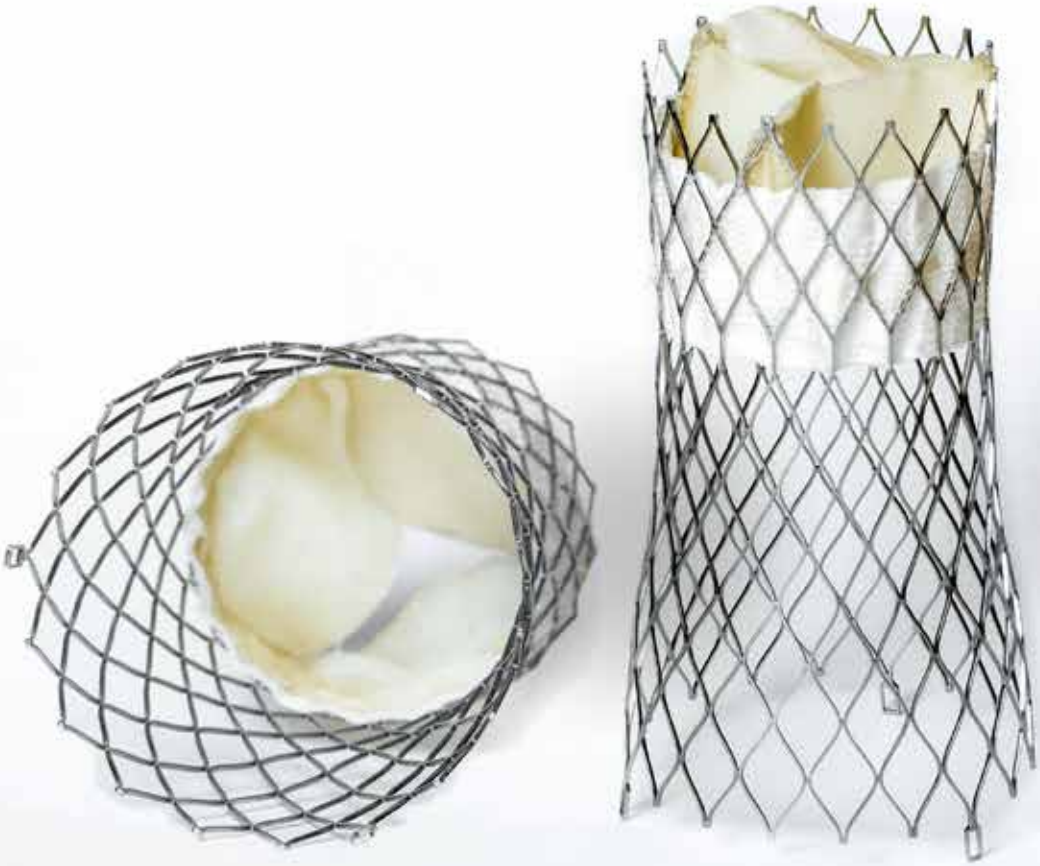
TRICVALVE®

TRANSCATHETER BICAVAL VALVES



TRAINING MATERIAL

P&F PRODUCTS & FEATURES
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TRICVALVE®

TRANSCATHETER BICAVAL VALVES

THE ONLY COMPLETE SOLUTION FOR TREATMENT OF TRICUSPID REGURGITATION USING CAVI.

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In Tricuspid Regurgitation (TR) the valve is leaky or doesn't close tight enough, causing blood to leak backwards across the valve.
In Tricuspid Stenosis the leaflets are stiff and do not open widely enough, causing a restriction in the forward flow of blood.

TR is frequently found in operative management of **left sided heart valve disease** (Mitral Regurgitation). [1]

Non-severe Tricuspid Regurgitation can be managed with medications (diuretics) that help remove fluids from the body.

0,8 %
of adults have mild to severe Tricuspid Regurgitation condition in the world.

But medical devices or prosthetics are needed to treat some cardiovascular diseases such as structural heart diseases usually caused by degenerative or congenital valve diseases and rheumatic disease. The conventional approach of open heart surgery is mainly divided into replacement of the diseased valve with a prosthetic heart valve (so called mechanical heart valve) or a biological heart valve. The choice of device depends mostly on the age of the patient and the availability of the device. Another surgical option is the repair of the diseased valve, mostly combined with the implantation of a surgical ring to reduce the size of the annulus of the native valve. This technique is mainly used in the mitral- and tricuspid valve.

1.6 million
US patients have tricuspid valve related issues requiring treatment.

The implantation of a pulmonary valve prosthesis is predominantly in congenital disease and therefore younger patient populations. As patients are getting older, more and more interventions for valvular disease are needed.

800.000
EU patients are contraindicated for valve surgery, due to high operative risk or technical contraindications.

Due to the advanced age and high surgical risk, many elderly patients are not referred for surgery or deemed inoperable. In search of new procedures for the treatment of valve disease for these patients with high surgical risk, the technical and procedural success of minimally invasive treatment has promoted innovation and development of minimal invasive transcatheter heart valve systems during the last 13 years. Reducing the size of the delivery catheters, along with technical improvements aimed at reducing postoperative paravalvular regurgitation, resulted in a significant reduction in CD mortality and improvement of quality of life.

35 %
of all the heart valve failure patients suffer from Tricuspid Regurgitation and require immediate attention.

Faced with the need for a device for tricuspid valve implantation, P+F Products + Features GmbH developed an innovative product that may make it even feasible to treat such patients with Severe Tricuspid Regurgitation with a minimal invasive transcatheter heart valve for the treatment of tricuspid insufficiency.

2 to 3 years
average survival rate of patients following onset of symtpoms.[2]

[1] Surgical approach to functional tricuspid regurgitation: should we be more aggressive?; Rogers JH, BollingSF. CurrOpinCardiol. 2014 Mar; 29(2): 133-9.
[2] Impact of Severe Tricuspid Regurgitation on Long Term Survival; Anita Sadeghpour, Mehri Hassanzadeh, Majid Kyavar, Hooman Bakhshandeh, Nasim Naderi, Behshid Ghadrdoost, Arezou Haghighat Talab. Res Cardiovasc Med. 2013 Aug; 2(3): 121–126. Published online 2013 Jul 31.

THE TRICVALVE® SYSTEM

TRICVALVE® TRANSCATHETER BICAVAL VALVES is a system of two self-expanding biological valves for the treatment of patients with hemodynamically relevant tricuspid insufficiency and caval reflux. The bioprostheses are implanted percutaneously into the inferior and superior vena cava without disturbing the native tricuspid valve.

It is especially intended for use for patients at extreme risk or who are inoperable for open surgical therapy.

Currently the ONLY solution specifically designed for the venous system, which is minimally invasive and addresses both SVC and IVC.

Alternative to open heart surgery, requiring only 30 minutes to perform and yields improvement that is immediate, reproducible and persistent.

The TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM consists of:

* SVC = superior vena cava; IVC = inferior vena cava

The TRICVALVE® TRANSCATHETER BICAVAL VALVES are already pre-mounted into the delivery system.

SIZES

TRICVALVE® MODEL	VALVE SIZE	PROXIMAL DIAMETER	DISTAL DIAMETER	LENGTH AFTER DEPLOYMENT
SVC 25	25	25	20	66,60
SVC 29	29	29	20	69,10
IVC 31	31	34	38	65
IVC 35	35	38	47	65

Table 1. TRICVALVE® sizes

TRICVALVE® TRANSCATHETER BICAVAL VALVES

The TRICVALVE® TRANSCATHETER BICAVAL VALVES are made of a tubular metallic structure of nitinol which is self-expandable and radiopaque with three valve leaflets of bovine pericardium sutured and complemented by a skirt of polyester to avoid paravalvular leaks. The bioprosthesis leaflets are processed with anti-calcification as well as chemical dehydration. It is designed to treat severe tricuspid regurgitation without removal of the defective tricuspid valve.

NITINOL FRAME

LONG SKIRT
to prevent PVL

BOVINE PERICARDIUM
leaflets and skirt

BOVINE PERICARDIUM
leaflets and skirt

SHORT SKIRT
to prevent hepatic vein occlusion

NITINOL FRAME

TRICVALVE® DELIVERY SYSTEM

TRICVALVE® DELIVERY SYSTEM for percutaneously access and delivery of the valves. The system is a single use, sterile device compatible with all the valve sizes.

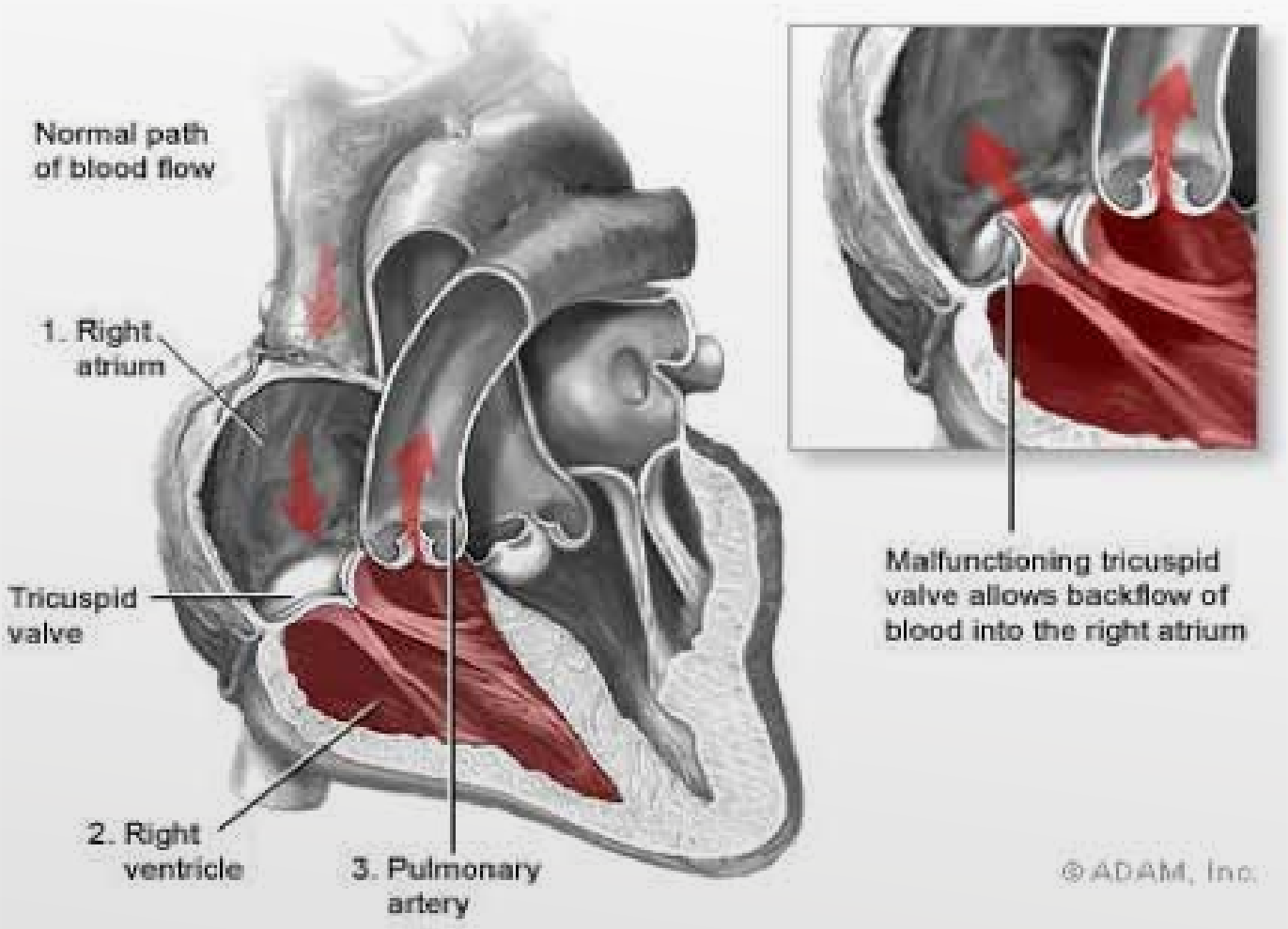
The TRICVALVE® DELIVERY SYSTEM has connectors in its system for safe and accurate bioprosthesis deployment. The distal end of the system has an atraumatic radiopaque tip and protective sheath. A capsule at distal end covers and maintains the bioprosthesis in a crimped position. A stabilizer tube is fixed at the handle and extends outside the catheter shaft. It provides a barrier between the inner catheter shaft and vessel walls, thus enabling the catheter to retract freely. The delivery system is compatible with 0.889mm (0.035 inch) guide wire.

The handle includes a macro slider for opening and closing the bioprosthesis housing and a micro adjusting knob to facilitate accurate release of the bioprosthesis. The micro knob rotates clockwise to open the housing and in anticlockwise direction for release. The delivery system has a flush port which is used to hydrate the bioprosthesis leaflets and remove air before usage.

TRICUSPID REGURGITATION AND CAVAL REFLUX

The tricuspid valve, or right atrioventricular valve, is on the right dorsal side of the heart, between the right atrium and the right ventricle. The function of the valve is to prevent backflow of blood into the right atrium. The normal tricuspid valve usually has three leaflets and three papillary muscles. They are connected to the papillary muscles by the chordae tendineae, which lies in the right ventricle.

Severe tricuspid regurgitation leads to a decrease in cardiac output, and significant symptoms of right heart failure develop, such as peripheral edema and congestive hepatosplenomegaly.



The implantation of self-expanding valves into the superior (SVC) and inferior (IVC) vena cava effectively reduce backward regurgitant flow and increase cardiac output.

The patients are elderly adults with a tricuspid disease who are considered to be inoperable by conventional open heart surgery and that conventional treatments do not have the effect of minimizing symptoms.

The TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM is not intended to cure the patient of tricuspid insufficiency but to bring about improved quality of life for patients considered inoperable by conventional or high-risk surgical surgeries.

- ↗ Improvement of NYHA functional class
- ↗ Improvement in the 6 Minute Walk Test Distance
- ↗ Improvement in quality of life

PATIENT SELECTION

The risks and benefits described below should be carefully considered for each patient before using TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM. The risks of long-term anticoagulant and/or antiplatelet therapy should be taken into account.

INCLUSION CRITERIA

- ✓ 18 years and older
- ✓ Patient with severe symptomatic tricuspid regurgitation demonstrated by echocardiography with significant backflow in the lower (IVC) and/or upper (SVC) vena cava and with a v-wave ≥ 25mmHg as demonstrated by right heart catheterization (measured in the IVC and/or SVC 2-4 cm above/below RA inflow) within 8 weeks prior to the implantation
- ✓ Suitable for TRICVALVE® implantation according to anatomic criteria by computed tomography
- ✓ The patient must have severe, tricuspid regurgitation leading to NYHA class III or IV
- ✓ The patient has LVEF ≥ 30%
- ✓ The patient shall be screened by a "Heart Team" – including an interventional cardiologist, cardiothoracic surgeon, and agreed as a candidate for the TRICVALVE® implantation.
- ✓ Patient/authorized legal guardian understands the nature of the procedure, is willing to comply with associated follow-up evaluations, and provides written informed consent.

EXCLUSION CRITERIA

- ✓ Known significant intracardiac shunt (e.g. ventricular septal defect) or congenital structural heart disease based on heart teams decision
- ✓ Requirement for other elective cardiac procedures e.g. PCI (percutaneous treatment of coronary artery) or CABG (coronary artery bypass surgery) up to 90 days after the procedure or 30 days before the procedure.
- ✓ Right ventricular failure (TAPSE ≤ 13 mmHg)
- ✓ Systolic pulmonary arterial pressure > 65 mmHg as assessed by Doppler echocardiography
- ✓ Liver cirrhosis Child C

CONTRAINDICATIONS

The TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM is contraindicated in patients who have any of the following conditions:

- ✓ Evolutionary or recent stroke;
- ✓ Cerebrovascular accident (CVA) evolutionary or recent;
- ✓ Recent myocardial infarction (<30 days);
- ✓ Known hypersensitivity, allergy or contraindication to device's components, e.g. nitinol;
- ✓ Known hypersensitivity to vitamin K antagonists, heparin and other oral anti-coagulants, or sensitivity to contrast medium that cannot be adequately premedicated;
- ✓ Sepsis, including active endocarditis;
- ✓ Thrombosis of the lower venous system or vena cava filter;
- ✓ Contraindication against a Transesophageal echo (TEE) during the procedure;
- ✓ Patients with Creatinine clearance <20 ml / min;
- ✓ Patients with vascular conditions (e.g. stenosis, tortuosity) that make insertion and endovascular access impossible to the upper and lower vena cava;
- ✓ Patients with bleeding diathesis or coagulopathy or patient refusing blood transfusion;
- ✓ Patients with active gastritis or peptic ulcer;
- ✓ Pregnancy.

TRICVALVE® CT ANGIOGRAM PROTOCOL

The selection of the patient requires the analysis of the measurements of the location of valve implants in the vena cava, for that it is necessary to use the following „Computed Tomography Angiogram" protocol. The images must be created using a Gated-ECG Cardiac Multidetector Computed Tomography (MDCT) or Cardiac Multi-slice Computed Tomography. The images must be transferred to a 3D Multi-Planar Reconstruction software (3D MPR), like Osiris, Horus, CVI42, 3Dmension, Terarecon and other similar programs.

! Correct sizing of the valve is essential to mitigate the risk of paravalvular leakage and migration of the valve.

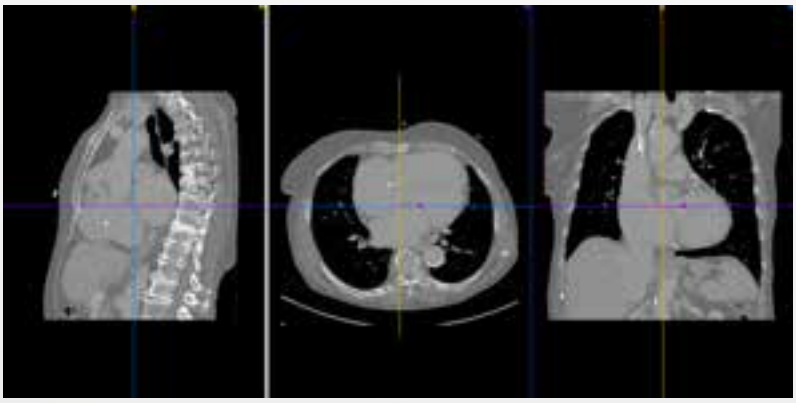


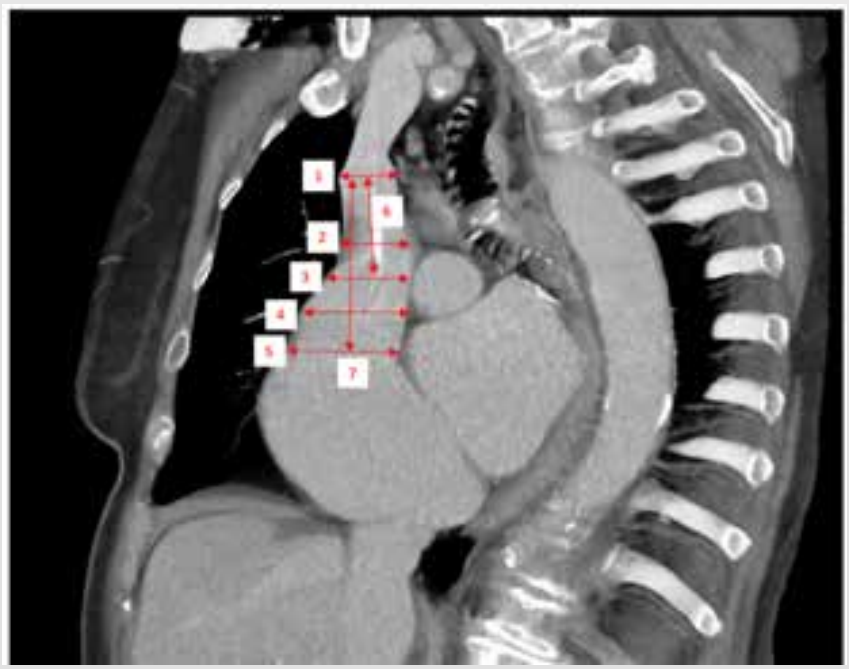
Figure 1. GATED-ECG MDCT OR MSCT

SUPERIOR VENA CAVA (SVC) | MEASUREMENTS

For implantation of SVC valve 7 measurements (all measurements in mm) are required as directed in the following checklist and figure 2.

1. Diameter of confluence;
2. Diameter of SVC at level of top of Pulmonary Artery;
3. Diameter of SVC at level of middle of Pulmonary Artery;
4. Diameter of SVC at level of bottom of Pulmonary Artery;
5. Diameter of SVC-Right Atrium junction;
6. Length between 1 and 3;
7. Length between 1 and 5.

Figure 2 SVC Measurements



CALCULATE THE DIAMETER VARIATION

- Between 2 and 3;
- Between 3 and 4.

HOW TO EXECUTE THE MEASUREMENT

Using the MPR plane, find the best projection at interest point of measurement and adjust the planes to be very orthogonal to SVC.

1. Put the center of line's intersection at the interest point. Repeat for the 3 planes presented in 3D MPR screen. (Figure 3).
2. Adjust the Coronal and Sagittal view, rotating the axis of image to obtain an orthogonal (perpendicular) view in these both visualizations. At the end, use the adjusted axial view to measure the perimeter and area of SVC in different interest points (use 10 to 15 points to create the polygon for area and perimeter measurement).

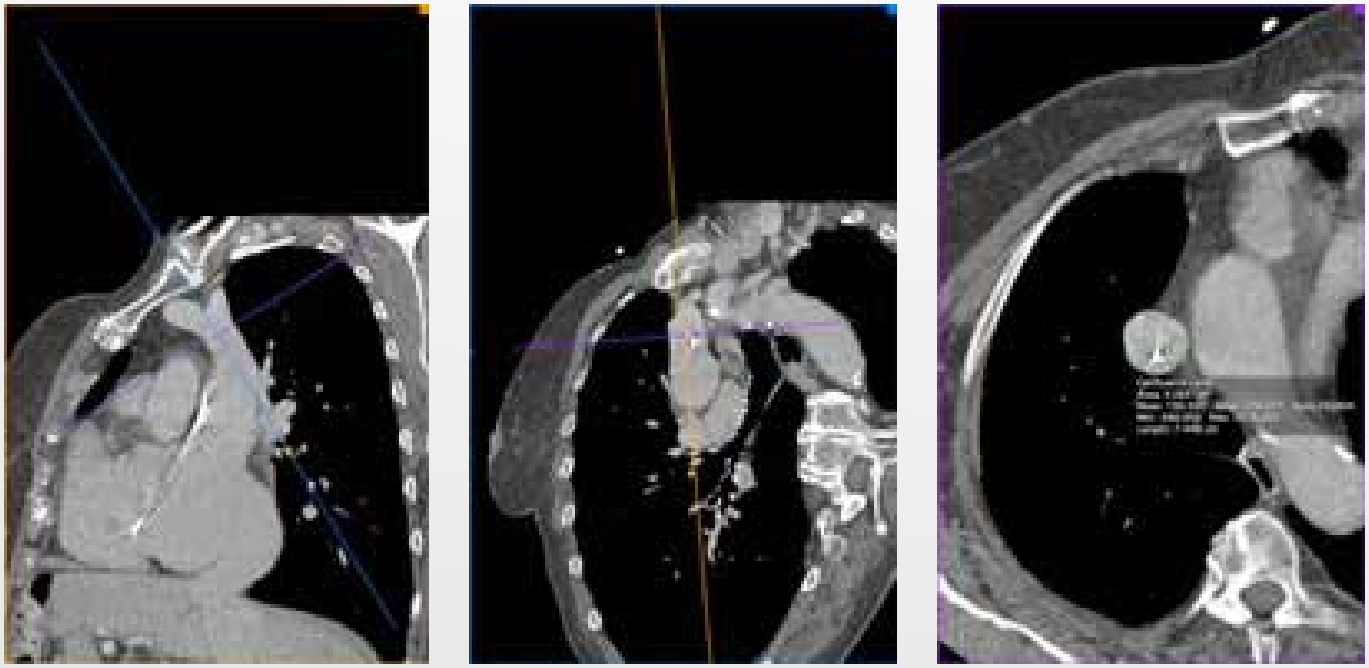


Figure 3. Adjust planes

3. Use the ruler to measure the distance between different planes of measurement. If the SVC presents angulation or tortuosity, use the open polygon tool to trace the length at the center of vein. The lengths between confluence and point of SVC at middle of Pulmonary Artery and between confluence and SVC-RA junction are fundamental to implantation planning.

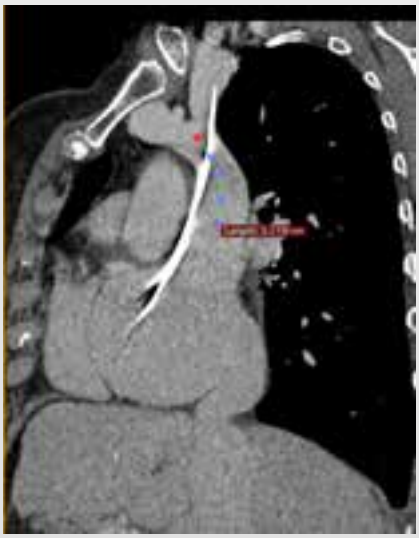
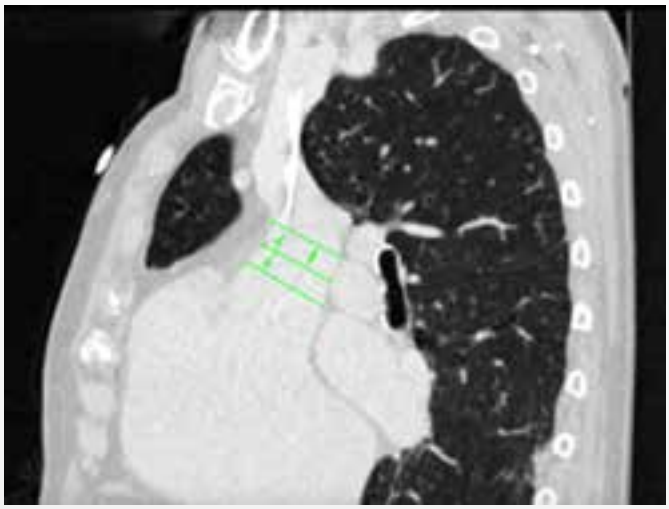


Figure 4. Trace length at center of vein

DIAMETER VARIATION



Use the measurements of SVC at three PA levels (top, middle and bottom) and distance between them.

Figure 5. Diameter variation

CALCULATE THE RELATION

- (Diameter of SVC@TOP PA – Diameter of SVC@Middle PA)/Length between TOP PA and Middle PA.
- (Diameter of SVC@Middle PA – Diameter of SVC@Bottom PA)/Length between Middle PA and Bottom PA.

The results from this calculation will be the rate of dilation of SVC per mm.

HOW TO CHOOSE THE SVC VALVE

To select the valve for SVC to be implanted it is obligatory to observe the valve measurements (Figure 6) and the Table 2 with the limits of the measurements.

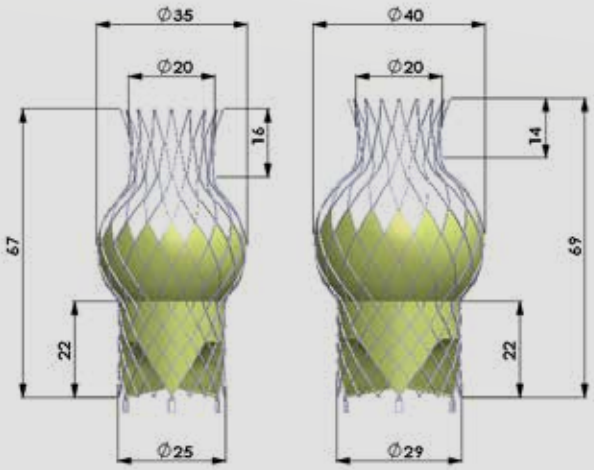


Figure 6. TricValve® for SVC - measurements

	SVC 25	SVC 29
Confluence	Larger than 14mm	
SVC TOP PA	19-31mm	22-34mm
SVC Middle PA	22-31mm	27-34mm
Diameter variation 1	Less than 0.50mm/mm	
Diameter variation 2		
Length Middle PA	Larger than 35mm	
Length to SVC-RA	Larger than 50mm	

Table 2. TricValve® for SVC - measurements

INFERIOR VENA CAVA (IVC) | MEASUREMENTS

For implantation of the IVC valve 5 measurements (all measurements in mm) are required as directed in the following checklist and figure 7.

1. IVC-RA transition diameter;
2. IVC at top of Hepatic Veins;
3. IVC just below Hepatic Veins;
4. IVC at 5cm below IVC-RA transition;
5. IVC-RA transition (1) to IVC top of HV (2) length.

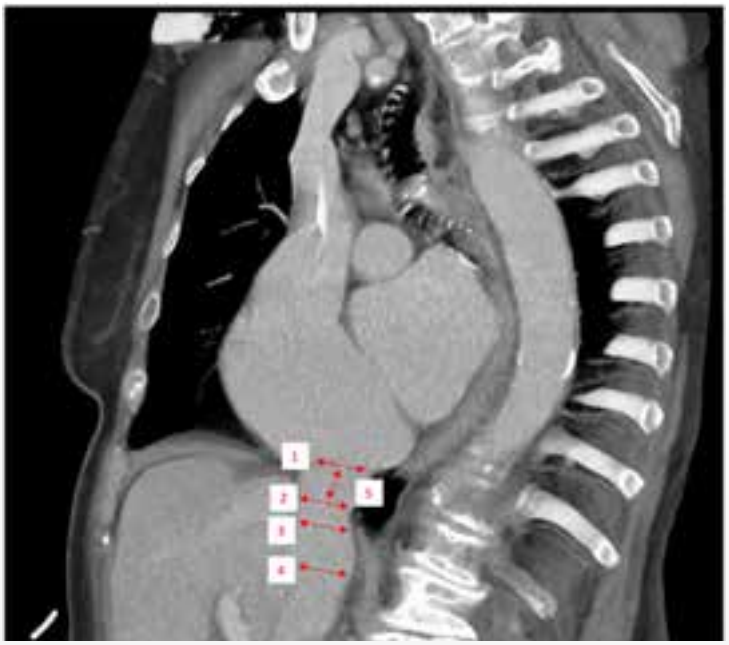


Figure 7. IVC measurements

HOW TO EXECUTE THE MEASUREMENT

Using the MPR plane, find the best projection at interest point of measurement and adjust the planes to be very orthogonal to IVC.

1. Put the center of line's intersection at the interest point. Repeat for the 3 planes presented in 3D MPR screen (Figure 8).

2. Adjust the Coronal and Sagittal view, rotating the axis of image to obtain an orthogonal (perpendicular) view in these both visualizations. At the end, use the adjusted axial view to measure the perimeter and area of IVC in different interest points (use 10 to 15 points to create the polygon for area and perimeter measurement).

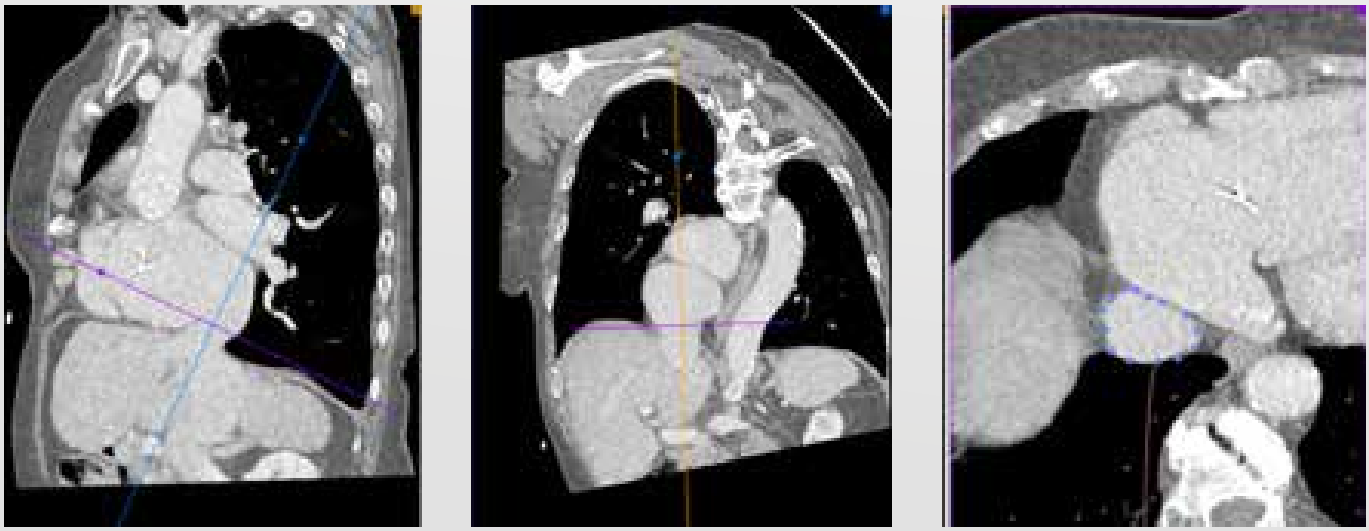
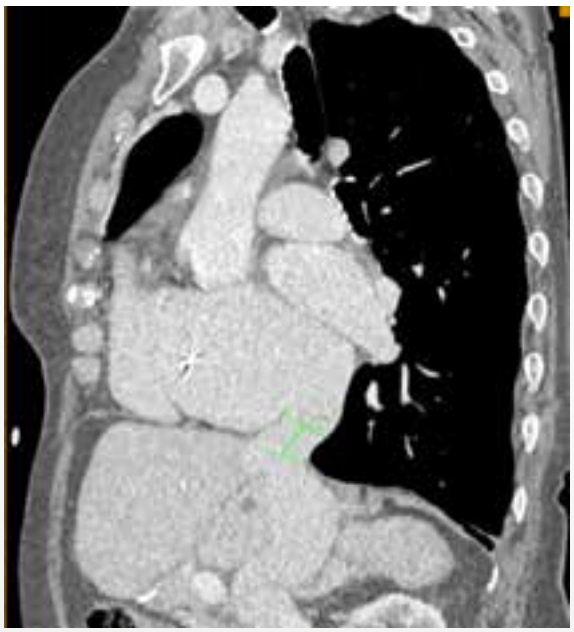


Figure 8. Adjust planes



3. Use the ruler to measure the distance between different planes of measurement. If the IVC presents angulation or tortuosity, use the open polygon tool to trace the length at the center of vein. The lengths between junction of IVC to RA and top of Hepatic Veins is fundamental to implantation planning (Figure 9).

Figure 9. Trace length at center of vein

HOW TO CHOOSE THE IVC VALVE

To select the valve for IVC to be implanted it is obligatory to observe the valve measurements (Figure 10) and the Table 3 with the limits of the measurements.

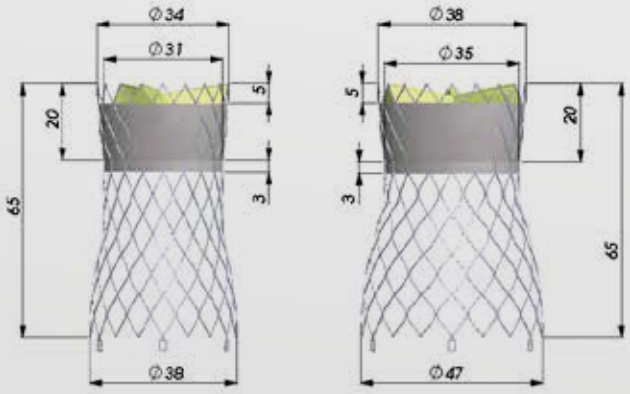


Figure 10. TricValve® for IVC - measurements

	IVC 31	IVC 35
IVC-RA junction	24 to 31mm	28 to 35mm
IVC top HV	24 to 31mm	28 to 35mm
Length IVC/RA junction - HVeins	Larger than 10mm	
IVC just below HV	21 to 35mm	27 to 43mm
IVC 5cm below RA junction	21 to 35mm	27 to 43mm

Table 3. TricValve® for IVC - measurements

TRICVALVE® IMPLANTATION

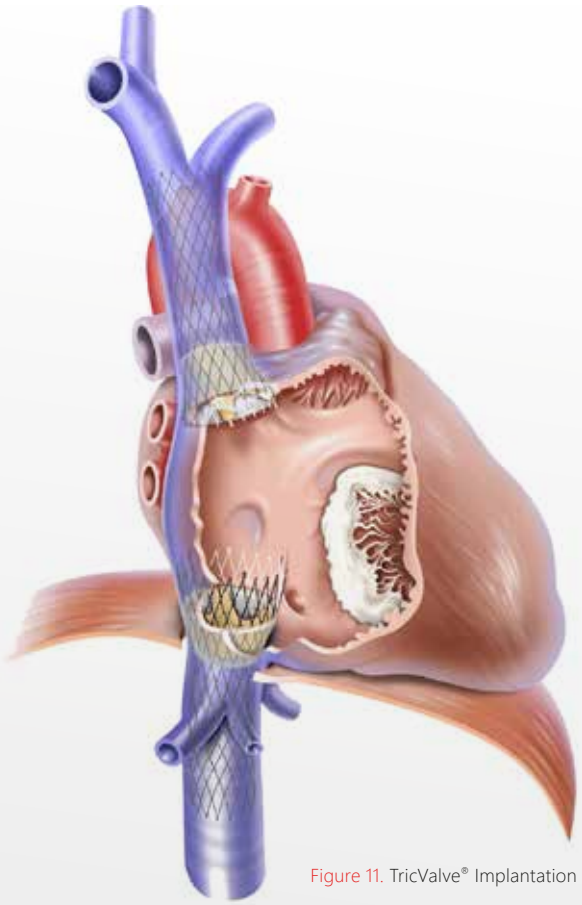


Figure 11. TricValve® Implantation

TRICVALVE® TRANSCATHETER BICAVAL VALVES are implanted in Superior Vena Cava (SVC) and Inferior Vena Cava (IVC). The delivery of the valves is done using a 28Fr flexible catheter via transvenous route.

It's the alternative to open heart surgery, requiring only 30 minutes to perform and yields improvement that is immediate, reproducible and persistent.

The TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM consist of:

- TRICVALVE® TRANSCATHETER BICAVAL VALVE for SVC
- TRICVALVE® TRANSCATHETER BICAVAL VALVE for IVC
- TRICVALVE® DELIVERY SYSTEM

ADDITIONAL EQUIPMENT

Additional equipment necessary for the implantation of the TRICVALVE® TRANSCATHETER BICAVAL VALVES:

- standard cardiac catheterization lab equipment;
- 20 ml sterile syringe;
- Fluoroscopy (fixed, mobile or semi-mobile fluoroscopy systems appropriate for use in percutaneous coronary interventions)
- Transesophageal (TEE) or Transthoracic Echocardiography capabilities;
- 2x Sheath 6F;
- 1x Standard Guidewire 0.0035;
- 1x Amplatz Super stiff guidewire;
- 1x Dilatator 14 F;
- 1x 5F Pigtail;
- 1x Standard right-heart balloon-Catheter (as used for right heart Cath);
- 2x Pro-glide (Optional).

This material is not part of the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM and must be supplied by the hospital prior to the surgical procedure.

WARNINGS

TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM is designed for single use only. Do not re-sterilize or reuse the devices. There is no data to support the sterility, non-pyrogenic and functionality of the devices after reprocessing or re-sterilisation.

- Verify that relevant patient anatomical parameters are suitable and within the specifications for performing the procedure.
- Incorrect sizing of the bioprosthesis may lead to paravalvular leak, migration, embolization and/or cardio-vascular rupture.
- Accelerated deterioration of the bioprosthesis may occur in patients with an altered calcium metabolism.
- Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the bioprosthesis.
- Caution should be exercised in implanting a valve in patients with clinically significant coronary artery disease.
- Caution should be exercised in patients with relevant left sided valve disease.
- Do not use the system if the tamper evident seal is broken, the temperature indicator has been activated or the valve is damaged, or the expiration date has elapsed.
- Do not use the catheter if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched).
- Follow the protocol for measuring relevant anatomical parameters of the patient before selecting the bioprosthesis for the treatment as described in the section "PATIENT SELECTION".
- After the bioprosthesis was inserted into a patient, do not attempt to reload it in the same or another release device. Dispose the bioprosthesis and catheter; do not attempt to reuse either component.
- Do not open the contents of the package until you are sure about the deployment and the appropriate size of the bioprosthesis.
- Do not handle or manipulate the bioprosthesis with sharp or pointed objects.
- Do not use the delivery system with any damage.
- Any mechanical failures of the delivery system may result in severe complications and severe damage to the patient.
- In order to avoid contamination of the delivery system, do not use gloves with powder.
- Use the products before the use by-date.
- Store the bioprosthesis at room temperature.
- Carefully remove the catheter from the packaging to prevent damage to the catheter.

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Do not use the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM

- If the temperature sensor of the sterile packaging has been activated;
- If the sterile package is damaged;
- If the bioprosthesis is damaged;
- If the delivery system is damaged;
- If the delivery system is unable to flush;
- If the expiration date has elapsed.

INSPECTION PRIOR TO USE

Once the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM is removed from the packaging, ensure all subsequent procedures are performed in sterile field.
Correct sizing of the bioprosthesis is essential to mitigate the risk of paravalvular leakage and migration of the bioprosthesis.

1. Before removing the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM from its primary packaging, carefully inspect the packaging for any evidence of damage that could compromise the sterility or integrity of the device (e.g., broken or missing seals, torn or punctured pouch).

Do not use the product after the expiry date has elapsed or if the integrity of the sterilized packaging has been compromised (e.g. damaged packaging).

2. Inspect the temperature indicator located within the packaging to ensure it has not been activated.

Do not use the bioprosthesis if the temperature indicator has been activated.

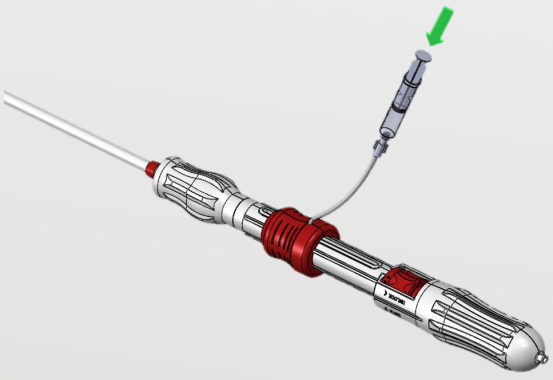
3. Visually check that the product is free of defects. Do not use if any defects are noted.

PREPARATION

Wipe the length of the catheter with a moist (saline) gauze.

1. The catheter with the loaded bioprosthesis is slightly open. Use the micro knob on the handle to close the catheter and then open until the tube extremity reaches the border of the bioprosthesis.

2. Attach a stopcock to the first flush port. Attach a 20-mlL syringe filled with saline to the stopcock on the first flush port and flush. Repeat step until removing air bubbles from the tube.

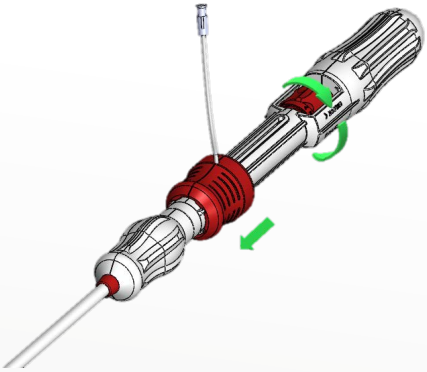


NOTE: The bioprosthesis leaflets are dehydrated when loaded in the delivery system and hence requires hydration using normal saline to achieve its required state for implantation. The hydration procedure is done by flushing the device with normal saline as per above mentioned procedure. It's important to remove all air bubble and flush with minimum of 60ml of saline solution and keep the bioprothesis wet during minimum 2 minutes.

3. Verify no catheter leakage is observed during any of the flushing steps. If leakage is found, use a new system.

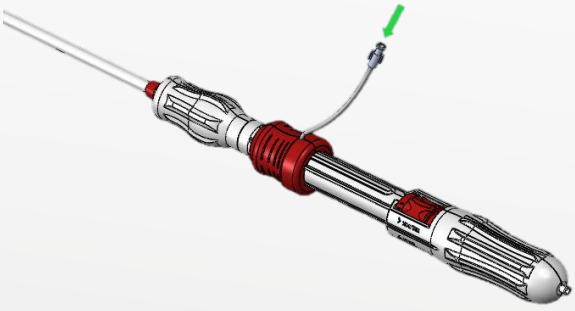
4. Attach a 10-ml syringe filled with saline to the guidewire port on the handle on the catheter and flush.

5. Close the capsule using the micro knob on the backside of the handle until the extension of the bioprosthesis is covered.



6. If necessary, flush the first port to remove any residual air bubble.

7. Connect the flushing line to the pressure line.



8. Conduct a final visual inspection of the loaded bioprosthesis to make sure the frame is free of creases or in folds beyond the second node from the inflow end. Ensure check is performed circumferentially around the entire bioprosthesis.

! If a crease or fold greater than 2 nodes long is noticed, do not use the bioprosthesis or delivery system.

VASCULAR ACCESS

NOTE: Vascular access should be achieved per hospital protocol (either percutaneously or via surgical cut down).

NOTE: The primary access vein will be used to introduce the valve and the delivery system; the secondary access vein will be used to introduce the reference pigtail.

1. Insertion of temporary pacemaker catheter if necessary.
2. Insert a 6-Fr introducer sheath into the secondary access vein.
3. A sheathless approach is also possible according to operator's distinction.
4. Administer anticoagulant according to hospital protocol. If heparin is administered as an anticoagulant, check the activated clotting time (ACT) after initial bolus of heparin and recheck every 30 minutes thereafter. Maintain ACT ≥250 seconds.

NOTE: Anticoagulant may be administered at any time prior to this point, but avoid delaying beyond this point.

IMPLANTATION PROCEDURE

1. Place a 5F arterial catheter in the left femoral artery used for continuous blood pressure monitoring.
2. Position a pulmonary catheter through the left femoral vein in the right pulmonary artery (rPA) to mark the crossing of the rPA with the SVC.
3. Introduce a 6F pigtail catheter through a 6F sheath in the right femoral vein.
4. Obtain an angiogram of the SVC prior to bioprosthesis deployment.
5. Exchange the pigtail for a straight 0.035 in. stiff guidewire with a soft tip.
6. Make a small skin incision.
7. Advance the TricValve® Delivery System over the guide wire through the femoral vein and the Inferior Vena Cava (IVC) into the RA and Superior Vena Cava (SVC).
8. Place the upper part of the SVC bioprosthesis in the confluence, with the belly of the SVC bioprosthesis positioned above the rPA crossing.
9. Confirm the catheter position under fluoroscopic and echocardiographic visualization and unload the uppermost 20 mm of the valve partially.
10. After the position is confirmed under fluoroscopy, fully deploy the SVC bioprosthesis by using the micro knob.
11. Retrieve the TricValve® Delivery System with the guidewire kept in place.
12. Pressure measurements may be taken to ensure correct prosthetic valve function.
13. Withdraw the catheter in the rPA to avoid interference with the IVC valve.
14. Insert the TricValve® Delivery System with the already loaded IVC bioprosthesis at the puncture site.
15. Position the IVC bioprosthesis at the height of the diaphragm with the skirt visible just above the hepatic vein inflow.
16. Align the constrained segment of the stent frame with the cavo-atrial junction by careful pullback of the catheter.
17. With a safety margin of 5 mm, take care to avoid a low or high valve position causing either hepatic vein obstruction or paravalvular regurgitation.
18. After a satisfactory position is confirmed, release the IVC bioprosthesis slowly from the catheter, observing the distal deployment. This avoids a jerky release of the bioprosthesis.
19. Under fluoroscopic guidance, confirm that the catheter tip is coaxial with the inflow portion of the bioprosthesis.
20. Withdraw the catheter to the femoral vein while maintaining guidewire position.
21. Close the capsule and remove the catheter through the femoral access.

NOTE: If the capsule does not close properly, gently rotate the catheter clockwise (<180°) and then counter clockwise (<180°) until the capsule closes.

! Ensure the capsule is closed before catheter removal. If increased resistance is encountered when removing the catheter through the introducer sheath, do not force passage. I

POST DEPLOYMENT

1. Remove the reference pigtail catheter over a standard guidewire.
2. Remove the 6-Fr introducer and close the access site per hospital protocol.
3. Administer anticoagulation and/or antiplatelet therapy as required according to hospital protocol.
4. Perform Transesophageal echocardiography (TEE Echo) immediately after the procedure, if needed.

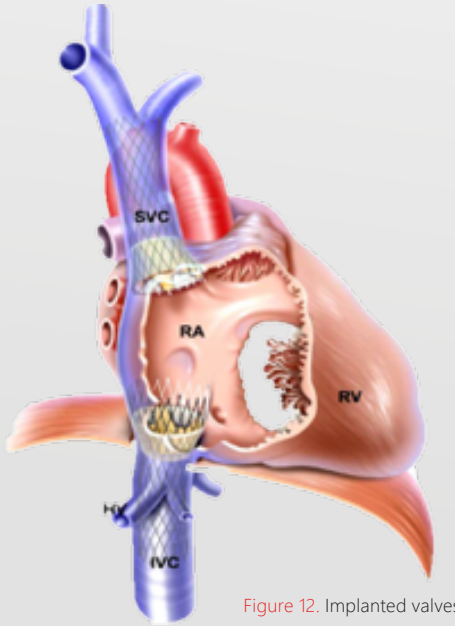


Figure 12. Implanted valves

POST-PROCEDURE CONTROL / MEDICATION

After the implantation, the patients are transferred to an intensive care unit for post operative monitoring. All patients should undergo anticoagulation therapy with Phenprocoumon (Marcoumar) for three months whereas an International Normalized Ratio (INR) between 2 and 3 is recommended. After this period, patients may be provided with anticoagulation therapy as judged by the investigator, lifelong anticoagulation is recommended.

MEDICAL TEAM TRAINING

Physicians using the the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM must have experience in

- Caval valve implantation (CAVI)
- Transfemoral access and catheterization
- Self-expandable Vena Cava Valve Bioprosthesis implantation using transcatheter/transfemoral procedures.

The use of the device is similar to other percutaneous valve implantation procedures and is having lower risks as it is being done through the venous route.

P+F Products + Features GmbH has a specific training program dedicated to train doctors in the use of the device. The initial procedures will be performed under supervision of company's technical advisors who have experience with the use of this device. An International Training Centre of Excellence is being setup in Portugal as a part of this program.

! The implantation of TRICVALVE® TRANSCATHETER BICAVAL VALVES should only be performed by doctors who have received a P+F Products + Features TricValve® Training.

For detailed information on the use of the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM, please refer to the Instructions for Use.

TRICVALVE® PUBLICATIONS

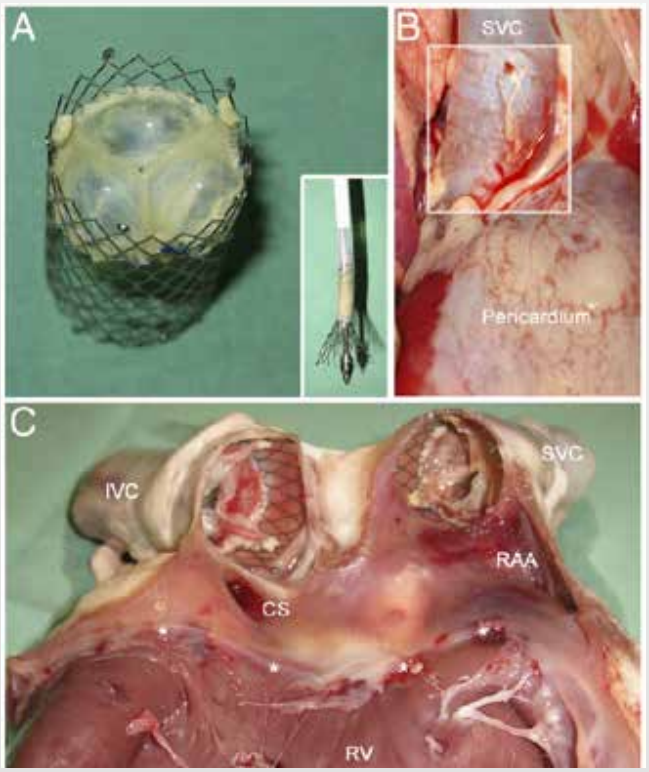
Several publications on pre-clinical studies and the first clinical experience with the TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM have already been published. The following is a brief summary of the most important results from the animal and clinical studies and the corresponding bibliographies.

PRE-CLINICAL PERFORMANCE DATA

In order to innovate the TR treatment, a study conducted by Lauten et al. in the year 2010 investigated the use of two self-expanding Nitinol stents containing a valve of biological tissue implanted by transcatheter approach in inferior and superior vena cava veins in 13 sheep, in which TR of grade III-IV were generated by the avulsion of the papillary muscle and chordae. This study showed that in high-grade Tricuspid insufficiency, percutaneous implantation of valve-bearing stents in the central venous position reduced venous regurgitation and improved hemodynamics in animal experimentation[1].

Regarding the valve implantation, the heterotopic approach in the Venae Cavae, compared to the orthotopic in the native Tricuspid valve, allows optimal valve fixation and presents a potentially lower risk of injury to cardiac structures, avoiding the introduction of foreign material into the right ventricle entryway. Thus, heterotopic valve implantation is feasible and has the potential to broaden the therapeutic options for patients with tricuspid valve disease.

The replacement of the heterotopic valve in animals with TR was performed by the same study group and published by Lauten et al. also in 2010. This study evaluated eight female sheep to establish research with the device of first generation, see picture below[2/3]. These studies from the research group of Lauten and contributors have shown that this technique allows for the amplification of potential therapeutic options for patients with important tricuspid regurgitation at high risk for open heart surgery[1/2].



Percutaneous Tricuspid Valve Replacement

(A) Porcine pulmonary valves were mounted to self-expanding nitinol stents of 28 or 26 mm in diameter. The devices were implanted using a 21-F delivery catheter.
(B) Macroscopic specimen showing the position of the valved stent in the superior vena cava (SVC) (highlighted area).
(C) Valve position in the SVC and inferior vena cava (IVC) after opening of the right atrium (RA) and right ventricular (RV) inflow tract. *Ruptured leaflets and chordae of tricuspid valve.

CS = coronary sinus;
RAA = right atrial appendage.

[1] Lauten et al., 2010. Percutaneous caval stent valve implantation: investigation of an interventional approach for treatment of tricuspid regurgitation. European Heart Journal (2010) 31, 1274-1281
[2] Lauten et al., 2010. Heterotopic valve replacement as an interventional approach to tricuspid regurgitation. Journal of the American College of Cardiology Vol. 55, No. 5, 2010 / ISSN 0735-1097/10
[3] Lauten et al., 2015. Transcatheter treatment of tricuspid regurgitation by caval valve implantation experimental evaluation of decellularized tissue valves in central venous position. Catheter Cardiovasc Interv 85: 150-160 (2015)

CLINICAL EXPERIENCE

Clinical studies have yet only been initiated as preliminary studies and with reduced follow-up, but compassionate implants have been performed with both TRICVALVE® TRANSCATHTER BICAVAL VALVES SYSTEM and other percutaneous valves already available on the market for mitral and aortic corrections.

First in man of "single valve implantation" in inferior vena cava and First in man of "bicaval valve implantation" in inferior and superior vena cava human clinical trials conducted between 2011-2016 by the Jena University.

Clinical experience with TRICVALVE® TRANSCATHTER BICAVAL VALVES SYSTEM started in 2011, when CAVI was first reported for compassionate use of patients with severe TR using investigational self-expandable valves. Since then, compassionate clinical use has confirmed the technical feasibility of CAVI, as well as the immediate and sustained hemodynamic improvement from the reduction of IVC and SVC backflow. However, due to the still limited availability of these devices, only few patients have been treated to date, and follow-up data are limited.

Recently, the feasibility, safety and efficacy of the TRICVALVE® TRANSCATHTER BICAVAL VALVES SYSTEM was previously assessed in an international, multicentric study which included 25 patients considered unsuitable for surgery upon decision by local heart teams and treated under a compassionate clinical use program. The total number of valves implanted within this study was 31 (including Sapien, TRICVALVE® TRANSCATHTER BICAVAL VALVES SYSTEM and Directflow). Due to the nature of the patient population, the period of treatment covered 6 years beginning March 2010 to February 2017.

Patients were followed up at least for 12 months after procedure. Patients were treated with single valve implantation (IVC only; n=19, 76.0%) or bicaval valve implantation (IVC and SVC, n=6, 24.0%). In these patients, either balloon-expandable (Sapien XT or Sapien 3: n=17, 78.3%) or self-expandable valves (TricValve® Transcatheter Bicaval Valves System n=7; 21.7%, Directflow n=1, 4.0%) were used for either single IVC- or bicaval valve implantation.

The study showed very promising results and confirmed the hemodynamic effects of the technique as well as the potential benefit that could be reached if implanted at the right moment in the course of the disease. At the moment P+F Products + Features GmbH is the only company worldwide developing such a dedicated device for CAVAL implantation only.

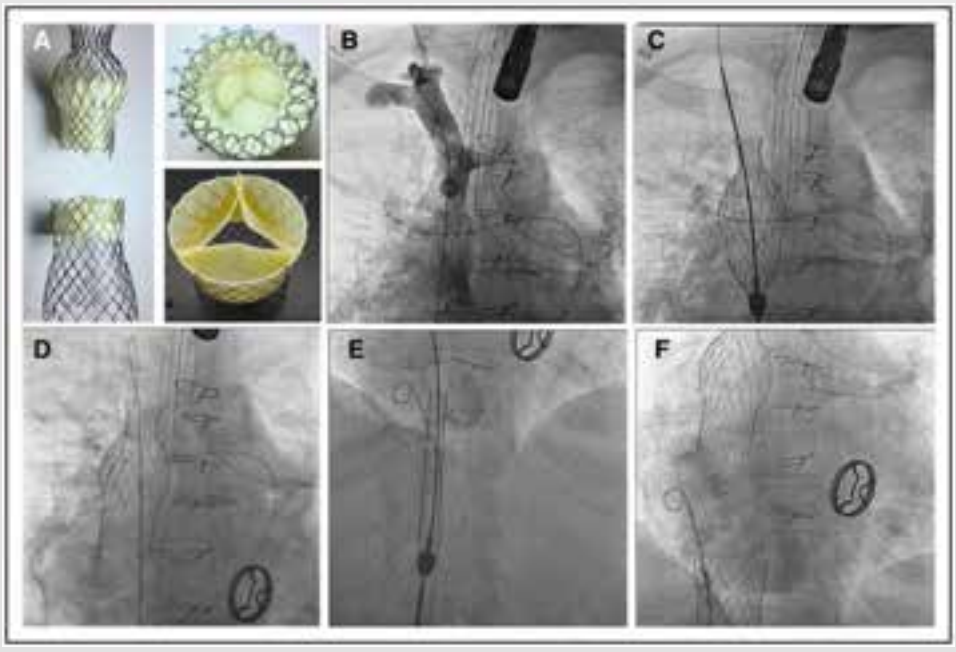


Figure 13. Caval valve implantation (CAVI) using TricValve®[3].

A The TricValve® Transcatheter Bicaval Valves.

B and C An angiogram of the right subclavian vein and SVC is obtained. A catheter marks the position of the right pulmonary artery.

D and E The device is developed above the IVC-right pulmonary artery crossing with the distal end at the level of the inflow of the lift brachiocephalic vein.

E and F The IVC valve is advanced into the right atrium (RA) in a 27F catheter and aligned with the distal valve segment ≈ 2 cm above the diaphragm protruding into the RA.

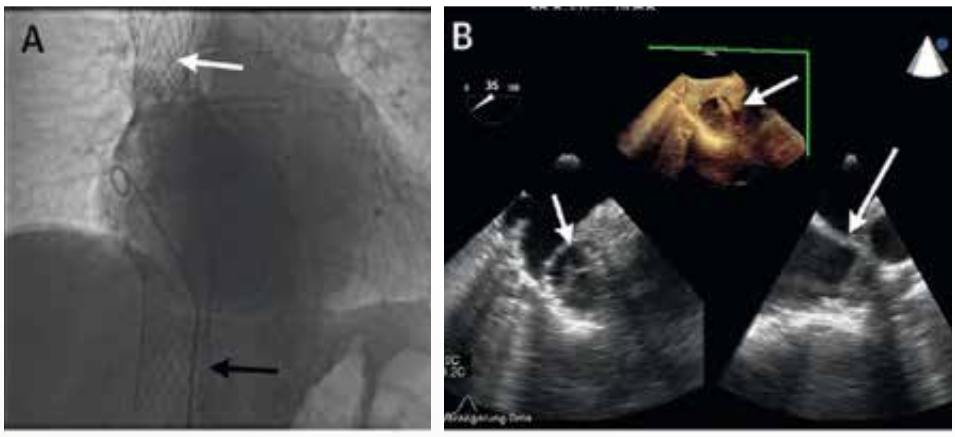


Figure 14. Bicaval Valve Implantation with the Self-Expandable TricValve®[1].

A Position of the self-expandable TricValve® in the superior vena cava (SVC) (white arrow) and inferior vena cava (IVC) (black arrow). The SVC valve is deployed with the landing zone of the enlarged mid-portion of the stent above the right pulmonary artery. The IVC valve is deployed with the upper, skirt-lined segment of the stent protruding into the right atrium and the device fully anchored in the IVC.

B Echocardiographic evaluation of prosthetic valve function in the SVC visualized by transesophageal echocardiography. Three-dimensional, short-, and long-axis views of the device after deployment are shown.

Overview published papers:

[1] Lauten et al., 2018. Caval Valve Implantation for Treatment of Severe Tricuspid Regurgitation. Journal of the American College of Cardiology 2018, Vol. 71, No. 10

[2] B. P. O. Neill, 2018. Caval Valve Implantation. Are 2 Valves Better Than 1? Circulation Cardiovascular Interventions 2018; 11:e006334, Editorial pp. 1–3

[3] Lauten et al., 2018. Interventional Treatment of Severe Tricuspid Regurgitation. Early Clinical Experience in a Multicenter, Observational, First-in-Man Study. Circulation Cardiovascular Interventions 2018; 11:e006061

[4] Figulla, Kiss, Lauten, 2016. Transcatheter interventions for tricuspid regurgitation – heterotopic technology: TricValve®. EuroIntervention 2016; 12:Y1-Y3

[5] Lauten et al., 2014. Caval valve implantation for treatment of tricuspid regurgitation: post-mortem evaluation after mid-term follow-up. European Heart Journal published November 14, 2013.

[6] Lauten et al., 2014. Percutaneous bicaval valve implantation for transcatheter treatment of tricuspid regurgitation: clinical observations and 12-month follow-up. Circulation Cardiovascular Interventions 2014; 7:268-272

[7] Lauten et al., 2012. Interventional perspective of tricuspid regurgitation – caval valve implantation from preclinical trials to fist human application. Journal of the American College of Cardiology 59, Issue 13, March 27, 2012

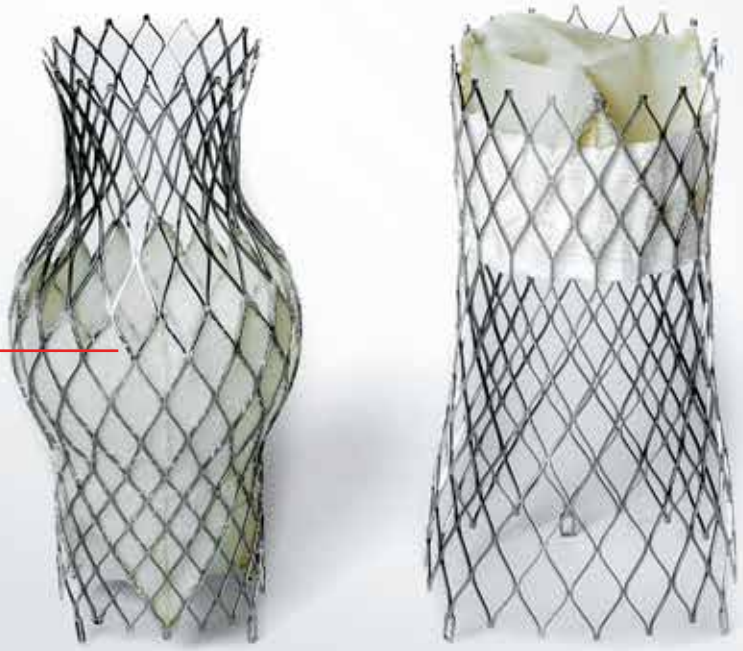
[8] Lauten et al., 2011. Heterotopic transcatheter tricuspid valve implantation: first-in-man application of a novel approach to tricuspid regurgitation. European Heart Journal 2011, 32, 1207-1213

TRICVALVE®

TRANSCATHETER BICAVAL VALVES

100 %

ORIGINAL SIZE



Product not yet commercially available.
CE certification under progress.

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