Pi-Cardia
Next-Generation Valve Repair

ShortCut™

INSTRUCTIONS FOR USE

USA

PROPRIETARY AND CONFIDENTIAL

Manufactured by:
Pi-Cardia Ltd.
5 David Fikes Street
Rehovot 7632805
Israel
Tel: +972-8-9484800
Fax: +972-8-9484801
info@pi-cardia.net

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1 IMPORTANT INFORMATION FOR THE USER

1.1 Device Description

The ShortCut™ (ShortCut) is a transfemoral catheter designed to split the bioprosthetic aortic valve leaflets prior to Transfemoral Aortic Valve Replacement (TAVR), to reduce the risk of coronary ostium obstruction and coronary access compromise and enable a valve-in-valve procedure for patients at risk of coronary obstruction.

The ShortCut is a sterile, single use, 16Fr device which is inserted through the femoral artery over a guide wire into the left ventricle. The ShortCut is comprised of the following parts:

a. **Distal Unit (DU)** - Distal end of the catheter which contacts the valve leaflets and splits them. It is comprised of the Splitting Element (SE) and the Positioning Arm (PA) (Figure 1). The DU is delivered in a sheathed 16Fr configuration that opens up to a size adequate with the aortic valve.

b. **Delivery System (DS)** – the catheter shafts connect the Handle and the DU, and delivers the required movements from the Handle to the DU. The DS is compatible with a 16Fr introducer sheath and delivered over a 0.035" Guide Wire (GW).
The outer shaft of the DS (Sheathing Tube) is used to sheathe the DU during introduction and removal from the body. The inner shafts of the DS, together with its pig-tailed tip, enable flexing and positioning of the DU on the valve.

c. **Handle** - The user interface, designed to control the DS and the DU and to enable correct positioning of the DU on the valve (Figure 2).

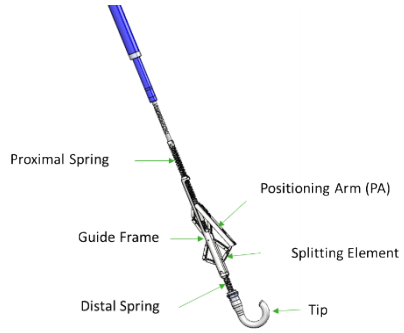

Figure 1: ShortCut Distal Unit

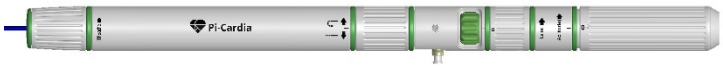

Figure 2: ShortCut Handle

The ShortCut is sterilized using Ethylene Oxide and is packaged in a blister inserted into a Tyvek™ pouch and stored in a labeled cardboard box.

1.2 ShortCut specifications

Diameter	16Fr (Sheathed)
Working length	1150 ± 15mm
Tip type	Pig-tailed

1.3 Mechanism of Action

Splitting of the leaflet is generated by using the Splitting Element (SE), which penetrates the leaflet from the ventricular side at the bottom of the leaflet. The Positioning Arm (PA), positioned on the aortic aspect of the leaflet, protects the surrounding tissue from injury and acts as a holder for the activated SE. Retracting the DU generates the splitting of the leaflet. The splitting action creates a triangular space within the leaflets, that allows blood flow to the coronary arteries.
Each ShortCut splitting sequence, including the SE activation, is designed to split one leaflet, either the left or the right coronary cusp. If required, the second leaflet may be split using the same ShortCut device after repositioning.

1.4 Indications for Use

ShortCut is indicated for use as a splitting device of bioprosthetic aortic valve leaflets to facilitate valve-in-valve procedures for patients at risk for coronary obstruction.
The ShortCut is designated as a prescription (Rx) device.

1.5 Intended Users

The ShortCut is intended for use by qualified interventional cardiologists or cardiac surgeons, who have completed all training required by Pi-Cardia.

1.6 Contraindications

Patients will not be eligible for the procedure if any of the following conditions apply:

1. Known hypersensitivity or contraindication to all intra-procedural anticoagulation and antiplatelet medication, or any product material.
2. Known allergy to contrast media that cannot be adequately controlled with premedication.
3. Active endocarditis on the aortic valve.
4. Thrombosis on the aortic valve.

1.7 Potential Adverse Events

Potential complications that can occur with the use of this device include but are not limited to:

1. Allergic reaction 2. Aortic regurgitation 3. Arrhythmia 4. Cardiovascular injury including perforation or dissection of vessels, aorta, ventricles, myocardium or valvular structures that may require intervention 5. Conduction system disturbance or injury which may require a permanent pacemaker 6. Congestive heart failure, cardiogenic shock 7. Coronary ostium obstruction 8. Death 9. Embolization including air, calcific valve material or thrombus	10. Femoral AV fistula or pseudoaneurysm 11. Fever 12. Hematoma Hemorrhage requiring transfusion or intervention 13. Infection including septicemia and endocarditis, pneumonia 14. Limb ischemia 15. Myocardial infarction 16. Pain or bleeding at the access site 17. Pericardial tamponade 18. Prolonged ventilation 19. Renal insufficiency 20. Stroke or transient ischemic attack 21. Vascular injury

1.8 Document Conventions and Graphical Symbols

This IFU uses the following symbols to indicate Warnings and Notes to the user so as to avoid misuse, use error and incorrect use of the system.

WARNING

Warnings indicate precautions and instructions which if not followed may result in personal injury or even death.

NOTE

Notes provide information to aid in obtaining optimal procedural or device performance.

2 GENERAL SAFETY WARNINGS

The ShortCut should only be used in patients once the physician has carefully read and fully understood the IFU. If the user has any questions or queries regarding the ShortCut use, they should contact Pi-Cardia (shortcut_info@pi-cardia.net).

1. Use of controls or adjustments, or performance of procedures other than those specified herein may be hazardous and might lead to patient injury. Therefore, personnel operating or maintaining the ShortCut should read this manual and become thoroughly familiar with all its safety requirements and operating procedures, BEFORE attempting to use or operate the ShortCut.
2. The ShortCut is intended for use by qualified interventional cardiologists or cardiac surgeons, who have completed all training required by Pi-Cardia.
3. The ShortCut was designed for single use only. Do not re-use or re-sterilize this product.

3 WARNINGS AND PRECAUTIONS

3.1 Warnings

1. ShortCut is intended for use in patients undergoing a valve-in-valve procedure. It should not be used unless the patient is undergoing a concomitant TAVR procedure.
2. ShortCut has not been investigated in a patient population that is not in a high risk of coronary ostia obstruction.
3. ShortCut has not been investigated for splitting native aortic valve leaflets.

3.2 Precautions

1. Avoid using the ShortCut if the leaflet planned to be intervened is torn.
2. Avoid using the ShortCut if patient has iliofemoral vessel characteristics that preclude safe insertion of the introducer sheath.
3. Avoid using the ShortCut in patients where the ascending aorta length is less than 60mm.
4. Avoid using the ShortCut in anatomies where the coronary ostia eccentricity is greater than 45° from cusp center.
5. Do not perform the procedure in a situation where visualization of the ShortCut or of the anatomy is compromised.
6. Avoid using the ShortCut in case of excessive target aortic leaflet calcification (no basal calcium-free window or potentially obstructive calcific masses) on baseline CT.

7. During all procedure steps in which the DU is located across the aortic valve, it is important to pay close attention to the valve hemodynamics.

4 DIRECTIONS FOR USE

4.1 Required Equipment

- Fluoroscopy appropriate for use in percutaneous interventions. If fluoroscopy does not provide adequate imaging for the purpose of proper PA positioning on the leaflet, use of transesophageal or transthoracic echocardiography should be considered.
- Guiding catheters
- Diagnostic Pigtail catheter (optional AL-1 catheter)
- Standard cardiac catheterization lab equipment, including:
  - Sterile rinsing bowls
  - Bag of Saline solution
  - Bag of Heparinized Saline solution
  - Pressure infusion bag with stand
  - Luer-lock syringes: 20 cc or larger
  - Standard 3-way stopcocks
  - Pre-shaped extra-stiff 0.035” guidewire, 275cm of length at the minimum
  - Introducer sheath 16 Fr, 30 cm
    In case additional procedure is planned during the same intervention, a larger introducer sheath diameter may be used.
  - Any standard cardiac catheterization laboratory equipment for facilitating the procedure, as determined by the physician.

4.2 ShortCut Package Evaluation

Step	Procedure
	**NOTE:** Always follow sterile technique during device preparation.
1	Verify valid expiration date on ShortCut labeling.
2	Before opening the Tyvek™ pouch, carefully examine the pouch and its seals and verify that there is no evidence of damage, piercing or broken seals.
	**WARNINGS:** **1. Do not use the ShortCut if any sign of damage or breach of the sterile barrier is observed or if the expiration date printed on the labeling is not valid.** **2. In case the expiration date is not valid, or there is any sign of damage or breach of the pouch, do not use and replace the ShortCut.**

4.3 Patient Preparation

1. Prepare the patient for catheterization per local procedures.
2. Administer pre-, intra-, and post-procedure medications and Heparin, and maintain ACT level according to applicable medical guidelines and physician discretion.
3. Prepare the patient per hospital standard for percutaneous catheterization with a 16Fr introducer sheath (or larger) for insertion of the ShortCut in one groin, and another introducer sheath for an additional standard catheter insertion in the other groin. Closure device usage is recommended.
4. Insert an extra-stiff guide wire (GW), over which the ShortCut will be inserted, through the 16Fr introducer sheath and place it in the left ventricle (LV). (See section 3.1 for required equipment).

4.4 ShortCut Preparation

4.4.1 ShortCut Package Opening and Examination

Step	Procedure
1	Remove the ShortCut from the cardboardbox. Inspect the Tyvek™ pouch and ensure there is no visual damage.,
2	Adhering to sterile technique at all times, carefully open the Tyvek™ pouch and pull the blister pack out. Place the blister pack on a sterile table.
3	Lift the blister pack cover and place aside. Only once the cover is removed, the ShortCut™ can be lifted and taken out of the blister. Remove the rest of the blister pack and place aside.
4	Examine the ShortCut™ device for any visual damage.
	**WARNING:** **Do not use the ShortCut if any sign of damage to the Tyvek™ Pouch or ShortCut ™device is seen.**
5	Test the different components of ShortCut: 1. Fully activate the splitting element by turning the activation knob clockwise all the way to hard stop, and fully deactivate the splitting element by turning the activation knob counter-clockwise until the hard stop. 2. Test the landing knob in each direction and then, turn the landing knob clockwise all the way until hard stop or until the distal unit is touching the tip. 3. Turn the rotation knob in each direction to test it and then rotate the positioning arm until it is pointing up (in the same direction as the markings on the handle). 4. Apply full flex to the device (by turning the flexing knob clockwise) and then fully removing flex from the device (turn counter-clockwise). 5. Test the sheathing knob in each direction, and then turn it clockwise until the external tube tip reaches the proximal end of the positioning arm. (Do NOT sheath the Positioning Arm.)

4.4.2 ShortCut Flushing

Step	Procedure
1	Connect a stopcock to the catheter's flushing port and close the side port of the stopcock.

2	Using a 20ml syringe, inject Heparinized Saline through the catheter internal lumen port, until Saline flows out of the catheter's Tip.
3	Move the syringe to the in-line port of the stopcock, hold the distal part of the catheter upwards (higher than the handle), and inject 20ml of heparinized saline.
4	While keeping the distal part of the catheter upwards and higher than the handle, remove the syringe from the stopcock leaving the flushing port inlet open to air.
5	Tap the external tube in order to let the saline fill the proximal part of the tube. Continue tapping the external tube for 1 minute.
6	Refill the syringe with heparinized saline. Reconnect the syringe to the flushing port stopcock and slowly inject heparinized saline until it flows out of the External Tube. Slowly inject the rest of the 20 mL of heparinized Saline while tapping the external tube to release all air bubbles in it.
7	Connect a Saline infusion line at 300mmHg pressure to the side port of the stopcock and open the stopcock to the pressurized Saline line.
8	Close the port to the catheter and allow flow of Saline from the pressure line to and out of the adjacent port into the syringe and fill the syringe with 20 mL of heparinized saline.
9	Close the port to the pressure line and inject 20ml of Heparinized Saline from the syringe into the catheter.
10	Close the port to the syringe, and open the port to the pressure line, so that Saline flows from the pressure line into the catheter. Remove the syringe from the stopcock.

4.4.3 Distal Unit Sheathing

Step	Procedure
1	Immerse the DU of the ShortCut in a bowl filled with Saline.
2	Examine the DU of ShortCut and gently shake the DU to remove any bubbles seen on it.
3	Turn the Sheathing Knob clockwise until the DU is completely sheathed, while keeping it immersed in Saline. (The support of a scrubbed assistant may be required)
	NOTE: Make sure that the tip of the External Tube does not overlap with the catheter's pigtail Tip.
4	Remove the DU from the Saline and hold it perpendicular to the Handle. Make sure that Saline flows out of the External Tube the whole time.
5	Immerse the DU of the ShortCut in a bowl filled with Saline.

Step	Procedure
6	Turn the Sheathing Knob counter-clockwise until DU is completely unsheathed, while keeping it immersed in Saline. Check for any bubbles release during un-sheathing.
7	In case bubbles are released during un-sheathing, repeat steps 2-6 until no bubbles are released during unsheathing.
8	Turn the Sheathing Knob clockwise until the DU is completely sheathed, while keeping it immersed in Saline.
9	While the distal end of the catheter is still immersed in saline, turn the Landing Knob counter-clockwise to un-land the DU (until it reaches the hard stop).
	**NOTE:** Make sure that the tip of the External Tube does not overlap with the catheter's pigtail Tip.

4.5 The ShortCut Procedure

- It is recommended to have a defibrillator available in the event of an emergency. Should the use of a defibrillator be required, ShortCut should be withdrawn prior to defibrillation.
- Use fluoroscopy for feedback regarding the ShortCut and DU sheathed state and position relative to the anatomy during each one of the procedure steps.

Note: Instructions are provided for both Left and Right leaflets split. Follow these as applicable, depending on the clinical situation.

4.5.1 Left Coronary Leaflet Procedure

Step	Procedure
1	Align the direction of the catheter with the patient's anatomy by placing the Handle on the table, while the printing on the Handle is facing upward.
2	**Advancing the ShortCut** View: LC side • If valve is not visible, position pigtail as a marker at the annulus level • Advance the ShortCut catheter, over GW into the 16Fr introducer sheath while keeping GW position in LV. • Advance the catheter until the bottom of the Guide Frame is aligned with the annulus level.
4	**Unsheathing** View: LC side

	• Turn Sheathing Knob CCW until Distal Unit is fully unsheathed and the knob reaches a hard stop • Maintain the bottom of the Guide Frame at the annulus level by pulling back the catheter and slightly pushing the GW • Verify visually that the PA is deployed • Verify Splitter Activation Knob is at zero. Turn the Splitter Activation Knob CW 2 clicks
5	**Orienting the Positioning Arm towards the LC Sinus** View: LC side • Rotate handle 90° CW, flushing port pointing upwards and hold position • Turn the Rotation Knob until the PA is positioned towards the LC sinus and seen in a side view
6	**Placing Positioning Arm in LC Sinus** View: LC side • Turn the Flexing Knob CW gradually until the PA moves as close to the inner arch and the LC sinus as possible • Pull on the GW to further move the PA towards the LC sinus. If needed, slightly push the catheter • Ensure the PA is in the sinus. Use contrast media to verify PA location
7	**PA Position in the LC Sinus** View: LC front & side view • Find correct position of PA Tip. • Perform the following catheter gentle movements, as needed, to finalize the position of the PA: Push the ShortCut against the outer arch curvature, turn Rotation Knob & use GW maneuvers (slight push/pull) • Verify the PA is in contact and has slight pressure on the annulus level of the valve.
	**WARNING:** **Avoid excessive manipulation of the GW. In case high friction is noted between the device and the GW, it is recommended to replace the GW.**
8	**Splitter Activation** View: LC side • While holding tension forward, slowly turn the Splitter Activation Knob CW until the knob reaches a hard stop; ensuring the PA position is maintained. • Verify, using fluoroscopy, full activation of the Splitter Element and engagement with the PA.
9	**Splitting the LC Leaflet**

	View: LC Side (zoom out to see LV and full arch) • Release flexing by turning the Flexing Knob **CCW** until it reaches a hard stop • **Turn** Sheathing Knob **CW** to advance the external tube tip until end of flexing tube • **Push on GW** and secure, visually verify position in the LV & outer curve • **Hold tension on GW whilst slightly pulling on the catheter** until the Splitting Element is disengaged OR until it has reached the middle of the AAO
10	**Deactivating the Splitting Element** View: LC Side • Gently pull on GW until Distal Spring at annular level. • Turn the Splitter Activation Knob **CCW** until the knob reaches a hard stop • Turn Landing Knob **CCW** until the knob reaches a hard stop • Turn the Rotation Knob until PA is pointing **towards** the **inner arch** curvature. If procedure is complete, continue with sheathing otherwise fully unsheathed by turning **Sheathing Knob CCW** until the knob reaches a hard stop
11	**Distal Unit Sheathing & Catheter Withdrawal** View: open arch (LAO) • Turn Sheathing Knob **CW** until Distal Unit is sheathed just before the Tip-Cone • Withdraw catheter to the descending aorta • Turn the Splitter Activation Knob **CW** until the tip is engaged with the external tube to complete sheathing process
	**WARNING:** **Do not perform a second split or a second attempt to split the same leaflet.**

- To continue to the RC leaflet – go to section 3.5.2
- To complete the procedure (sheathing) – go to section 3.5.3

4.5.2 Right Coronary Leaflet Procedure

Step	Procedure
1	**ShortCut Advancing** View: LAO/LC side view • If valve is not visible, position pigtail as a marker at annulus level • **Advance** the ShortCut catheter, over GW into the 16Fr introducer sheath while keeping GW position in LV. • Advance until bottom of the Guide Frame is aligned with annulus level.
2	**Unsheathing**

	View: LC Side view • **Turn** Sheathing Knob **CCW** until Distal Unit is fully unsheathed and reaches **hard stop** • Maintain the bottom of the Guide Frame at the annulus level by pulling back the catheter and slightly pushing the GW • Verify visually that the PA is deployed • Verify Splitter Activation Knob is at zero. Turn the Splitter Activation Knob **CW** 2 clicks
3	**Orienting the Positioning Arm towards the RC Sinus** View: LC Side view • If needed, turn Flexing Knob **CW** to orient the PA perpendicular to the annulus • Turn the **Rotation Knob** until the PA is positioned above the RC sinus
4	**Placing Positioning Arm in RC Sinus** View: LC Side view • **Pull on GW** and **slightly Push on the catheter** to further move the PA into RC sinus. • Make sure the PA is in the RC sinus. Use contrast media to verify PA location
5	**PA Position in the RC Sinus** View: RC front & Side view • Correct PA position to be placed in the desired location on both views. • Perform the following catheter movements, as needed in order to fine tune the position of the PA tip: Push the catheter against the outer arch curvature, turn Rotation Knob & use GW maneuvers (slight push/pull).
6	**Splitter Activation** View: RC side view • While holding tension forward, slowly turn the Splitter Activation Knob CW until it reaches a hard stop; ensuring the PA position is maintained. • Verify, using fluoroscopy, full activation of the Splitter Element and engagement with the PA.

7	**Splitting the RC Leaflet** View: RC Side (zoom out to see LV and full arch) • Release flexing by turning the Flexing Knob **CCW** until it reaches a hard stop. • **Turn** Sheathing Knob **CW** to advance the external tube tip until end of flexing tube • **Push on GW** and secure, visually verify position in the LV & outer curve • **Hold tension on GW whilst slightly pulling on the catheter** until the Splitting Element is disengaged OR until it has reached the middle of the AAO
8	**Deactivating the Splitting Element** View: RC Side • Gently push on catheter & pull on GW until Distal Spring at annular level • Turn the Splitter Activation Knob **CCW** until hard stop • Turn Landing Knob **CCW** until hard stop • If procedure is complete, continue with sheathing otherwise fully unsheathe by turning Sheathing Knob **CCW** until hard stop
9	**Distal Unit Sheathing & Catheter Withdrawal** View: open arch (LAO) • In LAO view, turn the Rotation Knob until PA is pointing **towards** the **inner arch** curvature • Turn Sheathing Knob **CW** until Distal Unit is sheathed just before the Tip-Cone • Withdraw catheter to the descending aorta • Turn the Splitter Activation Knob **CW** until the tip is engaged with the external tube to complete sheathing process

4.5.3 ShortCut Withdrawal

1	Slowly withdraw the ShortCut into the introducer sheath, while maintain the GW in the LV.

4.6 Post Procedure Patient Treatment

- Immediately after ShortCut withdrawal, TAVR procedure should be performed as planned according to local standard procedure.

4.7 ShortCut Disposal

The ShortCut is for single use only. After use, dispose of the catheter and packaging in accordance with hospital, administrative and/or local government policy.

5 CLINICAL STUDY SUMMARY

The ShortCut Study

5.1 Study Synopsis

Objective - To assess the safety and effectiveness of ShortCut for splitting bioprosthetic aortic valve leaflets, and to demonstrate coronary artery ostia patency following leaflet split, in subjects who are at risk for TAVR-induced coronary artery ostium obstruction following a valve-in-valve (ViV) procedure.

Design – Prospective, multi-center study sponsored by Pi-Cardia Ltd. The single-arm study analyzed sixty (60) subjects who were planned to undergo a percutaneous ViV procedure for an approved ViV indication, and who were determined at risk for TAVR-induced coronary artery ostium obstruction. The study included 23 sites worldwide: 13 in the US, 8 in EU and 2 in Israel.

Eligibility criteria summary

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

Key inclusion criteria included the following:

- Plan for a percutaneous ViV procedure for an approved ViV indication due to a failed bioprosthetic valve.
- Subject is at risk for TAVR-induced coronary artery ostium obstruction.

Key exclusion criteria included the following:

- Excessive aortic valve leaflet Calcium morphology.
- Leaflet planned to be intervened is torn pre-ShortCut access.
- Iliofemoral vessel characteristics that preclude safe insertion of the introducer sheath.
- Anatomy does not allow safe placement of a cerebral embolic protection device .
- Intervention ≤ 1 month prior to index procedure.
- Planned provisional stents.
- Coronary disease that should be treated, or treatment of coronary disease ≤ 1 month prior to index procedure.
- Carotid or vertebral artery disease that should be treated, or treatment of carotid stenosis ≤ 1 month prior to index procedure.
- CVA or TIA ≤ 6 months prior to index procedure.
- Inoperable for emergency open-heart surgery.
- Identified thrombotic material on the valve by either CT or Echocardiography.
-

Primary effectiveness endpoint - Overall leaflet splitting success using the ShortCut assessed intra-procedurally by echocardiography and or angiography. Per-subject leaflet splitting success was determined based on the splitting success of the first intervened leaflet, as follows:

  - Visualization of leaflet split, assessed by intraprocedural TEE immediately post-ShortCut procedure and prior to TAVR, OR

- Increase in aortic regurgitation from pre to post leaflet split, assessed by intraprocedural TEE or angiography.

Primary safety endpoint - Each of the following ShortCut device- and/or ShortCut procedure-related serious adverse events were assessed at discharge or at 7 days post-procedure, whichever occurred first:

- Mortality
- Stroke (fatal, disabling and non-disabling)

Additional Endpoints

The Secondary Effectiveness endpoints are:

- Per intervened leaflet splitting success was assessed intra-procedurally for each intervened leaflet according to the criteria described above for per-subject leaflet splitting success
- The following endpoints were assessed through 30 days post-index procedure:
  - Freedom from coronary artery ostia obstruction related to the intervened leaflet;
  - Freedom from coronary artery intervention related to the intervened leaflet.

The following Secondary Safety endpoints were assessed through 30 days post index procedure (according to VARC-3):

- All-cause mortality
- All-cause stroke (fatal, disabling and non-disabling)
- Coronary obstruction
- Myocardial infarction with new evidence of coronary artery obstruction requiring intervention
- Major vascular complications
- Cardiac tamponade
- Acute kidney injury
- Access-related type 3-4 bleeding

The Technical Success endpoints are composite of the following, which was assessed at exit from procedure room following the ShortCut™ procedure:

- Successful access, delivery, and retrieval of the ShortCut™ device
- Freedom from ShortCut device and/or ShortCut procedure-related mortality
- Freedom from ShortCut device and/or ShortCut procedure-related:
  - Surgery or intervention
  - Major vascular or access-related complications
  - Cardiac structural complication

Statistical Methods

The data is summarized listing the mean, standard deviation, median, minimum, maximum and number of subjects for continuous data, or listing count (frequency) and percentage for categorical data. The study was designed to provide 80% power to achieve significance for the primary effectiveness endpoint with a performance goal of 75% of subjects with evidence of a successful split. The study was not statistically powered to achieve significance for the primary safety endpoint;

however, a sample size of at least 60 subjects allows capturing at least 1 rare event, such as stroke or all-cause mortality, with an event rate of 2.8% or greater at high probability (>80%). Stroke or mortality rates in small ViV TAVR studies are reported at rates of 1.4% and 3.5%, respectively. Therefore, the study size is sufficient to observe stroke or mortality events for subjects receiving the ShortCut procedure within a 2-fold margin (i.e., 2.8%) of rates expected in ViV TAVR studies.

5.2 Accountability

A total of 137 subjects were screened for the study worldwide (US, Europe, and Israel). 66 of the 137 subjects were screening failures, 6 subjects dropped out of the study before treatment, and 5 subjects enrolled from OUS sites were considered not poolable by the conditions of the US protocol. Therefore, sixty (60) enrolled subjects were eligible for inclusion in the IDE Shortcut Pivotal study.

There were multiple reasons for the 66 screening failures, including but not limited to: subject not as risk for TAVR-induced coronary artery obstruction, subject not planning to undergo percutaneous ViV procedure for an approved indication, excessive aortic valve leaflet calcium morphology, and/or unsuitable anatomy or condition for the device or procedure.

The 5 OUS subjects that did not meet the US eligibility criteria per the approved IDE clinical protocol were considered non-poolable for the following reasons:

- Planned provisional stent (2);
- Coronary disease that should be treated or treatment of coronary disease =< 1 month prior to index procedure (1);
- Subject is not planned to undergo a percutaneous ViV procedure for an approved ViV indication (1);
- Surgery or interventional procedure ≤ 1 month prior to the index procedure (1).

Reasons for the 6 subjects that dropped out of the study and did not undergo the procedure are listed in Table 1 below.

Of the 60 subjects that initiated the overall transcatheter aortic valve procedure, 100% (60/60) underwent the index procedure with ShortCut. The 30-day visit compliance for the subjects was 95.0% (57/60), with 2 of the 3 missed visits due to death. Subjects disposition up to 90-day follow-up is provided in Table 1 below.

Table 1- Subjects Disposition

Disposition / Compliance Variable	US Subjects N (%)	OUS Subjects N (%)	All Subjects, N (%)
Consented Subjects	68	69	137
Passed Screening	35	36	71
IDE Study Eligible / Enrolled	35	31	66
Enrolled and Not Treated (Dropouts) [1]	4 (11.4)	2 (6.5)	6 (9.1)
Subject Withdrew Consent [2]	2 (50.0)	0	2 (33.3)
Investigator excluded/ withdrew subject [2]	0	1 (50.0)	1 (16.7)
Death [2]	1 (25.0)	1 (50.0)	2 (33.3)
Other [2]	1 (25.0)	0	1 (16.7)
Started Overall Procedure	31	29	60
Started Index Procedure [3]	31 (100.0)	29 (100.0)	60 (100.0)
At Least One Leaflet Split was Attempted [3]	31 (100.0)	29 (100.0)	60 (100.0)
Completed the Study According to Protocol [3]	28 (90.3)	27 (93.1)	55 (91.7)
30-Day Visit Completed [3, †]	29 (93.5)	28 (96.6)	57 (95.0)
90-Day Visit Completed [3, ‡]	28 (90.3)	27 (93.1)	55 (91.7)

[1] Percentages are based on the 'IDE Study Eligible / Enrolled' total per column.
[2] Percentages are based on the 'Enrolled and Not Treated' totals per column.
[3] Percentages are based on the 'Started Overall Procedure' totals per column.
† Two (2) subjects died 19 and 24 days post-procedure; One (1) subject did not perform the 30-days follow-up visit (but did return for 90-day visit).
‡ One (1) additional subject died 57 days post-procedure; One (1) subject is lost to follow-up; One (1) subject did not perform the 90-day follow-up visit.

5.3 Demographics

The mean subject age was 77.0±9.6 years, and most participants were female (70.0%). Most common comorbidities included significant renal impairment (73.3%) and coronary artery disease (43.3%). The majority of the subjects had isolated bioprosthetic valve stenosis (58.3%), 11.7% had isolated valve regurgitation and 30% had mixed bioprosthetic valve failure (stenosis and regurgitation). Information on the subject demographic and baseline characteristics is presented in Table 2.

Table 2 - Study Cohort Demographics and Baseline Characteristics

Demographic Parameter / Baseline Characteristic	**n = 60 n (%) or mean ± SD**
Age, yr	77.0 ± 9.6
Male	18 (30.0)
Female	42 (70.0)
Race / Ethnicity	
Asian	1 (1.7)
Black of African American	1 (1.7)
Hispanic/Latino	1 (1.7)
White	42 (70.0)
Unknown*	15 (25.0)
STS score, %	4.5 ± 2.4
EuroSCORE II	8.5 ±5.7
Surgical risk (assessed by the heart team)	
Intermediate / low	0 (0.0)
High	54 (90.0)
Extreme	6 (10.0)
NYHA Class	
I-II	20 (33.3)
III-IV	40 (66.7)
Left ventricular ejection fraction, %	54.2 ± 10.4
AV peak gradient, mmHg	65.3 ± 21.3
AV mean gradient, mmHg	38.1 ± 13.2
AVA, cm^2	1.0 ± 0.5
Failed Valve Type	
SAVR	58 (96.7)
TAVR	2 (3.3)
Failed Valve Disease	
Isolated aortic stenosis (AS)	35 (58.3)
Isolated aortic regurgitation (AR)	7 (11.7)
Mixed (AS and AR)	18 (30.0)
Failed bioprosthetic valve label size	
19 mm	8 (13.3)
21 mm	26 (43.3)
≥ 23 mm	26 (43.3)

* Unknown = Not applicable, Not asked, Asked but unknown, Not done, or Missing
BMI, body mass index; AVA, aortic valve area; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons; AV, aortic valve; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

All subjects (100%) were determined to be at risk for coronary obstruction. Key anatomical risk factors included mean VTC distance of 3.3±1.2 mm, mean VTS distance of 2.2±1.4 mm and coronary height<10mm for 91.7% of the subjects. Additional factors indicating risk for coronary obstruction in the study cohort are depicted in Table 3.

Table 3 - Study cohort risk factors of coronary artery ostia obstruction

	n = 60 n (%) or mean ± SD
Anatomical Risk Factors (per CT core lab analysis)	
Coronary height, mm*	6.9 ± 2.7
Coronary ostia eccentricity (°deg)	10.6 ± 8.0
Coronary height <10 mm*	55 (91.7)
Sinus of Valsalva width, mm*	27.9 ± 3.3
Sinus of Valsalva height, mm*	16.2 ± 3.2
VTC distance, mm*	3.3 ± 1.2
VTS distance, mm*	2.2 ± 1.4
Bioprosthetic Valve Factors (per site evaluation)	
Supra-Annular Position	16 (26.7)
Internal Stent Frame	23 (38.3)
No Stent Frame	4 (6.7)
Long, Thick, or Bulky Bioprosthetic Leaflets	11 (18.3)
Stents Posts That Extend Beyond Sinotubular Junction	17 (28.3)
Intended Over-Expansion / Fracture of Bioprosthetic Valve frame during TAVR	17 (28.3)
Transcatheter Valve factor (per site evaluation)	
Extended Sealing Cuff	19 (31.7)
High Implantation	20 (33.3)
None of the above	32 (53.3)

VTC, virtual transcatheter heart valve-to-coronary-artery; VTS, virtual transcatheter heart valve to sinotubular junction.

5.4 Results

Procedural Outcomes

All procedures were performed under general anesthesia utilizing TEE and all used an embolic protection device. A single leaflet split was performed in 63.3% of subjects and two leaflets split in 36.7% of subjects. ShortCut procedure time was 31±18 min (single split 26.9 ± 19.7 min, dual split 37.0±14.7 min). In all subjects, valves were implanted successfully following the ShortCut procedure. One subject required emergency open-heart surgery for replacement valve implant due to index procedure-related adverse event (guidewire perforation of left ventricle). Selected procedural outcomes are provided in Table 4 below.

Table 4 - Summary of Procedural Outcomes

Procedure Detail	**n = 60 n (%) or mean ± SD**
Transfemoral access for TAVR	60 (100.0)
Embolic protection device placed	60 (100.0)
Intervened Leaflet	
Left	30 (50.0)
Right	8 (13.3)
Left and Right	22 (36.7)
Overall procedure time (skin-to-skin), min*	119.7 ± 51.3
ShortCut procedure time, min**	30.6 ± 17.9
One leaflet split, min	26.9 ± 19.7
Two leaflet split, min	37.0 ± 14.7
ShortCut procedure contrast media volume, ml	23.3 ± 43.9
ShortCut procedure fluoroscopy time, min	16.8 ± 10.1
ViV TAVR procedure time, min***	7.9 ± 7.1

*Total procedure time - time from access site incision to access site closure.

**ShortCut procedure time: time between ShortCut insertion to its full retrieval including imaging time for split documentation.

***n=59; Data does not exist for 1 subject who had surgical implant procedure rather than TAVR.

Fifty-three subjects (53/60) were treated using only the first ShortCut device attempted. In six cases (6), the first device was removed prior to cutting a leaflet and a second device was used to make either a single split (3) or dual split (3). For one subject (1), the first device successfully performed the first leaflet split and a second device was used to make the second leaflet cut. Overall, fifty-nine subjects (59/60) had all leaflet intervention(s) performed by a single (either first or second introduced) ShortCut device, as shown in Table 5 below.

Table 5 - Procedural Outcomes Per Device and Intervened Leaflet

ShortCut Procedure Outcome	**First ShortCut Device (n=60), n (%)**	**Second ShortCut Device (n=7), n (%)**	**Overall**
ShortCut Successfully Reached the Left Ventricle [1]	59 (98.3)	7 (100.0)	
ShortCut Successfully Positioned on Leaflet(s) [1]	56 (93.3)	7 (100.0)	
Number of subjects for whom splitting performed [1]	54 (90.0)	7 (100.0)	60 (100.0)
LCC Split Only [2]	27 (50.0)	3 (42.9)	30 (50.0)
RCC Split Only [2]	8 (14.8)	0 (0.0)	8 (13.3)
RCC and LCC [2]	19 (35.2)	4 (57.1)	22 (36.7)
Withdrawn Successfully [1]	58 (96.7)	7 (100.0)	

[1] Percentages are based on the number of devices per column.

2 Percentages are based on the 'Number of subjects for whom splitting performed' totals per column.

Primary Effectiveness Endpoint

The primary effectiveness endpoint of per-subject leaflet splitting success was achieved in all subjects(100%) by one of the two pre-defined methods using intra-procedural echocardiography or angiography, and was statistically significantly higher (p<.001) then the study performance goal of 75%, as shown in Table 6.

Table 6 - Per-Subject Splitting Success

Primary Efficacy Endpoint	**Subjects with Successful First Split (n=60), n (%)**	**95% Confidence Interval**	**P-Value**
Evidence of Split	60 (100.0)	(94.0, 100.0)	<.001
Split visualization by Echocardiography	54 (90.0)	(79.5, 96.2)	
Increase in transvalvular AR by Echocardiography or Angiography	55 (91.7)	(81.6, 97.2)	

Confidence intervals were calculated using Clopper-Pearson method.
P-value was calculated using Exact Binomial test versus the performance goal of 0.75.

Primary Safety Endpoint

The primary safety endpoint of stroke or deathby discharge or 7 day post index procedure was analyzed per CEC adjudication and is provided in Table 7. There was no deaths (0.0%) within 7 days post-procedure or by discharge. There was one stroke (1.7%) occurring at 4 days post-procedure that was determined not related to the ShortCut device and possibly related to ShortCut procedure.

Table 7 - Mortality or Stroke Through Discharge or 7-Day Follow-Up

Primary Safety Endpoint	**Related to Either ShortCut Device or Procedure (n=60) n (%)**
Mortality	0
Stroke	1 (1.7)
Fatal stroke	0
Disabling*	1 (1.7)
Non-disabling **	0

* Disabling Stroke (mRS ≥2 and increase of at least 1 from baseline)
** Non disabling Stroke (mRS <2 or without increase from baseline)

Additional Endpoints

The Secondary Effectiveness endpoints of Per-intervened leaflet splitting success and freedom from coronary artery ostia obstruction or interventions are summarized in Tables 8 and 9 below:
When considering all splitting attempts, successful leaflet split was demonstrated in 80 out of the 82 (97.6%) intervened leaflets. For the two cases in which successful leaflet split was not determined, one case indicated unsuccessful split per the pre-established conditions and the other case was inconclusive due to inadequate imaging.

Table 8 - Per-Leaflet Splitting Success

Per-Leaflet Splitting Effectiveness Endpoint	Intervened Leaflet with Successful Split (n=82), n (%)
Evidence of a split	80 (97.6)
Split visualization	73 (91.3)
Increase in transvalvular AR	68 (85.0)

There were 3 cases of coronary artery ostia obstruction (5%) within 30 days of the procedure, as well as 1 additional case of coronary artery intervention without evidence of coronary ostia obstruction.

Table 9 - Coronary Artery Ostia Obstruction or Intervention within 30 Days Post-procedure

Secondary Effectiveness Endpoints	Total Subjects (n=60), n (%)
Freedom from Coronary Artery Ostia Obstruction related to the intervened leaflet	57 (95.0)
Freedom from Coronary Artery Intervention related to the intervened leaflet	56 (93.3)

The Secondary Safety endpoints were assessed through 30 days post-index procedure according to VARC-3 and per CEC adjudication, as presented in Table 10 below:

Table 10 - Safety Endpoints Through 30 Days Post-procedure

Secondary Safety Endpoints	Total Subjects (n=60), n (%)
All-cause mortality	2 (3.3)
Cardiovascular mortality	0 (0.0)
Non-cardiovascular mortality	2 (3.3)
All-cause stroke	1 (1.7)
Coronary obstruction	3 (5.0)
Myocardial infarction with new evidence of coronary artery obstruction requiring intervention	2 (3.3)
Major vascular complications	0 (0.0)
Cardiac tamponade	1 (1.7)
Acute kidney injury (AKI)	2 (3.3)
Access-related type 3-4 bleeding	0 (0.0)

The Technical Success endpoints evaluated at exit from procedure room following the ShortCut procedure on a per-subject basis are summarized in Table 11 below. One subject had cardiac tamponade caused by the guidewire position who underwent open-heart valve replacement, accounting for both reported technical failure reasons.

Table 11 - Technical Success Endpoints following ShortCut Procedure

Technical Success Endpoints	**Total Subjects (n=60), n (%)**
Overall Technical Success	59 (98.3)
Successful access, delivery, or retrieval of the ShortCut™ device	60 (100.0)
Freedom from ShortCut device and/or procedure related mortality	60 (100.0)
Freedom from ShortCut device and/or procedure related:	59 (98.3)
- surgery or intervention	59 (98.3)
- major vascular or access-related complications	60 (100.0)
- cardiac structural complication	59 (98.3)

Adverse Events

The total number of events adjudicated by the CEC for treated subjects from the point of index procedure through the study was 91 events. Following CEC adjudication, the reviewed events were classified as 40 serious adverse events (SAE) and 51 adverse events (AE), as shown in Table 12 below.

Table 12 - Summary of Adverse Events and Serious Adverse Events Through 90-Day Study Duration

Type of Event	**Adjudicated events n (%)**	**Events with relatedness to the ShortCut device or procedure, n (%)**
Total # as adjudicated *	91	25
SAE [1]	40 (44.0)	9 (36.0)
AE [1]	51 (56.0)**	16 (64.0)

[1] Percentages are based on the total number of events per column.

* Additional 23 AEs, determined by site as non-serious and not related to the ShortCut device or procedure or the overall ViV, were not adjudicated by the CEC, per protocol.

** 3 out of the 51 AEs were adjudicated as 'no event'.

Three total deaths occurred in the study cohort: two deaths prior to 30 days (see Table 11) and one additional death within 90 days. The deaths were determined to be non-cardiovascular causes and were not not related to ShortCut device or procedure, as shown in Table 13below.

Table 13 - Critical Adverse Events Through 90-Day Study Duration by Relation to ShortCut Device or Procedure

Adverse Event	**Not Related to ShortCut***	**Related to ShortCut***	**Total Subjects (n=60), n (%)**
All-cause mortality	3 (5.0)	0 (0.0)	3 (5.0)
Cardiovascular mortality	0 (0.0)	0 (0.0)	0 (0.0)
Non-cardiovascular mortality	3 (5.0)	0 (0.0)	3 (5.0)
All-cause stroke	0 (0.0)	1 (1.7)	1 (1.7)
Myocardial infarction with new evidence of coronary artery obstruction requiring intervention	2 (3.3)	0 (0.0)	2 (3.3)

* Assesses "Not Related" or "Related" that includes Possibly / Probably / Definitely Related AEs to either ShortCut Device or Procedure, per CEC adjudication.

5.5 Conclusions

Key findings of the ShortCut Study include:

- The primary effectiveness endpoint of per-subject leaflet splitting success using the ShortCut was achieved for the first intervened leaflet in 100% subjects, which was significantly higher ($p < 0.001$) then the study performance goal of 75%.
- There was no mortality (0.0%) and one stroke (1.7%) within 7 days post-procedure or at discharge, which is comparable to death and stroke rates expected for patients undergoing ViV TAVR.
- Coronary obstruction was reported in three subjects (5%); however, these events were adjudicated as not related to the ShortCut device or procedure, and all were successfully managed via coronary intervention post-TAVR. An observed occurrence of 5% coronary obstruction is not unreasonable in the study patient population of high risk for coronary obstruction receiving ViV.
- Technical success was achieved in 98.3% of the subjects.

The ShortCut Pivotal Study demonstrates that the splitting of failed bioprosthetic aortic valve leaflets using ShortCut is safe and effective in subjects at high risk for coronary obstruction undergoing ViV TAVR.

6 LABELS AND SYMBOLS

The following table provides a description of the label symbols that appear on the ShortCut packaging.

	Manufacturer
	Medical Device
	Reference (catalog) number
	Lot Number
	Serial number
	UDI
	Use By
	Importer information
	Distributor information
	Consult Instructions for Use
	Ethylene Oxide sterilized
	Single sterile barrier system with protective packaging outside
	Do Not Re-Use
	Fragile, handle with care
	Do not use if package is damaged

	Do not re-sterilize
	Prescription Use Only

7 LIST OF ACRONYMS

ACT	Activated clotting time
CAU	Caudal
CRA	Cranial
DU	Distal Unit
DS	Delivery System
Fr	French (unit)
GW	Guide Wire
LC	Left Coronary
LV	Left Ventricle
PA	Positioning Arm
RAO	Right Anterior Oblique
RC	Right Coronary
SE	Splitting Element
STJ	Sinotubular Junction
TAVR	Transcatheter Aortic Valve Replacement
TTE	Trans-Thoracic Echocardiography

8 PATENTS

Pi-Cardia owns multiple issued patents and pending patent applications in multiple jurisdictions around the world that cover or relate to various aspects of the technology embedded in the ShortCut. For additional details regarding Pi-Cardia's patent estate relating to the ShortCut, please see Pi-Cardia's ShortCut patent marking page at https://www.pi-cardia.net/technology-shortcut.

9 DISCLAIMER

The ShortCut should only be used in the manner prescribed in this IFU. Changes or modifications not expressly approved by Pi-Cardia Ltd or use of the device in any other manner than indicated in this IFU could affect the safety or effectiveness of the ShortCut. Neither Pi-Cardia Ltd nor any of its

directors, employees or affiliates, shall be held responsible in any manner for any bodily injury and/or property damage arising from operation or use of this device other than that which adheres to the instructions and safety precautions contained herein and in all supplements hereto and according to the terms of the warranty provided herein.

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Signatory Table

Action Name	User Name	Title	Signature Date
Send for Review (Written By)	Ira Rosenblit	Regulatory Affairs Associate	10-Oct-2024 10:56
Review	Ronnie Levy	COO	10-Oct-2024 12:05
Review	Hadas Givon	VP RA & Clinical Operations	10-Oct-2024 14:51
Send for Approval	Ira Rosenblit	Regulatory Affairs Associate	10-Oct-2024 15:05
Approve	Hadas Givon	VP RA & Clinical Operations	10-Oct-2024 15:12
Approve	Keren Jan-Wolf	Senior QA Specialist	10-Oct-2024 15:33
Approve	Ronnie Levy	COO	10-Oct-2024 15:47
QA Approval	Keren Jan-Wolf	Senior QA Specialist	10-Oct-2024 15:52

* Dates are displayed according to the system time zone: (GMT+03:00) Israel Daylight Time (Asia/Jerusalem)