147** (99.32%)	**51** (98.08%)	**198** (99%)	**1.24%** (-2.71%, 5.21%)[$]	0.45[$]
Device Success	**147** (99.32%)	N/A			

& Seven subjects did not have time to hemostasis recorded in the manual compression group.
$ Wald asymptotic confidence intervals and Fishers exact test applied.

Table 11: Secondary effectiveness end-points – procedure and device success.

Conclusions

The results from the **Celt ACD®** Pivotal Clinical Trial demonstrated that patients who underwent interventional cardiac or peripheral vascular intra-arterial procedures using a 6F introducer sheath and were treated with the **Celt ACD®** VCD had statistically and clinically significant decreased times-to-hemostasis when compared to patients treated with manual compression. In addition, the study demonstrated that the major and minor access site-related complication rates for patients treated with the **Celt ACD®** VCD were non-inferior to the major and minor access site-related complication rates for patients treated with manual compression. The study data support use of the **Celt ACD®** VCD in both interventional patients and diagnostic patients because interventional patients typically have longer times-to-hemostasis than do diagnostic patients due to the antiplatelet and anticoagulant medications that interventional patients receive before and during the catheterization procedures, and because interventional patients serve as a worst-case scenario for potential VCD-related complications. The study provides scientifically valid evidence that the **Celt ACD®** VCD is safe and effective when used in accordance with the device labelling.

Celt ACD® Pivotal Clinical Trial Results-Celt ACD 7F

(Note Table Numbering is specific to this section)

Following the 207-patient 6F **Celt ACD®** VCD study and in accordance with an agreement with the US FDA, an additional 34 interventional device patients were recruited. These patients were recruited across 3 clinical investigation sites in Europe. In these patients, who were fully anticoagulated, a 7F **Celt ACD®** device was deployed to close an arterial puncture made with a 7F sheath. The control group for the 7F **Celt ACD®** VCD study consisted of the manual compression control patients from the 6F **Celt ACD®** VCD study.

The **Celt ACD®** 7F clinical investigation plan was reviewed and approved by the Ethics Committee at each participating clinical investigation site. All patients granted their consent prior to participating in the study.

All patients participating in the trial were fully anti-coagulated and following the interventional vascular procedure a femoral angiogram was performed to identify the site of the 7F sheath puncture and also to estimate the width of the femoral artery at the puncture entry point. If possible, the activated clotting time (ACT) was measured when part of normal catheterization laboratory procedure. At that point, if all the criteria for entry into the trial were satisfied, the patient had their arterial puncture closed using a **Celt ACD®** 7F device.

Results

All patients in the study met the general inclusion criteria and general exclusion criteria. The baseline characteristics of age, gender, heights, weight and BMI are shown below in Table 12. The mean age of all patients was 67 years, the mean height was 172 cms and the weight was 81Kgs. The number of male patients enrolled in the trial was 25 versus 9 female patients which is a reflection of the general referral pattern for patients undergoing percutaneous vascular interventional procedures at the investigation sites. Also measured were the baseline systolic and diastolic blood pressure and the prevalence of hypertension and diabetes in the 34 patient group. The site of femoral access on the right side was 33 and on the left side was 1. The activated clotting time (ACT) data was recorded in 23 patients.

Baseline Characteristics	CELT ACD (7F) N=34
Age in years (mean, 95% CI) (SD, Range)	**67** (63.99, 70.01) SD=8.62 (47, 80)
Height in cm (mean, 95% CI) (SD, Range)	**172.44** (168.83, 176.05) SD=10.35 (150, 193)
Weight in kg (mean, 95% CI) (SD, Range)	**81.13** (76.17, 86.09) 14.20 (55.8,107)
BMI (kg/m2) (mean, 95% CI) (SD, Range)	**27.09** (26.15, 28.02) SD=2.68 (21.30, 33.09)
Male (%) **Female** (%)	**25** (73.5%) **9** (26.5%)
Femoral artery site Right N (%) Left N (%)	**33** (97.1%) **1** (2.9%)
Type anticoagulant: Unfractionated heparin	**34** (100%)
Systolic blood pressure (pre; n=22) (mean, 95% CI) (SD, Range)	**135.55** (125.12, 145.97) SD=24.95 (100, 204)
Diastolic blood pressure (pre; n=22) (mean, 95% CI) (SD, Range)	**79.68** (75.10, 84.27) SD=10.97 (60, 110)
Activated clotting time (N=23) (ACT) in secs (mean, 95% CI) (SD, Range)	**311.57** (212.1, 411.0) SD=229.97 (157, 1000)

Table 12 – Baseline Characteristics (Source Table 1, File002/IDE Final Report)

Effectiveness Endpoints:

Time to Hemostasis (TTH)

Table 13 below presents the results for TTH in minutes. The data were significantly skewed (non-normal), therefore, medians and inter-quartile range (25th to 75th percentile) are also presented with means and 95% confidence intervals. The median TTH was 0.33 minutes.

Time to Hemostasis (mins)	All patients (n=34)
Mean (mins)	1.44
95% CI for mean TTH	(0.39, 2.49)
Median (mins)	0.33
Inter-quartile range (IQR)	(0, 1)
Range (min, max)	(0, 15)

Table 13: Primary effectiveness endpoint–TTH (Source Table 2, File002/IDE Final Report)

Table 14 below presents the TTH categorized by intervals of duration. For the **Celt ACD®** 7F the majority (94.1%) of subjects achieved TTH within 5 minutes.

N (%) of patients within time interval		0 mins	0.1-5 mins	5.1-10 mins	10.1-15 mins
	CELT ACD 7F N=34	13 (38.2%)	19 (55.9%)	1 (2.9%)	1 (2.9%)

Table 14: TTH by post-procedural time interval for achieving hemostasis (Source Table 3, File002/IDE Final Report)

Time to Dischargeability (TTD) & Time to Ambulation (TTA).

Table 15 below shows data on TTD were available on only n=19 (56%) and were non-normal. The median time was just under 24 hours.

N (%) of patients within time interval of dischargeability	Interval (hrs)	<2 hrs	2-4 hrs	4-6 hrs	6-8 hrs	8-10 hrs	10-11.9 hrs	>= 12hrs
	Celt ACD (7F) (n=19)$	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	19 (100)

$ data not available on all subjects

Table 15: TTD by post-procedural time interval for 7F patients. (Source Table 5 File 002).

Table 16 and Table 17 below shows the TTA analysis for patients in the 7F Study. Mean TTA was 345.5 minutes.

Time-to-ambulation (TTA in minutes)	CELT ACD (7F) (n=25)&
Mean (SD)	345.5 (136.2)
95% CI for mean	(289.3,401.7)
Median (mins)	347
Inter-quartile range (IQR)	(240,436)
Range (min, max)	(34,540)

Table 16: Time to ambulation (TTA) by post-procedural time interval for interventional ITT patients (Source Table 6 File 002)

N (%) of patients ambulated within time interval		<2 hrs	2-3.9 hrs	4-5.9 hrs	6-7.9 hrs	8-9.9 hrs	10-11.9 hrs	>=12 hrs
	CELT ACD (7F) (n=25)$	2 (8.0)	2 (8.0)	9 (36.0)	7 (28.0)	5 (20.0)	0 (0)	0 (0)

$ Data not available on all subjects

Table 17: TTA by post-procedural time interval for CELT ACD® (7F). (Source Table 7 File 002)

Device Success

The device success in the 7F study was 94.1% (32/34) due to 2 **Celt ACD®** device implants not being properly positioned by the user in the femoral artery puncture site, resulting in embolization of the implants.

Major Complications

The 4 major complications reported in the study are reported below in Table 18.

	MAJOR COMPLICATIONS	CELT ACD (7F) (N=34)	Excluding 'definitely not' device related
1	Vascular repair or the need for vascular repair (via surgery, ultrasound -guided compression, transcatheter embolization, or stent-graft.	0	0
2	Retroperitoneal bleeding.	0	0
3	Access-site-related infection requiring intravenous antibiotics and/or extended hospitalisation.	0	0
4	Permanent access site-related nerve injury.	0	0
5	Surgery for access site-related nerve injury.	0	0
6	Access site related bleeding requiring transfusion.	0	0
7	Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram.	0	0
8	Any complication requiring surgery, vascular repair, or transfusion is a major complication and not a minor complication.	0	0
9	**OTHER**		
	ST elevation after procedure	1	0
	Death after Myocardial infarction	1	0
	Brain Stem Ischemia.	0	0
	Device Migration from the FA access point.	2	2
TOTAL - MAJOR COMPLICATIONS, N (%)		4 (11.76%)	2 (5.88%)
DIFFERENCE IN MAJOR COMPLICATION RATE WITH MANUAL COMPRESSION (from 6F Trial) (95% CI)		8.37% (-3.4%, 20.45%)$	2.49% (-6.67%, 11.65%)$
p-value		0.79#	0.38&

$ Farrington-Manning 95% confidence limits;
# Farrington-Manning method (test for margin of 4%, z=0.80);
& Farrington-Manning method (test for margin of 4%, z=0.31)

Table 18: Major complications as reported by the Clinical investigation sites. Source Table 8 File 002)

Of these 4 major complications, 2 were as a result of cardiac problems and were therefore not device-related. The remaining 2 major complications were embolizations of the **Celt ACD®** implant in the right leg and were a result of intra-arterial deployment of the **Celt ACD®** as a result of incorrect technique used during device deployment. In both cases the implant was retrieved radiologically and implanted in the right femoral artery wall.

Minor Complications

	Minor Complications	CELT ACD (7F) (N=34)	Excluding 'definitely not' device related	Excluding 'tract oozing'
1	Access site haematoma ≥ 6 cm.	0	0	0
2	Ecchymosis > 5 mm.	1	1	1
3	Locally induced vasovagal episode requiring therapy.	0	0	0
4	Pseudoaneurysm, documented by ultrasound that does not require intervention.	0	0	0
5	Arteriovenous (AV) fistula documented by ultrasound that does not require intervention.	0	0	0
6	Access site-related bleeding requiring > 30 minutes to re-achieve hemostasis.	3	3	0
7	Late access site-related bleeding (i.e. following hospital discharge). (Note – Incorrectly categorised bleeding in recovery phase)	3	2	0
8	Transient loss of ipsilateral lower extremity pulse.	0	0	0
9	Ipsilateral deep vein thrombosis.	0	0	0
10	Transient access site-related nerve injury.	0	0	0
11	Access site-related vessel laceration (not requiring surgical repair or intervention).	0	0	0
12	Access site wound dehiscence.	0	0	0
13	Localised access site infection treated with intramuscular or oral antibiotics.	0	0	
14	Pseudoaneurysm treated with ultrasound-guided thrombin injections or ultrasound-guided fibrin adhesive injection.	0	0	0
15	Ipsilateral lower extremity arterial emboli.	0	0	0
16	**OTHER**			
TOTALS-MINOR COMPLICATIONS (N, %)		**7 (20.6%)**	**6 (17.6%)**	**1 (2.94%)**
DIFFERENCE IN MINOR COMPLICATION RATE WITH MANUAL COMPRESSION (from 6F trial) (95% CI)		**12.11% (-3.22%, 27.45%)$**	**9.17% (-5.48%, 23.8%)$**	**-5.53% (-14.63%, 3.59%)$**
p-value		**0.87#**	**0.77&**	**0.06^**

$ Farrington-Manning 95% confidence limits;
# Farrington-Manning method (test for margin of 4%, z=1.1);
& Farrington-Manning method (test for margin of 4%, z=0.73);
^ Farrington-Manning method (test for margin of 4%, z=1.59)

Table 19: Minor complications as reported by the clinical investigation sites. (Source Table 9 File 002)

Unanticipated Adverse Events
There were no unanticipated adverse events reported during period of this 7F study.

Patient Discontinuation
There were no patient discontinuations in this 7F study.

Patient Complaints
There were no reported patient complaints during the study at any of the sites.

Device Failures and Replacements
There were no device failures or replacements during the trial.

Comparison to the 6F study
The mean TTH for the 7F device of 1.44 mins was found to be similar to that of the **Celt ACD®** in the pivotal study, 0.99 mins, and both mean TTHs from the 7F and pivotal study were significantly shorter than the TTH in the manual compression group at 17.54 mins. The mean TTAs were also similar between the 7F device and the **Celt ACD®** from the pivotal trial, which were 345.5 min (5.8 hrs) and 360.0 min (6.0 hrs), respectively. The time to Dischargeability (TTD) was longer for the 7F device compared to the pivotal study, with 53% discharged within 24 hours for the 7F device and a similar percentage within 12 hours for the **Celt ACD®** in the pivotal trial. Major complications were higher for the 7F device (5.88%, excluding definitely not device related) than either the **Celt ACD®** (0.68%) or manual compression (3.39%) groups from the pivotal study. Minor complications, which are the secondary safety endpoint, were higher with the 7F device (17.6%, excluding definitely not device related, decreased to 2.94% when clinical ooze patients excluded) than either the **Celt ACD®** (4.73%) or manual compression group (8.47%) from the pivotal study.

Conclusion for 7F study:
The results of the supplemental 7F **Celt ACD®** VCD clinical study support the safety and effectiveness of the 7F **Celt ACD®** VCD when used in accordance with the device labelling.

SECTION K – CLOSURE

PROCEDURE CAUTION:

a. Each stage of the deployment has been designed to proceed in a smooth and orderly manner. If resistance is felt at any stage, this means that the previous step of the deployment has not been fully completed.

b. In the event that post-deployment excessive bleeding occurs with the removal of the **Celt ACD® PLUS** Vascular Closure Device, apply either manual or mechanical pressure as would normally be used when an arterial puncture closure device is not in use. In addition, take an x-ray to confirm the implant is visible in the femoral artery. If the implant is not visible, embolization should be suspected and a clinical decision regarding further clinical management should be made.

Indicator Arrows:
Numbered indicator arrows are printed onto the body of the handle to ensure that the device is deployed correctly (Fig. 2).

Arrow 1 is printed onto the handle indicating that it is the first step in the deployment sequence. The handle should be rotated in a clockwise direction (indicated by the arrow direction) to deploy the distal wings (Step 3).

Arrow 2 is also printed onto the handle indicating that the handle should be turned in a counter-clockwise direction to deploy the proximal wings (Step 5).

Arrow 3 is printed onto both sides of the ejector lever indicating the direction in which the lever should be pressed to eject the implant (Step 7). Additional information such as the French size and the trade name for the device, **Celt ACD® PLUS** are also printed onto the device.

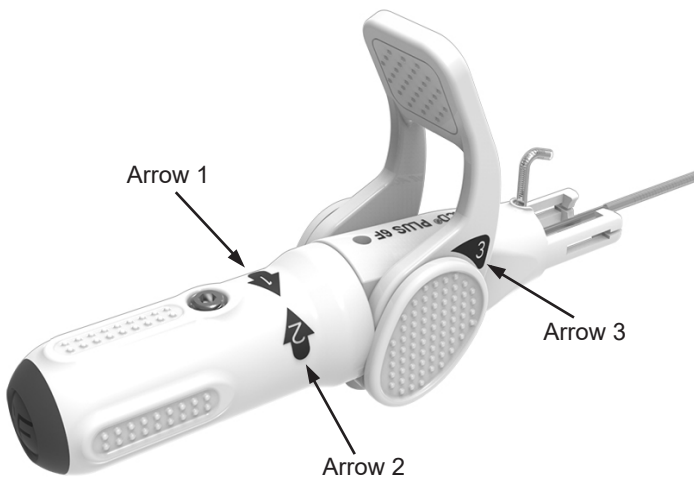
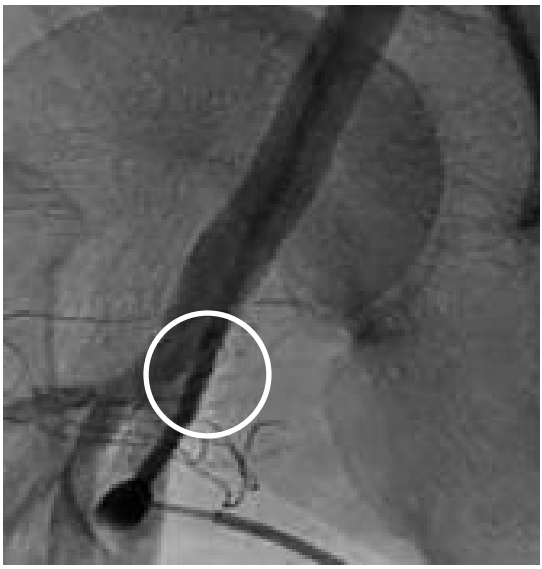


Fig. 2

Step 1:

a. Refer to the pre-procedure fluoroscopic image A below to confirm the site of puncture by the sheath into the artery.



Fluoroscopic Image: A

b. Under strict sterile conditions and using an aseptic technique, remove the **Celt ACD® PLUS** Vascular Closure Device from its packaging.

c. Insert the tip of the **Celt ACD® PLUS** Vascular Closure Device through the valve in the introducer sheath and advance the flexible guide tube into the lumen of the sheath (Fig. 3).

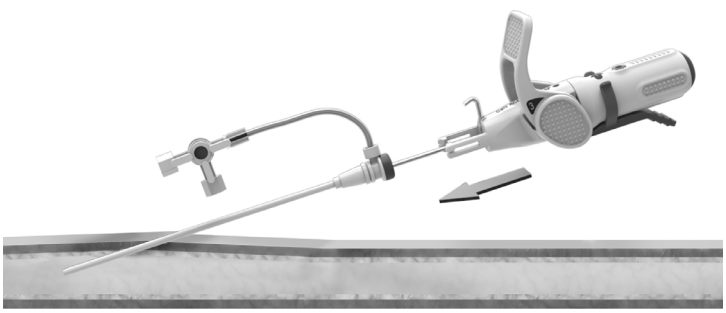


Fig. 3

Step 2:

a. Continue to advance the **Celt ACD® PLUS** Vascular Closure Device through the introducer sheath and into the femoral artery until the latches extending from the front of the handle are touching the valve of the sheath. The blood signal will now become visible from the Blood Outlet (Fig. 4).

b. The blood signal and Fluoroscopic co-control may be used to confirm the position of the device within the arterial lumen (Fig. 4).

c. Holding the device in a fixed position, pull the valve of the introducer sheath toward the handle of the delivery system and into the latches extending from its front end. Ensure that the valve of the introducer sheath is securely attached to the device.

IMPORTANT:
Do not continue to deploy the implant unless the Celt ACD® PLUS Vascular Closure Device is properly engaged with the introducer sheath and the blood signal is visible.

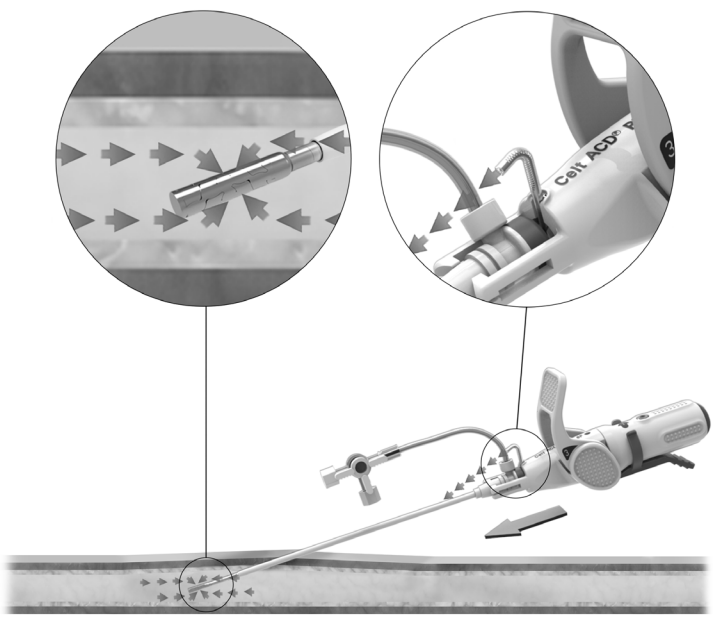
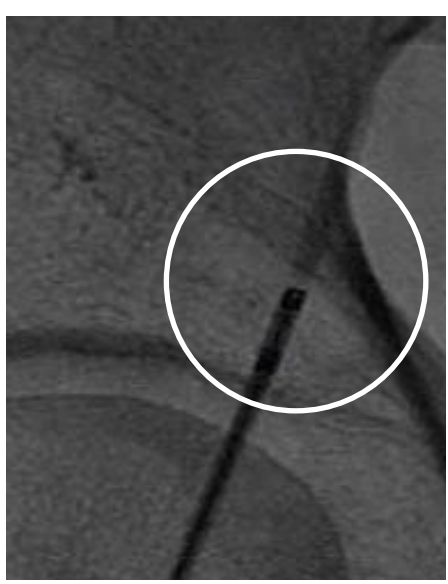


Fig. 4



Fluoroscopic Image: B

Step 3:

a. Holding the device and the introducer sheath, withdraw both from the patient until the distal tip of the sheath is close to the puncture hole but remains within the arterial lumen. The blood signal should still be visible. Fluoroscopic control may be used for guidance.

b. Prior to operating the device, remove the red locking tab by pressing down on the locking tab lever (Fig. 5).

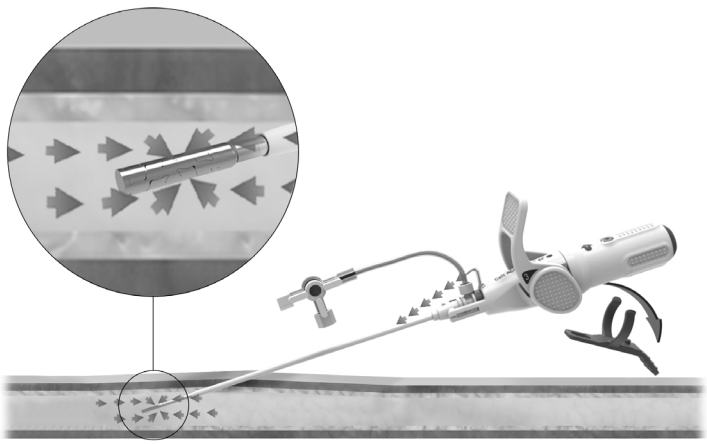


Fig. 5

c. Holding the **Celt ACD® PLUS** Vascular Closure Device with one hand, grip the end of the handle with the other hand and turn it **GENTLY** in a **clockwise direction**, as indicated by **Arrow 1**, until it pops back to a stop position (Fig. 6). The opening of the distal wings of the implant may be observed under fluoroscopy.

The blood signal will still be visible from the Blood Outlet after the deployment of the distal wings (Fig. 6).

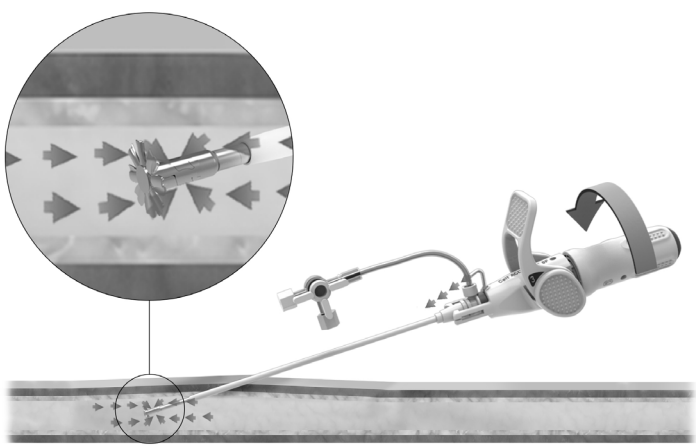
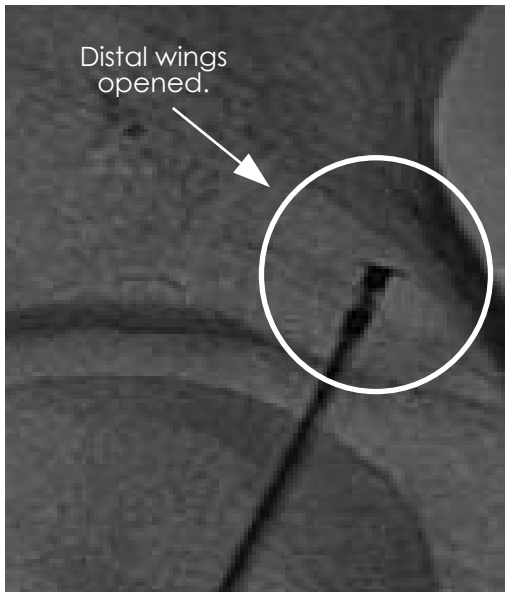


Fig. 6



Fluoroscopic Image: C

IMPORTANT:
Check to ensure that the handle has moved back leaving a gap, as illustrated below (Fig. 7), before proceeding to the next step.

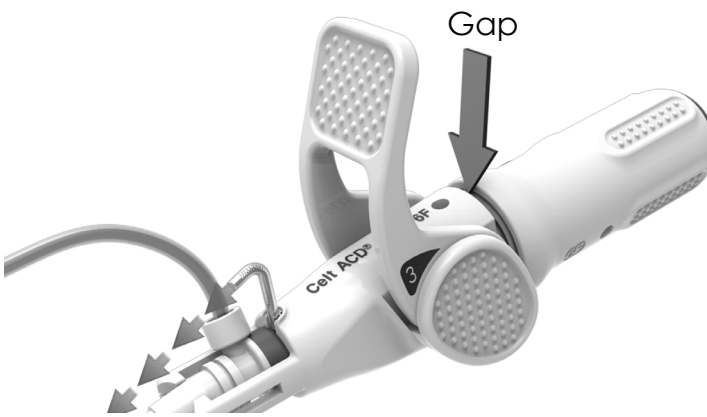


Fig. 7

Step 4:

a. Holding the **Celt ACD® PLUS** Vascular Closure Device with one hand and the valve of the introducer sheath with the other hand, withdraw both the device and the sheath from the patient until resistance is felt (Fig. 8).

b. The blood signal should **NOT** be visible, therefore confirming that the Distal Wings are correctly located against the interior arterial wall.

c. If a fluoroscopic image is taken and compared with a pre-deployment fluoroscopic image, the position of the distal wings at the puncture wall should correlate the puncture sheath entry site as seen on the pre-deployment fluoroscopic image.

IMPORTANT:
Ensure that the introducer sheath remains attached to the handle during withdrawal (Fig. 8).

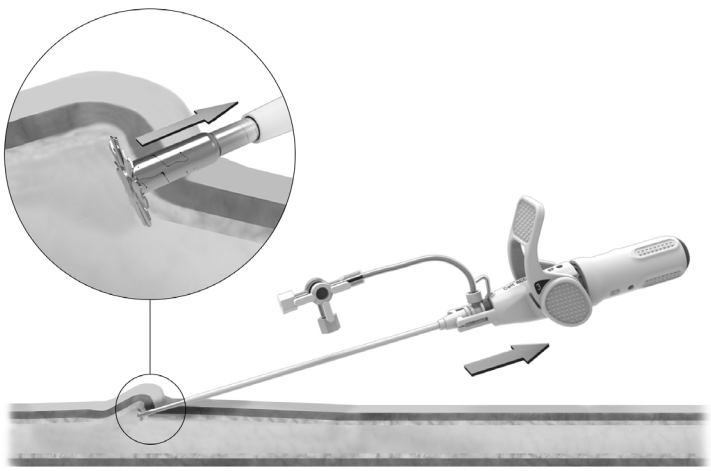
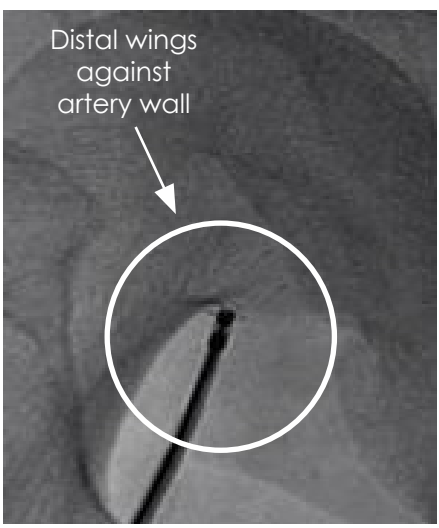


Fig. 8



Fluoroscopic Image: D

Step 5:

a. To deploy the proximal wings, firstly check to ensure that the valve of the sheath remains attached to the device and that the blood signal has stopped. **Hold the device as close to vertical as possible (Fig. 9)**.

b. **While maintaining upward tension** on the device and the vertical orientation, turn the handle **GENTLY** in a **counter -clockwise** direction, as indicated by **Arrow 2**, until it pops back to the second stop position (Fig. 9) and the proximal wings open.

c. Fluoroscopic control may be used to observe the proximal wings opening on the external surface of the artery to form a "sandwich" with the arterial puncture edges between the wings.

IMPORTANT:
Check to ensure that the handle has moved back leaving an increased gap (as shown below in Fig. 9) before proceeding to the next step.

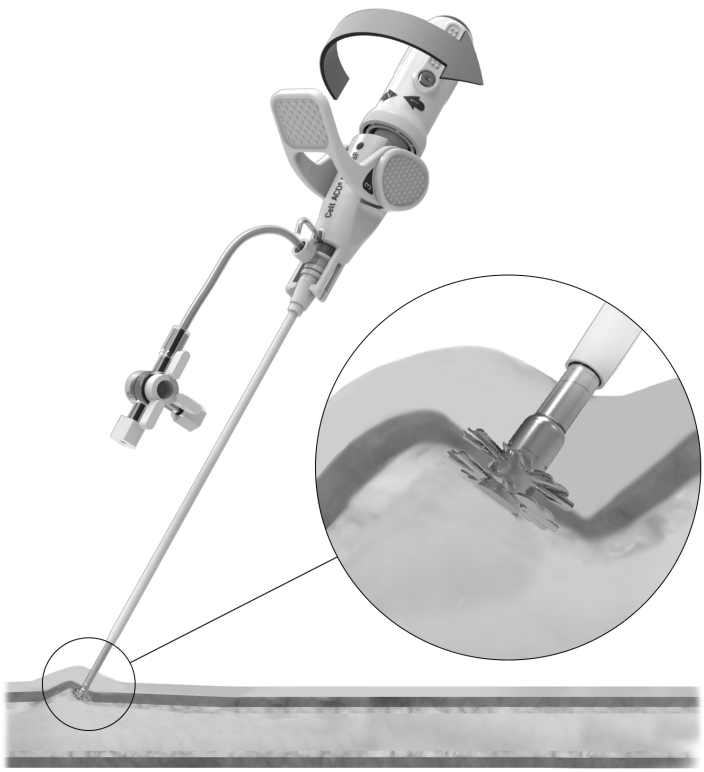
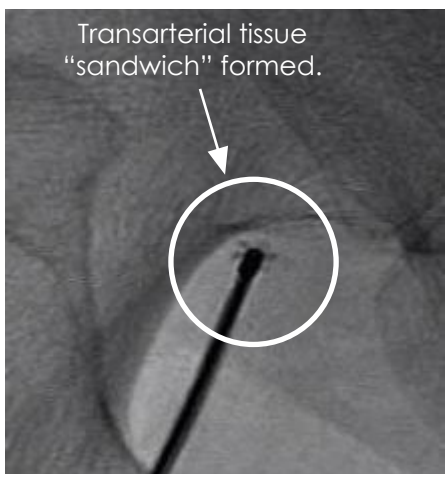


Fig. 9



Fluoroscopic Image: E

Step 6:

a. Carry out a sandwich "Push-Pull" test by gently pushing the device backward and forward (Fig. 10). If deployment is correct, it will not be possible to advance the deployed implant into the artery. The blood signal should **NOT** be visible.

b. If a fluoroscopic image is taken, the implant will be observed to remain in a fixed position.

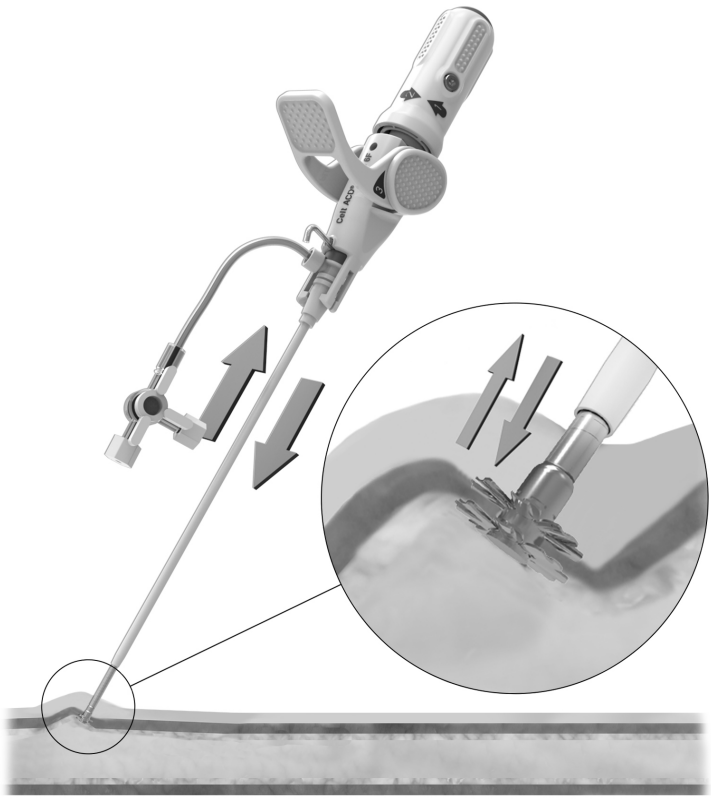
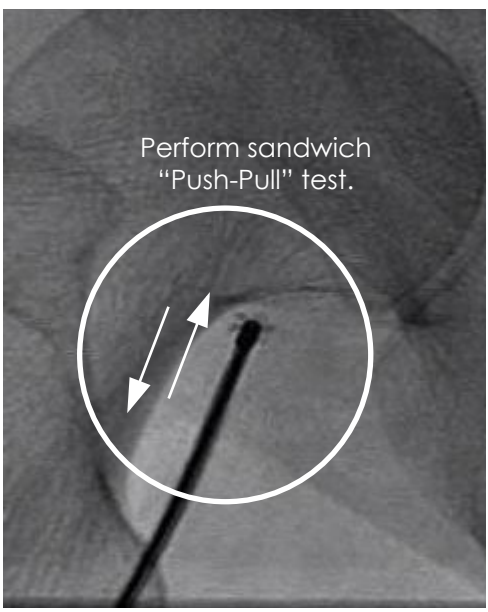


Fig. 10



Fluoroscopic Image: F

Step 7:

a. It is now safe to eject the implant from the delivery system by pressing down on the ejector lever, as indicated by **Arrow 3**, until it abuts the handle (Fig.11).

b. If a fluoroscopic image is taken, the separation of the delivery device from the implant may be observed.

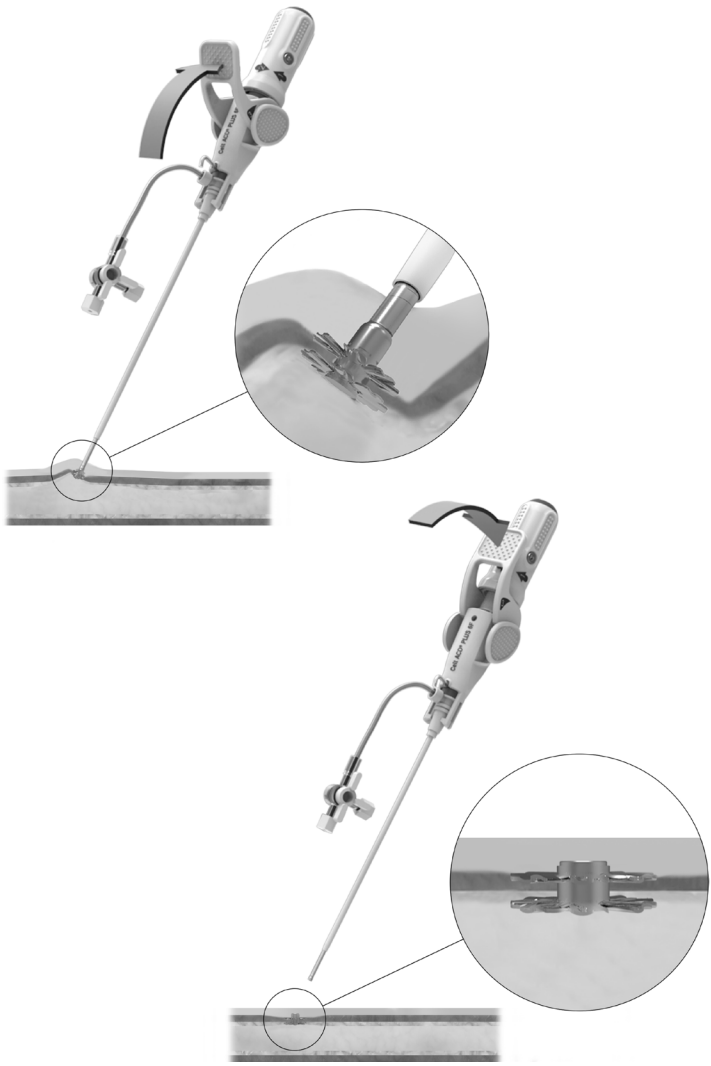
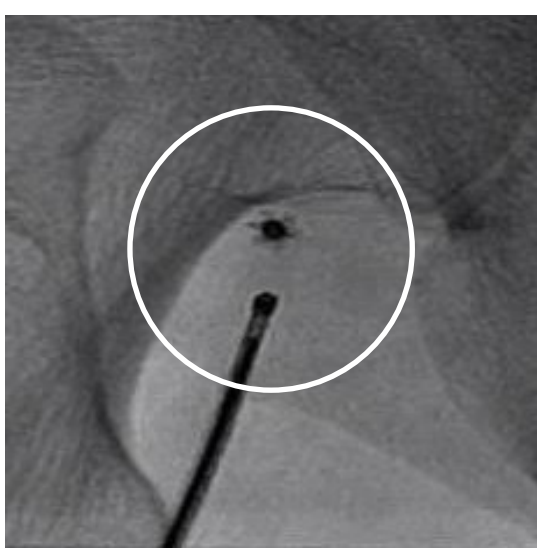


Fig. 11



Fluoroscopic Image: G

Step 8:

a. Remove the device and introducer sheath from the patient and dispose of both appropriately (Fig.12).

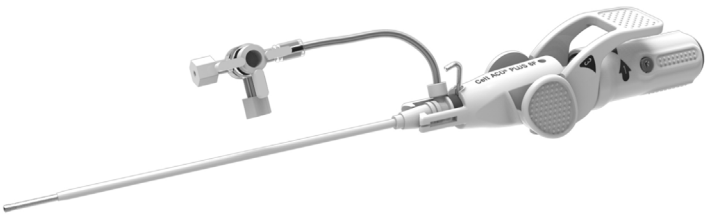


Fig. 12

b. If required a final fluoroscopic picture will show the implant stabilised in the arterial wall.

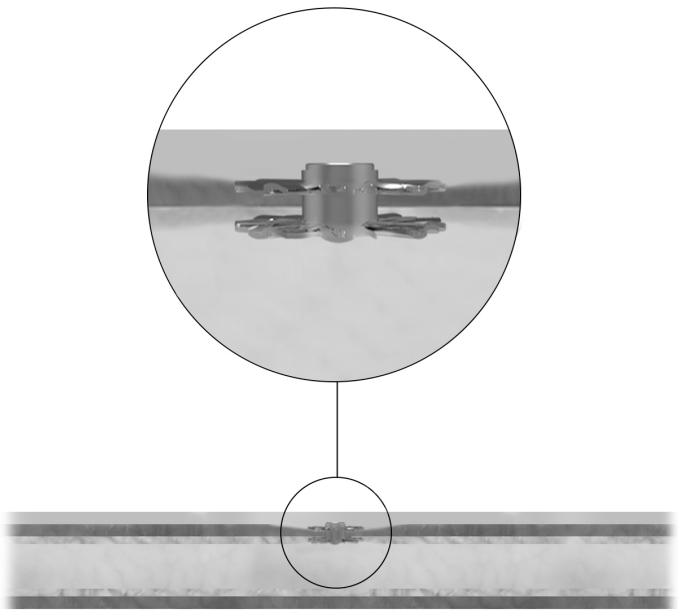
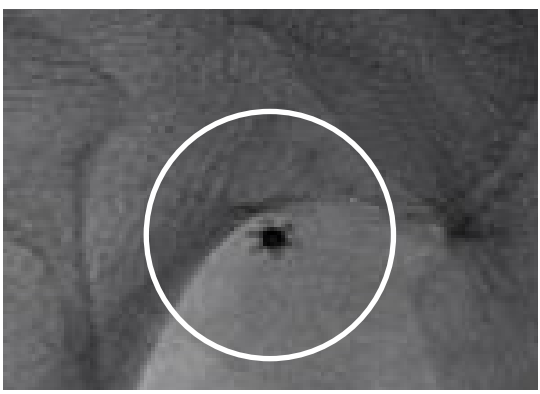


Fig. 13



Fluoroscopic Image: H

POST PROCEDURE PATIENT MANAGEMENT:

- Apply an appropriate dressing to the puncture site.
- Assess the insertion site as per hospital protocol.

RECOMMENDATION FOR PATIENT AMBULATION AND DISCHARGE

In determining whether to ambulate or discharge an individual patient, it is important to consider all clinical factors including but not limited to anticoagulation regimen, antiplatelet and thrombolytic agents administered, oozing or bleeding from the access site, venous access site hemostasis and the overall clinical condition of the patient.

Section L – Symbols for Medical Device Labelling

"Read the documentation"

"Method of sterilization, E-Beam irradiation"

"Do not resterilize"

"Do not reuse"

"Keep dry"

"Keep out of direct sunlight"

"Lot number/Batch code"

"Do not use product if packaging or sterile barrier has been previously opened or damaged"

"Use by"

"Manufacturer"

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

"Non Pyrogenic"

"Caution, refer to accompanying documents"

"Medical Device"

"Reference"

"Contents"

"Single Sterile Barrier System"

Section M – MRI Safety Information

MR Conditional

Non-clinical testing demonstrated that the **Celt ACD®** Vascular Closure Device is MR Conditional. A patient with this device can be scanned safely in an MR system immediately after placement under the following conditions:

- Static magnetic field of 3-Tesla or less.
- Maximum spatial gradient magnetic field of 1,500-gauss/cm (15-T/m) (extrapolated) or less.
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg for 15 minutes of scanning (i.e. per pulse sequence) in the First Level Controlled Operating Mode of operation for the MR system.

Under the scan conditions defined for the **Celt ACD®** it is expected to produce a maximum temperature rise of 2.1˚C after 15 minutes of continuous scanning (i.e., per pulse sequence).

In non-clinical testing, the image artifact caused by the **Celt ACD®** extends approximately 10 mm from this device when imaged using a gradient echo pulse sequence and a 3-Tesla MR system.

HOW SUPPLIED:

The **Celt ACD® PLUS** Vascular Closure Device is supplied sterile and non-pyrogenic in unopened undamaged packaging. Products are sterilized by ebeam irradiation and intended for single use only. Do not resterilize. The device and the primary packaging do not contain latex. Store in a cool, dry place.

USA