



State-of-the-art intra-procedural imaging for the mitral and tricuspid PASCAL Repair System

Rebecca T. Hahn * and Susheel K. Kodali

Columbia University Medical Center, New York Presbyterian Hospital, 177 Fort Washington Avenue, New York, NY 10032, USA

Received 19 December 2020; editorial decision 11 February 2021; accepted 22 February 2021; online publish-ahead-of-print 17 June 2021

Advanced intra-procedural imaging techniques have been integral to technical and procedural success transcatheter devices. A novel leaflet approximation therapy, the PASCAL Transcatheter Valve Repair System (Edwards Lifesciences, Irvine, CA, USA) has demonstrated high procedural success, acceptable safety, and significant clinical improvement in patients with severe mitral and tricuspid regurgitation and has CE mark approval in Europe with pivotal trials underway in the USA. This review outlines the pre-procedural imaging views and advanced transoesophageal imaging protocols both mitral and tricuspid valve device implantation.

Keywords

mitral regurgitation • tricuspid regurgitation • transcatheter repair

Introduction

Despite the poor outcomes associated with untreated significant mitral (MR) and tricuspid regurgitation (TR), surgical interventions to treat these valvular conditions have been underutilized^{1,2} resulting in a large population of symptomatic patients with limited options. Recent trials have shown significant benefits with transcatheter edge-to-edge repair (TEER) device for primary³ and secondary⁴ MR. A novel leaflet approximation therapy, the PASCAL Transcatheter Mitral Valve Repair (TMVr) System (Edwards Lifesciences, Irvine, CA, USA) has demonstrated high procedural success, acceptable safety, and significant clinical improvement in compassionate use patients.⁵ The 1-year results of the PASCAL TrAnScatheter Mitral Valve RePair System (CLASP) early feasibility study (NCT03170349) showed low complication rates and high survival, sustained MR reduction, and significant improvements in functional status and quality of life.⁶

The compassionate use of the PASCAL Transcatheter Tricuspid Valve Repair (TTVr) device for TR reported a 30-day mortality of 7.1%, acceptable safety metrics⁷ with 85% achieving mild or

moderate TR following device placement ($P < 0.001$). The single-arm, multicentre, prospective CLASP TR Early Feasibility Study (NCT03745313) recently reported its 30 days results showing a favourable safety profile with low major adverse events rate and no mortality at 30 days. The PASCAL TTVr device received CE mark in May 2020.

Although multiple prior imaging reviews have been published outlining the intra-procedural imaging for TEER guidance,^{8,9} there are differences in the procedural steps for the PASCAL device. Both the pivotal CLASP IID/IIF trial (NCT03706833) for degenerative and functional MR as well as the pivotal CLASP II TR trial (NCT04087145) for TR, are currently enrolling, and require pre-procedural transoesophageal echocardiography (TEE) for determination of valve morphology, severity of disease and adequacy of required intra-procedural imaging. This review will outline the standard TEE views for both pre-procedural and intra-procedural imaging and highlight the procedural differences with TEER. Patients whose images were used in this review were participants of the CLASP and CLASP TR studies. The studies were approved by the Columbia University Institutional Review Board.

*Corresponding author. Tel: +1 212 305 7060; Fax: +1 212 342 3660. E-mail: rth2@columbia.edu

© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

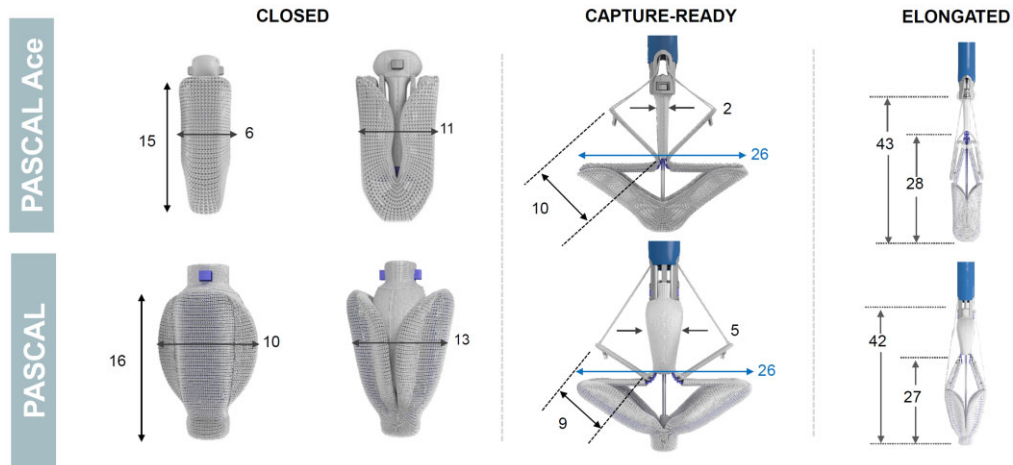


Figure 1 The PASCAL Repair System. There are features unique to the PASCAL repair system including a central spacer and adjacent paddles and clasps that attach the implant to the native leaflets to reduce regurgitation. (Note: all dimensions are in millimeters).

Mitral Valve View	Example	Tricuspid Valve View	Example
4 Chamber MV View (ME) Biplane: 4Ch/2CH		4 Chamber TV (ME)	
Commissural MV View (ME) Biplane: Commissural/LAX		RV Inflow/Outflow View ME (SWEEP)	
3 Chamber MV View (ME)		4 Chamber TV (DE)	
Transgastric MV SAX and LAX Views		Alternate Grasping Views (ME and DE)	
3D Volumes MV and IAS (ME)		TG TV SAX	
		DT RV view	
		3D Volumes	

Abbreviations: 3D = three-dimensional, DE = distal esophageal, DT = deep transgastric, IAS = interatrial septum, LA = left atrium, LAX = long axis, LV = left ventricle, ME = mid-esophageal, MV = mitral valve, SAX = short axis, TG = transgastric, TV = tricuspid valve

Figure 2 Primary imaging views for the mitral and tricuspid valve. The primary imaging views used for pre-procedural planning and intra-procedural guidance are shown in this figure.

PASCAL repair system

Features unique to the PASCAL repair system including a central spacer and adjacent paddles and clasps that attach the implant to the

native leaflets to reduce regurgitation and is available in two sizes (Figure 1). The narrower width of the ACE device has been favoured for manoeuvring through dense chordal structures. The spacer and paddles are a single structure of interwoven nitinol wires acting as a

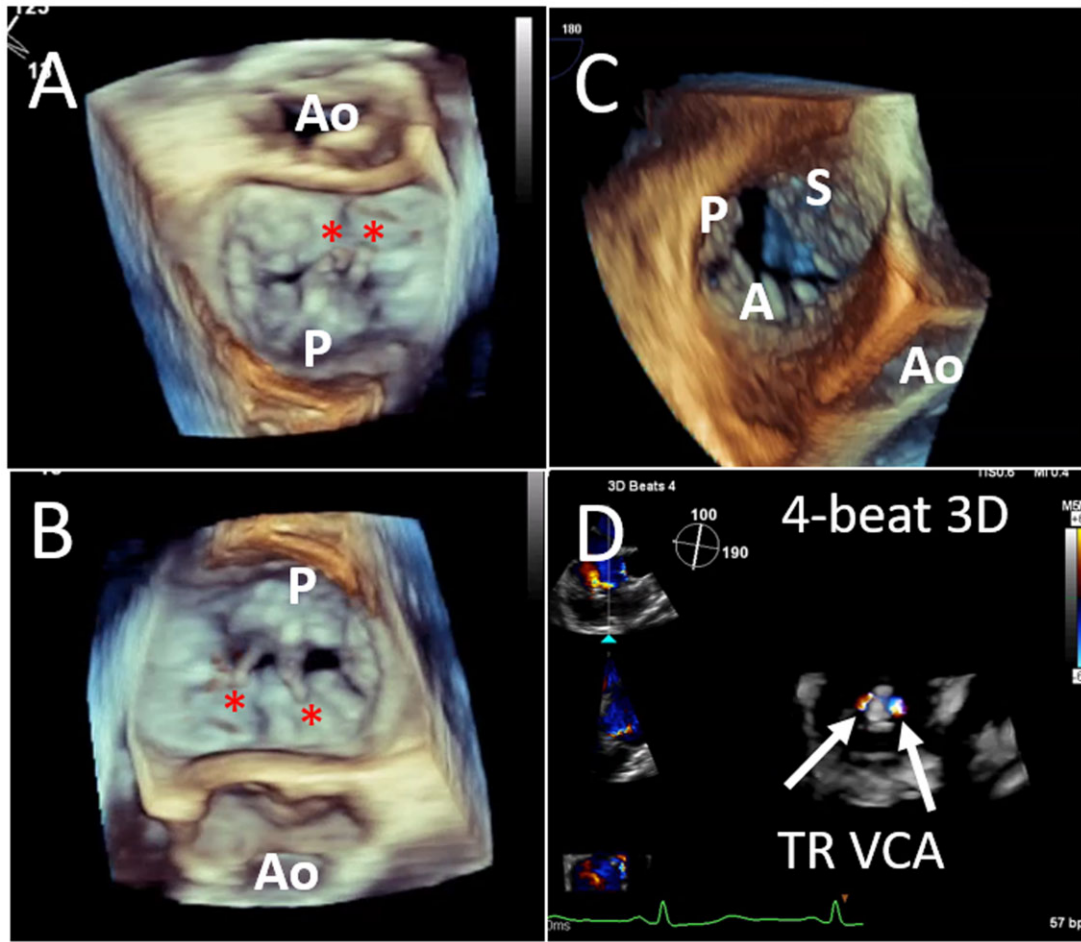


Figure 3 Three-dimensional imaging of the mitral and tricuspid valves. Standardized imaging display for the *en face* view of the MV with both lateral and Z-plane rotation (A) and without Z-plane rotation (B); ruptured P2 chordae are seen (asterisk). A real-time 3D *en-face* view of the TV without Z-plane rotation, results in leaflet orientation similar to the transgastric view (C). Creating multi-beat colour Doppler 3D volumes of the systolic regurgitant jet, allows planimetry of the MR VCA post-device (D). MR, mitral regurgitation; MV, mitral valve; TV, tricuspid valve; VCA, vena contracta area.

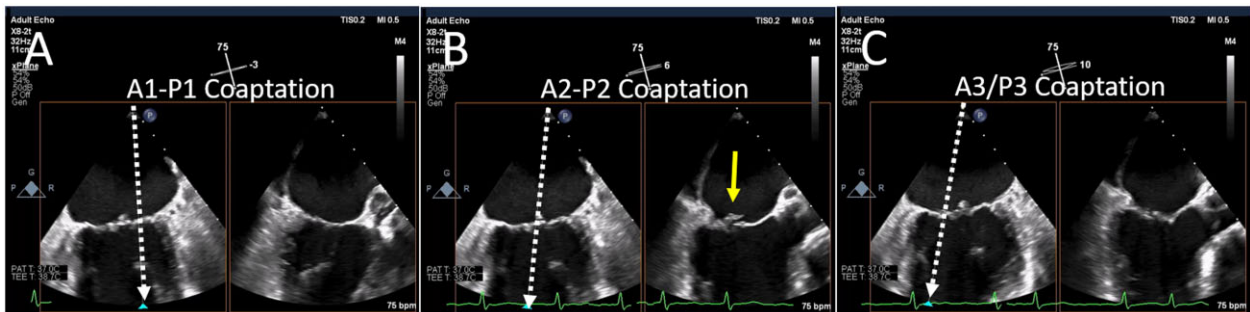


Figure 4 Biplane imaging from the MV commissural view. Using simultaneous biplane imaging with the mid-oesophageal MV commissural view as the primary image, a sweep of the entire commissure can be performed. (A) The position of the orthogonal image (white arrow) at the lateral commissure (A1-P1 scallops). (B) The position of the orthogonal image at the midline (A2-P2 scallops) where a small flail posterior scallop is imaged (yellow arrow). (C) The position of the orthogonal image at the medial commissure (A3-P3 scallops). MV, mitral valve.

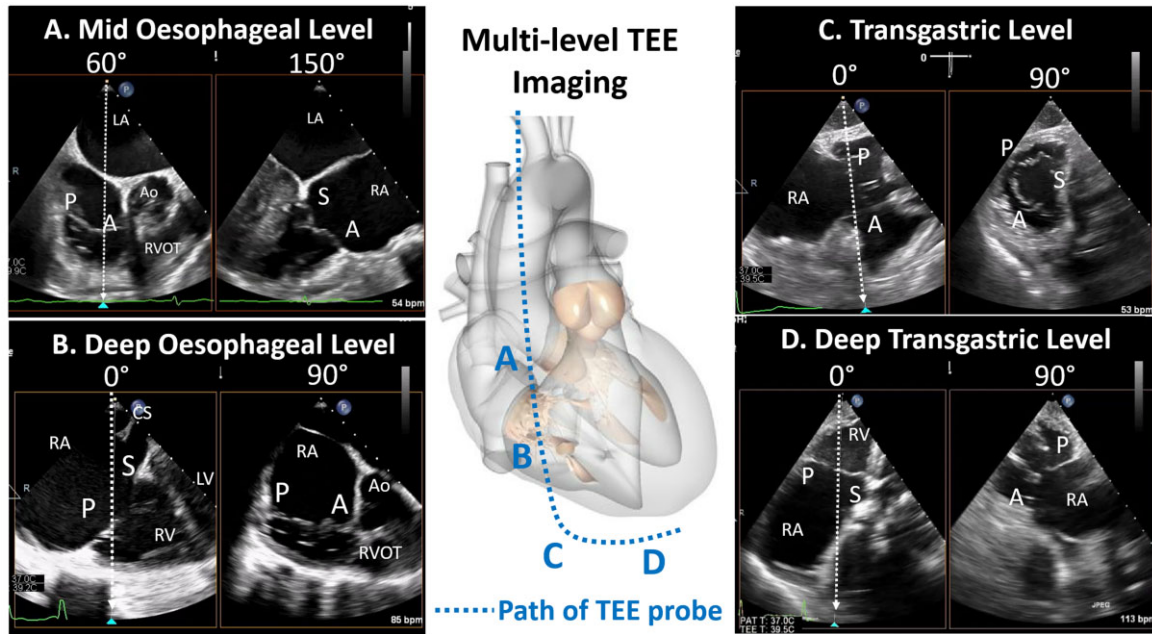


Figure 5 Four levels of imaging for the tricuspid valve. The path of the oesophagus allows for the generation of four imaging levels for the tricuspid valve: mid oesophageal level, deep oesophageal level, transgastric and deep transgastric. A, anterior leaflet; Ao, aorta; LA, left atrium; LV, left ventricle; P, posterior leaflet; RA, right atrium; RV, right ventricle; S, septal leaflet.

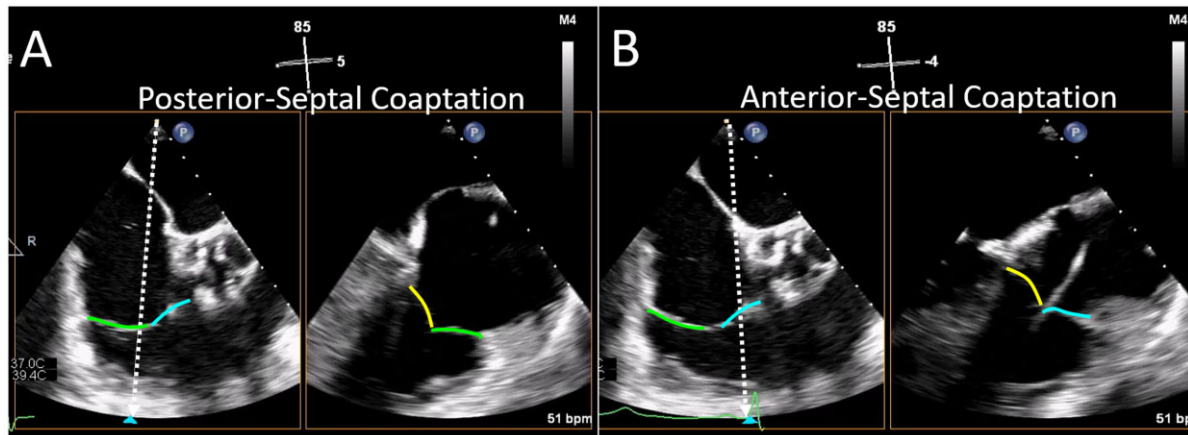


Figure 6 Biplane imaging from the TV commissural view. The mid-oesophageal right ventricular inflow-outflow view (at ~50–80°) is considered the TV ‘commissural’ view with the anterior (blue line) and posterior (green line) leaflets imaged and the septal leaflet (yellow line) behind the imaging plane. Moving the orthogonal biplane cursor towards the posterior wall (A) images the posterior and septal leaflets. Moving the orthogonal biplane cursor towards the aorta (B) images the anterior leaflet near the aorta and the septal leaflet. TV, tricuspid valve.

flexible frame to capture the leaflets and minimize leaflet stress.^{10,11} The nitinol clasps have a horizontal row of four retention elements near the top of the clasps intended to run parallel to the mitral leaflet collagen fibres, potentially reducing leaflet injury. The clasps can be

actuated simultaneously or independently when grasping the leaflets allowing for optimization of leaflet insertion. An elongation mechanism allows positioning and repositioning with less risk of chordal entrapment.

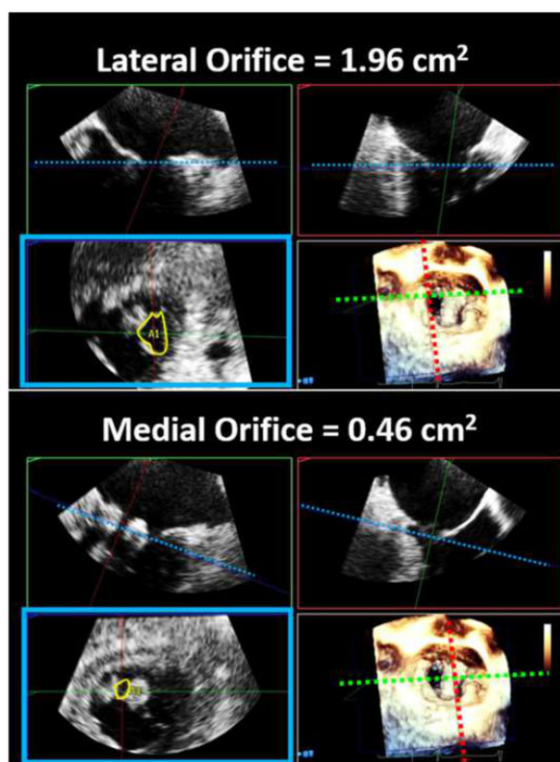


Figure 7 Post-device orifice area. Three-dimensional imaging is used to directly planimeter the MV orifice areas separately since the medial and lateral orifices are not typically in the same horizontal plane. Aligning the short-axis plane at the tips of leaflet in diastole (blue lines) allows the lateral orifice area (A) to be planimetered from the short-axis view (blue box). Realigning the short-axis plane for the medial orifice is shown in (B). MV, mitral valve.

Transoesophageal echocardiography imaging protocols

The PASCAL repair system is implanted under TEE and fluoroscopic guidance. The imaging protocols will be divided into the following sections: (i) standard views for pre-procedural planning, (ii) pre-procedural assessment of valve morphology and function, and (iii) guidance of the procedure. Each step will be divided into mitral-specific and tricuspid-specific imaging protocols.

Standard views for pre-procedural planning

Appropriate 2D and 3D imaging with Doppler should be performed prior to and following device placement to quantify valve function. Figure 2 shows the primary imaging levels and views required for assessment of MV and TV morphology and function utilizing the probe manipulations described in prior guidelines.¹² The standard four levels of imaging include: high oesophageal (HE), mid oesophageal (ME), shallow transgastric (TG), and deep transgastric (DT). For the MV

and TV, the HE level is rarely used. A new distal oesophageal (DE) imaging level has been added for imaging the TV.

Because of anatomic variability not only of the cardiac structures themselves but also the relationship of the oesophagus to the heart structures, it is important to confirm complex valvular anatomy using 3D imaging.¹³ The 'surgeon's view' imaging display for the *en face* view of the MV (Figure 3A) is advocated¹⁴ which requires varying degrees of Z-plane rotation depending on the acquisition image. The 3D *en face* MV view acquired from the 2D commissural view will image the posterior leaflet in the near field prior to Z-plane rotation (Figure 3B); some imagers/interventionalists prefer this image which minimizes image manipulation and mimics the 2D image by positioning the lateral commissure on the right and the medial commissure on the left side of the screen. Similarly the 3D *en face* TV view acquired from the 2D commissural view (and without Z-rotation), positions the interventricular septum on the right side of the screen, the aorta at 5 o'clock and the posterior leaflet in the near field (Figure 3C), an orientation similar to the TG SAX view.¹⁵ Creating multi-beat colour Doppler 3D volumes without splice artefacts for measurement of systolic regurgitant jet vena contracta area (VCA) is possible even with irregular rhythms (Figure 3D).

Mitral valve

Because of the relative positions of the oesophagus and left atrium, aligning the annulus perpendicular to the insonation beam may require right flexion in addition to retroflexion. Aligning the annulus perpendicular to the insonation beam has the following advantages: (i) both biplane images are typically perpendicular to leaflet coaptation (which allows simultaneous imaging of the clasp arms); (ii) orientation of the real-time multi-planar 3D image or 3D *en face* view is easier; and (iii) the trajectory of the system is more accurately assessed.

The ME MV commissural view at a transducer angle between 50° and 70°, is often seen as the 'home' view for the PASCAL system (Figures 2 and 4). Using biplane imaging, the orthogonal imaging plane can be positioned across the commissural line, and thus sweep from the lateral commissure of A1/P1 (right sector, Figure 5A) to the mid-line (A2/P2, Figure 4B), and finally the medial commissure (A3-P3, Figure 4C), without and with colour flow Doppler. TG views may be useful not only for Doppler of the aortic valve (i.e. to calculate forward stroke volume) but also to evaluate the MV (Figure 2). Although short-axis views of the MV are rarely used given the use of ME 3D imaging, occasionally acoustic shadowing prevents an adequate assessment of the tissue bridge and the TG short-axis view can be helpful. In addition, commissural regurgitant jets may be aligned with the insonation beam only from the TG views (Figure 2).

Tricuspid valve

The TV is the largest and most apically positioned of the four cardiac valves with a normal orifice area between 7 and 9 cm²¹⁶ requiring a larger field of view with greater depth of imaging, both factors resulting in a loss of spatial and temporal resolution. In addition, given the position of the TV in relation to the oesophagus the annulus cannot be aligned perpendicular to the insonation angle in the ME and DE views and imaging the thin TV leaflets throughout the cardiac cycle using lateral resolution, is also more challenging. Finally, the TV leaflet morphology is highly variable creating a complex regurgitant orifice.¹⁶

Table 1 Anatomic considerations for the PASCAL Repair System

	Inclusion	Suggested anatomic exclusions
Mitral regurgitation	<ul style="list-style-type: none"> • Primary severe, symptomatic MR • Secondary severe, symptomatic MR 	<p>Mitral valve anatomy precludes proper device deployment and function, including:</p> <ul style="list-style-type: none"> • Evidence of moderate to severe calcification in grasping area • Evidence of severe bi-leaflet/multi scallop prolapse involvement • Presence of significant cleft or perforation in grasping area • Leaflet mobility length <8 mm • Presence of two or more independent significant jets • Mitral valve orifice area <4.0 cm² • Echocardiographic evidence of intracardiac mass, thrombus, or vegetation • Echocardiographic evidence of severe right ventricular dysfunction per core lab assessment
Tricuspid regurgitation	<ul style="list-style-type: none"> • Primary severe, symptomatic TR • Secondary severe, symptomatic TR 	<p>Tricuspid valve anatomy precludes proper device deployment and function, including:</p> <ul style="list-style-type: none"> • Evidence of severe calcification in the annulus or subvalvular apparatus • Evidence of moderate to severe calcification in grasping area • Excessive chordae structure in grasping area • Presence of perforation in grasping area • Severe leaflet tethering or immobile leaflet • Primary non-degenerative tricuspid disease (e.g. carcinoid, rheumatic, endocarditis, traumatic, pacemaker lead-induced, iatrogenic, tricuspid stenosis) • Previous tricuspid valve repair or replacement that would interfere with device placement • Presence of trans-tricuspid pacemaker or defibrillator leads which would prevent proper TR reduction due to interaction of the lead with the leaflets

MR, mitral regurgitation; TR, tricuspid regurgitation.

Thus, all probe manipulations and four-probe levels are required for imaging the TV (Figure 2 and 5).^{12,16}

Similar to MV imaging, the 'home view' for the TV is the ME RV inflow-outflow view (mechanical rotation of ~60°) (Figure 6). From this view (either at the ME or DE level), the anterior leaflet is near the aorta and the posterior leaflet near the posterior free wall with the septal leaflet out-of-plane. Using this as the primary view, simultaneous biplane imaging can be used to image the entire coaptation line with the septal leaflet: from the aortic side (anterior-septal commissure) to the lateral side of the valve (posterior-septal commissure). The ME RV inflow-outflow view can thus be considered the TV 'commissural' view. Colour Doppler from the TV commissural view shows the long-axis of the typically elliptical or crescent-shaped jet along the length of the septal leaflet (Figure 2), and a sweep of the commissural line will thus identify the location of the regurgitation orifice. Importantly, the DE view typically images the TV through only right heart structures with no intervening left heart structures (i.e. prosthetic mitral devices) and may circumvent the acoustic shadowing from left heart structures.

The TG level of imaging is essential for TV interventions. Right flexion with ante-flexion creates the TG RV inflow-outflow view and simultaneous biplane imaging at the TV leaflet tips results in a short-axis view of the TV. A single plane short-axis view can be obtained by using only anteflexion, at a mechanical rotation of between 25° and

60°.¹⁵ From the short-axis view, the coaptation gaps at the tips of the three leaflets, as well as the exact origin of the TR jet can be assessed. This view may be particularly useful for aligning the clasp arms, particularly when 3D imaging is limited. Further insertion of the probe towards the apex of the heart results in the DT views which aligns the Doppler insonation angle for more accurate measurement of transvalvular flow velocities (Figure 2).

Assessment of valve morphology and function

Precise identification of atrioventricular valve morphology and function is required for pre-procedural planning in order to confirm: (i) severity of regurgitation, (ii) number and location of regurgitant jets, and (iii) suitability of anatomy for the PASCAL repair system. Although suitability for TEER has been delineated,¹⁷ defining morphologic suitability for the PASCAL repair system remains speculative at this time although investigators have shown that poor TEER patients may be candidates for this device.⁵

Mitral valve

Mitral valve morphology: both degenerative and functional MR may be appropriate targets for the PASCAL therapy with anatomic

Table 2 Procedural steps for implantation of the PASCAL Repair System**Procedural steps**

- I. Mitral valve implantation of the PASCAL Repair System
 - a. Transseptal puncture—mitral specific
 - b. Advancing the delivery system (2D and 3D guidance)
 - c. Catheter trajectory, implant position, and orientation above leaflets
 - d. Clasp identification
 - e. Positioning and orientation below the leaflets
 - f. Clasping the leaflets:
 - i. Simultaneous
 - ii. Independent
 - iii. Single leaflet optimization (for optimal result)
 - g. Pre-release assessment
 - i. MR severity (closed implant)
 - ii. Confirm leaflet insertion with open implant
 - iii. Mitral valve orifice area and gradient
 - h. Elongation—when needed to reposition or to introduce a second device
 - i. Implant release
 - j. Post-delivery assessment
 - i. MR severity
 - ii. Mitral valve orifice area and gradient
- II. Tricuspid valve implantation of the PASCAL Repair System
 - a. Positioning in the right atrium
 - b. Advancing the delivery system (2D and 3D guidance)
 - c. Catheter trajectory, implant position, and orientation above leaflets
 - d. Clasp identification
 - e. Confirming position and orientation below the leaflets
 - f. Clasping the leaflets:
 - i. Simultaneous
 - ii. Independent
 - iii. Single leaflet optimization (for optimal result)
 - g. Pre-release assessment
 - i. TR severity (closed implant)
 - ii. Confirm leaflet insertion with open implant
 - iii. Tricuspid valve orifice area and gradient
 - h. Elongation—when needed to reposition
 - i. Implant release
 - j. Post-delivery assessment
 - i. TR severity (closed implant)
 - ii. Tricuspid valve orifice area and gradient

MR, mitral regurgitation; TR, tricuspid regurgitation.

differences previously reviewed.^{17,18} MV anatomy which may preclude leaflet coaptation device implant or sufficient reduction in MR are shown in *Table 1*. Specific patient characteristics should always be considered when determining anatomic eligibility. For instance, a patient with a body surface area of 1.5 m² could have significant reduction in MR without an increase in MV gradient with a baseline MV area of <4.0 cm².

Mitral valve function: a comprehensive assessment of MV function both at baseline and following device placement includes:

- (1) Assessment of MV orifice area and diastolic transmitral gradient: peak and mean transmitral gradients should be recorded along with heart rate.¹⁹ In the PASCAL compassionate use report, a single device resulted in a mean MV area reduction of ~47% and mean gradient = 3.0±1.0 mmHg.⁵ Because gradients are dependent on loading conditions and chamber compliance, planimetry of the MV orifice at baseline and post-device, should also be performed using 3D volumes (*Figure 7*). Two devices resulted in a mean MV area reduction of ~59% and mean gradient = 4.0±1.0 mmHg.
- (2) Location and Severity MR: using the ME commissural view, simultaneous biplane imaging with a 'sweep' of the MV coaptation zone (*Figures 2 and 4*) allows the imager to identify the location and approximate size of the regurgitant jet(s). Standard measures of MR severity should be performed as per society guidelines.^{20,21} However intra-procedurally, the most efficient method for assessing MR severity both at baseline and following device placement is planimetry of the 3D VCA (*Figure 3D*).²² Finally, following transcatheter leaflet repair, 3D VCA has been shown to accurately assess MR severity²³ and predict outcomes.²⁴
- (3) Pulmonary venous inflow: systolic reversal of pulmonary vein inflow is a specific sign for severe MR.²⁰ Following leaflet repair, improvement of forward systolic flow in the pulmonary veins has become an important measure of device efficacy, and a predictor of improved outcomes.^{25,26}
- (4) Other parameters: following device placement, recent American Society of Echocardiography guidelines suggest other indicators of improvement in MR severity including: appearance of spontaneous contrast in the left atrium, an increase in forward stroke volume and a reduction in ejection fraction.²⁷

Tricuspid valve

Tricuspid valve morphology: similar to MV morphology, TR can be divided in primary and secondary disease. Primary TR is relatively rare with one study showing cardiac implantable devices the most frequent cause.²⁸ Secondary TR is far more common and can be morphologically characterized as atrial functional and ventricular functional TR.²⁹

Tricuspid valve function: a comprehensive assessment of TV function both at baseline and following device placement includes:

- (1) Assessment of TV orifice area and diastolic transtricuspid gradient: planimetry of the TV orifice should be performed using 3D multi-planar reconstruction and peak and mean transtricuspid gradients should be recorded along with heart rate.
- (2) Location and severity of TR: using the 2D ME RV inflow-outflow view and 3D biplane sweep of the TV coaptation zone, location and approximate size of the regurgitant jet(s) can be determined. Standard measures of TR severity should be performed as per society guidelines.^{20,21} However new methods of assessing severity of TR¹⁶ as well as an extended severity grading scheme³⁰ is currently being used in early feasibility and pivotal trials of transcatheter TV

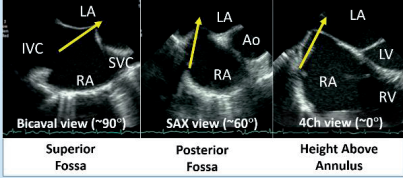
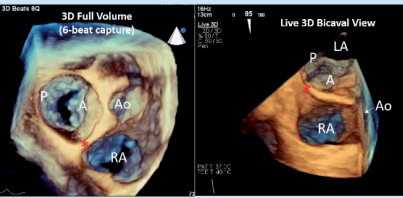
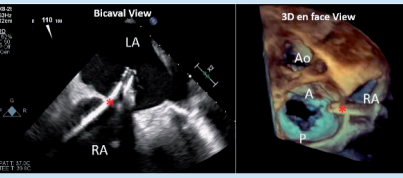
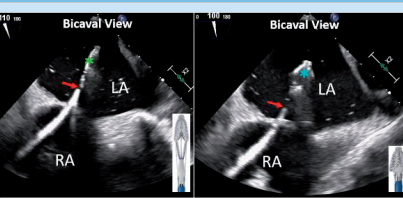
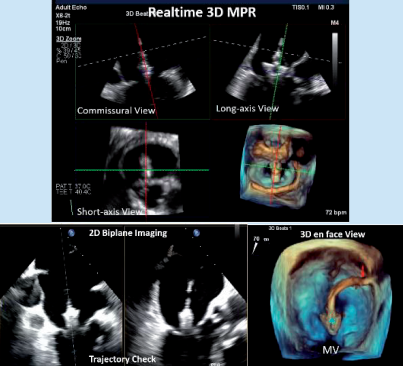
Mitral Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
Procedural Step for PASCAL Repair System: Transseptal puncture and introduction of catheters		
<ul style="list-style-type: none"> Locate the position and direction of transseptal catheter puncture ~4.5 cm above the annular plane in the mid-to-posterior fossa (adjacent to the mitral commissural line) with a posterior and superior direction of the catheter 3 Imaging views are used to confirm the position: bicaval view (superior/inferior position), SAX view (anterior/posterior position) and the 4Ch view (height above the annular plane). 	 	<ul style="list-style-type: none"> Mal-positioned transseptal puncture results in difficulty achieving the optimal trajectory of the implant 3D Imaging of the interatrial septum helps identify the location of the medial MV commissure and transseptal puncture site (red asterisk)
<ul style="list-style-type: none"> Position the PASCAL delivery system so that the tip (double-echodensity, red star) is across the interatrial septum (IAS). 		<ul style="list-style-type: none"> Maintaining the guide across the interatrial septum is recommended but not absolutely required to steer the implant in the left atrium.
Procedural Step for PASCAL Repair System: Advancing the Delivery System		
<ul style="list-style-type: none"> Follow the entrance of the elongated implant (green asterisk) into the left atrium, ensuring that the implant is clear of adjacent anatomy. (Note: Guide catheter tip noted by red arrow) Image implant closure (blue asterisk) 		<ul style="list-style-type: none"> Avoid trauma to adjacent structures with guide or elongated implant 3D imaging is optional
<ul style="list-style-type: none"> Guide manipulation of the steering mechanisms to position the implant (blue asterisk) above the desired mitral valve scallops. Confirm the appropriate catheter trajectory, implant position 		<ul style="list-style-type: none"> 3D imaging is essential and the primary imaging modality for guiding implant the valve and confirming appropriate catheter trajectory Real-time 3D multi-planar reconstructions allows for live imaging of the 2 orthogonal long-axis view, short-axis view and 3D en face view

Figure 8 Procedural steps for PASCAL mitral device implantation. (A) The imaging requires for transseptal puncture, advancing the delivery system (2D and 3D guidance) and implant orientation. (B) The next procedural steps of positioning and orientating the device below the leaflets, clasp the leaflets and pre-delivery assessment. (C) The imaging necessary for post-implant assessment of mitral valve function as well as haemodynamic benefit, and safe removal of the delivery catheter.

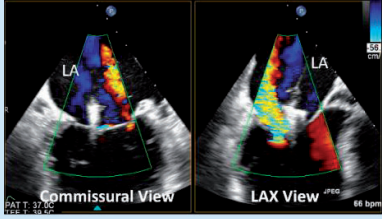
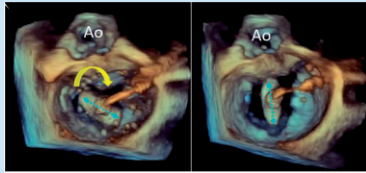
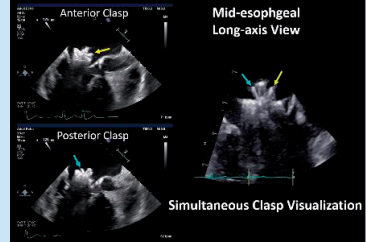
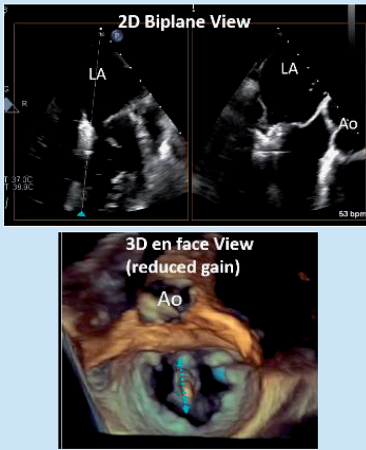
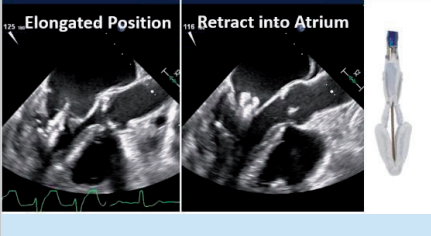
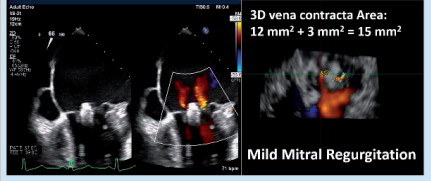
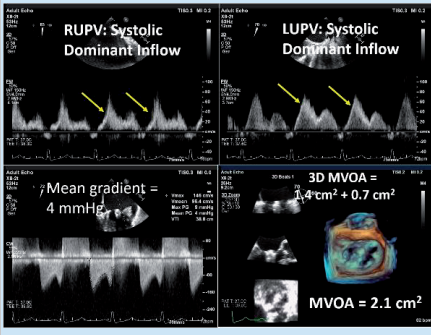
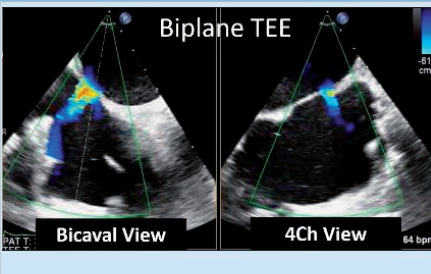
Mitral Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
Procedural Step for PASCAL Repair System: Orient Implant and Identify Anterior and Posterior Clasp		
<ul style="list-style-type: none"> Using color Doppler as a guide, position the implant over the desired location relative to the regurgitant orifice 		<ul style="list-style-type: none"> If the regurgitant orifice is not at the A2-P2 coaptation, ideal implant orientation may not necessarily be perpendicular to the line of coaptation
<ul style="list-style-type: none"> Guide the orientation/rotation of the implant paddles orthogonal to the commissure line at the desired location of implantation 		<ul style="list-style-type: none"> Inappropriate orientation may result in failure to grasp adequate anterior and posterior tissue risking single leaflet device attachment
<ul style="list-style-type: none"> Determine which slider controls which clasp Determine the correct imaging plane enables imaging of both clasps simultaneously 		<ul style="list-style-type: none"> 2D single plane, biplane or 3D imaging can be used Simultaneous fluoroscopic imaging is essential
Procedural Step for PASCAL Repair System: Confirming position and orientation below the leaflets		
<ul style="list-style-type: none"> Confirm location of the implant relative to the regurgitant lesion Advance the delivery system beneath the leaflets using 2D (single or biplane) imaging. Note that stored frictional force in the catheters cause the implant to rotate upon advancement and retraction of the device and orientation confirmation should always be performed 		<ul style="list-style-type: none"> Although 2D imaging may be the first clue to implant rotation (both paddles no longer imaged in a single plane), 3D imaging should be used to confirm the location and orientation of the implant Reducing the gain of the 3D image allows clear visualization of the implant beneath the thin mitral valve leaflets without changing the level of imaging
Procedural Step for PASCAL Repair System: Clasping the leaflets		

Figure 8 Continued.

Mitral Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
<ul style="list-style-type: none"> Continuously image as the implant is retracted Once leaflets are laying on inner paddles the clasps are dropped and imaging verifies leaflet insertion: visualization of clasp bounce should be seen however does not ensure adequate leaflet length capture Simultaneous capture of leaflets is most commonly performed, however independent grasping may be performed After capture of both leaflets, single leaflet optimization may be performed for optimal result 		<ul style="list-style-type: none"> High frame rate (FR) and line density (LD) are required thus performing this step typically requires 2D single plane (highest FR,LD), or 2D biplane (lower FR, LD) imaging Real-time 3D (with or without multi-planar imaging) results in the lowest FR and LD however can be used if visualization of leaflet motion is adequate
<p>Procedural Step for PASCAL Repair System: Pre-release assessment</p>		
<ul style="list-style-type: none"> Confirm the following: <ol style="list-style-type: none"> adequate tissue bridge and leaflet insertion between paddles and spacer, appropriate location of the implant, appropriate reduction in MR Use of biplane imaging with the commissural view as the primary view, permits imaging of long-axis views on either side of the implant to confirm capture of both leaflets 		<ul style="list-style-type: none"> On initial closure note reduction in MR (may see acute increase in BP, reduction in LA pressure) Measurement of leaflet lengths before and after closure ensures adequate grasped leaflet length. (NOTE: Independent clasp opening can be performed for these measurements)
<ul style="list-style-type: none"> Following implant closure and prior to release of the implant assess: <ol style="list-style-type: none"> Mitral valve orifice area and gradients, Residual regurgitant severity Hemodynamic benefit (improvement in systolic forward flow): <ol style="list-style-type: none"> Pulmonary venous inflow LV outflow tract stroke volume New onset "smoke" in the LAA 		<ul style="list-style-type: none"> 3D planimetry of both the mitral valve area and the color Doppler vena contracta area should be performed using multi-planar reconstruction (not imaged here)

Figure 8 Continued.

Mitral Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
<ul style="list-style-type: none"> If the implant requires repositioning in the atrium, it is set in the elongated position and slowly retracted into the atrium 		<ul style="list-style-type: none"> In the elongated position, entanglement in chordae is minimized
Procedural Step for PASCAL Repair System: Post-release assessment		
<ul style="list-style-type: none"> Following release of the implant verify the same parameters as noted above: <ol style="list-style-type: none"> Mitral valve orifice area and gradients, Residual regurgitant severity Hemodynamic benefit (improvement in systolic forward flow): <ol style="list-style-type: none"> Pulmonary venous inflow LV outflow tract stroke volume New onset “smoke” in the LAA 		<ul style="list-style-type: none"> Standard quantitative methods (i.e. PISA, quantitative Doppler) cannot be performed accurately following PASCAL Quantitation of MR relies on 3D color Doppler planimetry of the vena contracta area
<ul style="list-style-type: none"> Determine whether second implant is required 		<ul style="list-style-type: none"> Desirable mean transmitral gradient is < 5 mmHg Desirable valve area is >2.0 cm²
Procedural Step for PASCAL Repair System: Image the delivery catheter to assure safe withdrawal		
<ul style="list-style-type: none"> Image the removal of the delivery catheter Document the resulting interatrial atrial defect Document the absence of a pericardial effusion 		<ul style="list-style-type: none"> Closing the iatrogenic atrial septal defect can be considered depending on the presence of a significant shunt (either left-to-right or right-to-left).

Abbreviations: 2D = two-dimensional, 3D = three-dimensional, A = anterior mitral valve leaflet, Ao = aorta, IAS = interatrial septum, IVC = inferior vena cava, LA = left atrium, LUPV = left upper pulmonary vein, LV = left ventricle, MR = mitral regurgitation, MVOA = mitral valve orifice area, P = posterior mitral valve leaflet, RA = right atrium, RUPV = right upper pulmonary vein, RV = right ventricle, SVC = superior vena cava

Figure 8 Continued.

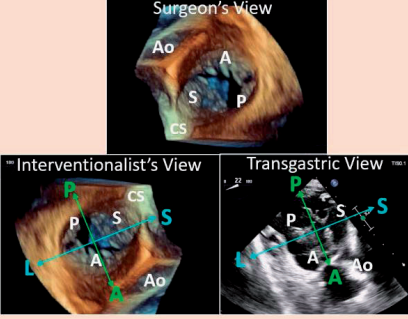
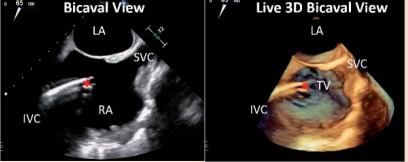
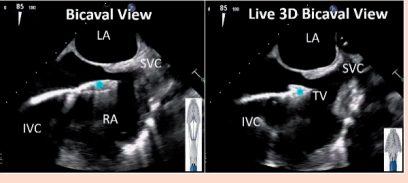
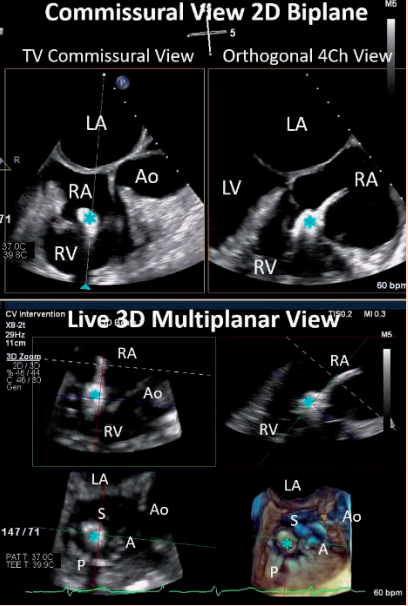
Tricuspid Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
Procedural Step for PASCAL Repair System: Pre-Procedural Assessment		
<ul style="list-style-type: none"> Interventionalist and Imager should agree on the orientation and nomenclature to be used throughout the procedure. 2 standard orientations are acceptable: the surgeon's view with the anterior leaflet on top, or the interventionalist's view with the anterior leaflet on the bottom of the 3D image. The latter orientation is the same as a 2D transgastric view and thus may be preferred. 		<ul style="list-style-type: none"> Directional indicators show the septal-lateral plane (blue arrow) and the anterior-posterior plane (green arrow). Note: the tricuspid valve frequently is composed of either only 2 leaflets, or >3 leaflets. Deep folds in the leaflets may also result in the appearance of additional leaflets
Procedural Step for PASCAL Repair System: Advancing the Delivery System		
<ul style="list-style-type: none"> Position the PASCAL™ delivery system so that the tip (double-echodensity, red star) is 1-2 cm into the RA from the IVC/RA junction 		<ul style="list-style-type: none"> 3D narrow sector from the bicaval view allows imaging of the tricuspid TV in the elevational plane
<ul style="list-style-type: none"> Follow the entrance of the elongated implant (blue star) into the right atrium, ensuring that the implant is clear of adjacent anatomy. Image implant closure (blue asterisk) 		<ul style="list-style-type: none"> Avoid trauma to adjacent structures with guide or elongated implant 3D imaging is optional
<ul style="list-style-type: none"> Guide manipulation of the steering mechanisms to position the implant (blue asterisk) above the desired tricuspid valve leaflets. Confirm the appropriate catheter trajectory, implant position 		<ul style="list-style-type: none"> 3D imaging is essential and the primary imaging modality for guiding the implant to the valve and confirming appropriate catheter trajectory Real-time 3D multi-planar reconstructions allows for live imaging of the 2 orthogonal long-axis views, short-axis view and 3D en face view

Figure 9 Procedural steps for PASCAL tricuspid device implantation. (A) The imaging requires for pre-device assessment, advancing the delivery system (2D and 3D guidance) and positioning and orientating the device below the leaflets. (B) The next steps of clamping the leaflets and pre-delivery assessment. (C) The imaging necessary for post-implant assessment of tricuspid valve function as well as haemodynamic benefit.

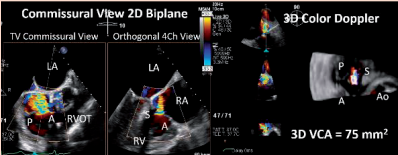
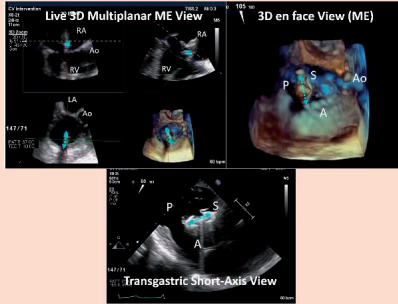
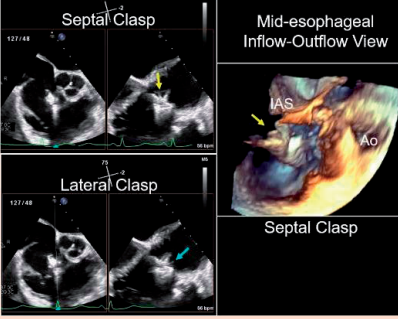
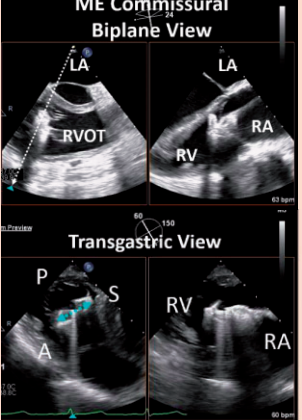
Tricuspid Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
Procedural Step for PASCAL Repair System: Orient Implant and Identify Anterior and Posterior Clasp		
<ul style="list-style-type: none"> Using color Doppler as a guide, position the implant over the desired location relative to the regurgitant orifice 		<ul style="list-style-type: none"> Most TR regurgitant jets occur along the septal leaflet coaptation line
<ul style="list-style-type: none"> Guide the orientation/rotation of the implant arms to along the commissure line at the desired location of implantation 		<ul style="list-style-type: none"> 3D multiplanar or en face views are essential. 2D transgastric short-axis view should be used to confirm
<ul style="list-style-type: none"> Determine which slider controls the individual clasps Determine the correct imaging plane which enables imaging of both clasps simultaneously 		<ul style="list-style-type: none"> 2D single plane, biplane or 3D imaging can be used. In this example the yellow arrow indicates the septal clasp and the blue arrow indicates the lateral clasp
Procedural Step for PASCAL Repair System: Confirming position and orientation below the leaflets		
<ul style="list-style-type: none"> Image the delivery system advance beneath the leaflets using 2D (single or biplane) imaging. Confirm location and orientation of the implant using 2D imaging from multiple imaging levels 		<ul style="list-style-type: none"> Transgastric short-axis views should be used to confirm orientation 2D transgastric views can be used to visualize leaflets (or leaflet tips) between the paddles and the spacer however this view will not typically allow a measurement of the leaflet length within the paddles or clasps.

Figure 9 Continued.

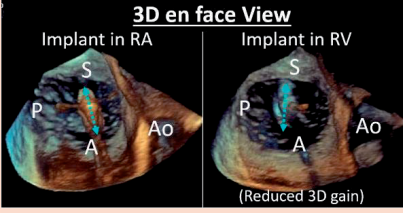
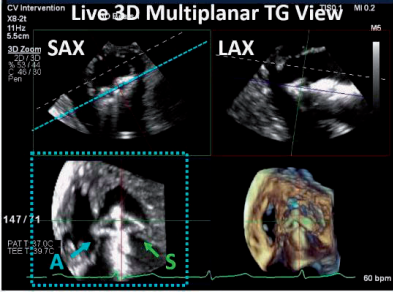
Tricuspid Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
<ul style="list-style-type: none"> Confirm location and orientation of the implant using 3D imaging from multiple imaging levels 	<p>3D en face View</p> 	<ul style="list-style-type: none"> If an adequate 3D en face rendering is obtained, reducing the gain of the 3D image allows clear visualization of the implant beneath the tricuspid valve leaflets
<p>Procedural Step for PASCAL Repair System: Clasping the leaflets</p>		
<ul style="list-style-type: none"> Continuously image both paddles and leaflets as the implant is retracted Once leaflets are laying on Inner paddles the clasps are dropped and imaging verifies leaflet insertion: clasp "bounce" may not be seen in the setting of lower systolic force Simultaneous capture of leaflets or independent grasping can be performed. After capture of both leaflets, single leaflet optimization may be performed for optimal result 	<p>ME Commissural View 2D Biplane</p>  <p>Live 3D Multiplanar TG View</p> 	<ul style="list-style-type: none"> Although 2D single plane (highest FR,LD), or 2D biplane (lower FR, LD) imaging are preferred, mid-esophageal 2D imaging of the anterior clasp is frequently shadowed by the spacer (blue box, blue arrow) 3D live multiplanar transgastric views can be used to visualize both leaflets in the paddles (blue box). NOTE: transgastric biplane imaging (LAX view) is not typically able to image leaflet insertion
<p>Procedural Step for PASCAL Repair System: Pre-release assessment</p>		

Figure 9 Continued.

Tricuspid Valve Imaging Recommendations	Examples of Imaging	Caveats of Imaging
<ul style="list-style-type: none"> Confirm the following: <ol style="list-style-type: none"> adequate tissue bridge and leaflet insertion between paddles and spacer, appropriate location of the implant, appropriate reduction in TR Use of biplane imaging with the commissural view as the primary view, permits imaging of long-axis views on either side of the implant to confirm capture of both leaflets Always confirm leaflet grasp in the transgastric views <ul style="list-style-type: none"> Following implant closure and prior to release of the implant assess: <ol style="list-style-type: none"> Tricuspid valve orifice area and gradients, Residual regurgitant severity Hemodynamic benefit (hepatic venous inflow) If the implant requires repositioning in the atrium, it is set in the elongated position and slowly retracted into the atrium 		<ul style="list-style-type: none"> Measurement of leaflet lengths before and after closure ensures adequate grasped leaflet length. (NOTE: Independent clasp opening can be performed for these measurements) Reduction in TR on initial closure 2D transgastric views with open paddles are essential for imaging leaflets on the paddles: with the clasps down the leaflet tips should reach to the center of the device (or at least >50% of respective paddle length) in both systole and diastole. 3D real-time multiplanar imaging can also be used to confirm leaflet insertion between the paddles and spacer <ul style="list-style-type: none"> 3D planimetry of both the tricuspid valve area and the color Doppler vena contracta area should be performed using multi-planar reconstruction (not imaged here) In the elongated position, entanglement in chordae is minimized

Figure 9 Continued.

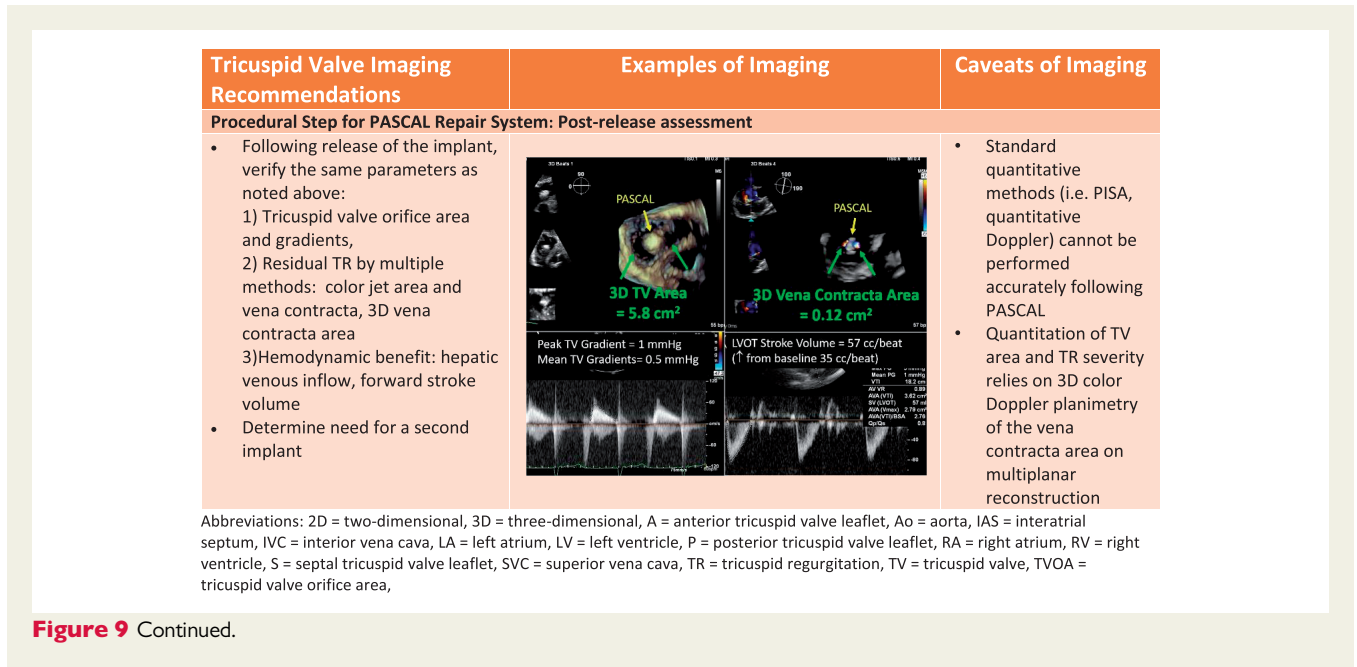


Figure 9 Continued.

- devices. Recent studies have correlated the extended grading scheme with outcomes.^{31,32}
- (3) Hepatic venous inflow: systolic reversal of hepatic vein inflow is thought to be a specific sign for severe TR.²⁰ Following the leaflet repair, improvement of forward systolic flow has been seen.²⁷

Intra-procedural guidance

Intra-procedural guidance of leaflet coaptation devices rely heavily on maximizing the strengths of both 2D and 3D imaging.³³ Because of these unique structural and mechanistic features of the PASCAL and ACE devices, imaging can differ from the TEER device. General procedural considerations include: imaging the number and location of chordae which may determine whether to use the PASCAL or the ACE device, and the frequent use of multiple imaging planes to circumvent the acoustic shadowing created by the spacer.

Differences between the imaging steps for the TEER and PASCAL system include the safe introduction of the elongated device followed by implant closure and shortening prior to redirecting to the atrioventricular annular plane. Manoeuvring the shortened device reduces the risk of injury (i.e. the lateral left atrial wall for the mitral and interatrial septum for the tricuspid device). In order to utilize independent leaflet grasping, the individual clasps must be identified. Finally, repositioning by retraction of the elongated device infrequently causes injury to the subvalvular or valvular structures, but nonetheless must be carefully monitored during repositioning of the device.

The procedural steps outlined in Table 2, are shown with the essential TEE imaging views for the mitral device (Figure 8A–C) and tricuspid device (Figure 9A–C).

Discussion

The PASCAL repair system to treat MR and TR is currently in pivotal trials with pre-procedural TEE required for inclusion, and intra-

procedural imaging essential for technical success. The inherent advantages of 2D (greater resolution) and 3D (improved anatomic visualization) should always be considered during each procedural step. The imaging levels and views for the MV have been standardized for commercially available TEER however imaging of the TV remains a challenge given the relationship between the TV and oesophagus previously discussed. Implantation of the TV device typically requires greater probe manipulations and use of multiple imaging planes (ME, DE, TG, and DT) as well as multiple imaging modalities (2D and 3D) to optimize visualization of leaflets within the clasps and confirm adequate leaflet grasp. Extensive probe manipulation as well as longer procedures, increase the risk of complications from TEE imaging.³⁴ Additional imaging modalities such as transthoracic and intracardiac echocardiography (2D and 3D) have been successfully used during these procedures when TEE imaging is limited.^{9,35} As 3D intracardiac phased array probes become commercially available this imaging modality has the potential to supercede TEE imaging for the TV.

Conclusions

The novel PASCAL transcatheter valve repair system (Edwards Lifesciences, Irvine, CA, USA), has received CE mark for treatment of both MR and TR of either primary or secondary aetiology. Both devices are currently in pivotal trials. Because this device relies heavily on TEE imaging the current imaging review may be useful in patient selection and technical success of the procedure.

Conflict of interest: R.T.H. is a speaker and consultant for Edwards Lifesciences and is the Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she

receives no direct industry compensation. S.K.K. reports no relationships relevant to the contents of this article to disclose.

References

- lung B, Delgado V, Rosenhek R, Price S, Prendergast B, Wendler O, And the EORP VHD II Investigators et al. Contemporary presentation and management of valvular heart disease: the EURObservational Research Programme Valvular Heart Disease II Survey. *Circulation* 2019;**140**:1156–69.
- Benfari G, Antoine C, Miller WL, Thapa P, Topilsky Y, Rossi A et al. Excess mortality associated with functional tricuspid regurgitation complicating heart failure with reduced ejection fraction. *Circulation* 2019;**140**:196–206.
- Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med* 2011;**364**:1395–406.
- Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM et al. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;**379**:2307–18.
- Praz F, Spargias K, Chrissoheris M, Bullesfeld L, Nickenig G, Deuschl F et al. Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgitation: a multicentre, prospective, observational, first-in-man study. *Lancet* 2017;**390**:773–80.
- Webb JG, Hensey M, Szerlip M, Schäfer U, Cohen GN, Kar S et al. 1-Year outcomes for transcatheter repair in patients with mitral regurgitation from the CLASP Study. *JACC Cardiovasc Interv* 2020;**13**:2344–57.
- Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovas Imaging* 2017;**18**:1342–3.
- Wunderlich NC, Siegel RJ. Peri-interventional echo assessment for the MitraClip procedure. *Eur Heart J Cardiovas Imaging* 2013;**14**:935–49.
- Hahn RT, Nabauer M, Zuber M, Nazif TM, Hausleiter J, Taramasso M et al. Intraprocedural imaging of transcatheter tricuspid valve interventions. *JACC Cardiovasc Imaging* 2019;**12**:532–53.
- Zhang Y, Wang VY, Morgan AE, Kim J, Handschumacher MD, Moskowitz CS et al. Mechanical effects of MitraClip on leaflet stress and myocardial strain in functional mitral regurgitation - a finite element modeling study. *PLoS One* 2019;**14**: e0223472-e.
- Caballero A, Mao W, McKay R, Hahn RT, Sun W. A comprehensive engineering analysis of left heart dynamics after MitraClip in a functional mitral regurgitation patient. *Front Physiol* 2020;**11**:432.
- Hahn RT, Abraham T, Adams MS, Bruce CJ, Glas KE, Lang RM et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr* 2013;**26**: 921–64.
- Badano LP, Agricola E, de Isla LP, Gianfagna P, Zamorano JL. Evaluation of the tricuspid valve morphology and function by transthoracic real-time three-dimensional echocardiography. *Eur J Echocardiogr* 2009;**10**:477–84.
- Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *J Am Soc Echocardiogr* 2012;**25**:3–46.
- Hausleiter J, Braun D, Orban M, Latib A, Lurz P, Boekstegers P et al. Patient selection, echocardiographic screening and treatment strategies for interventional tricuspid repair using the edge-to-edge repair technique. *EuroIntervention* 2018;**14**:645–53.
- Hahn RT. State-of-the-art review of echocardiographic imaging in the evaluation and treatment of functional tricuspid regurgitation. *Cir Cardiovas Imaging* 2016;**9**: e005332. doi: 10.1161/CIRCIMAGING.116.005332. PMID: 27974407.
- Bonow RO, O'Gara PT, Adams DH, Badhwar V, Bavaria JE, Elmariah S et al. 2020 Focused update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol* 2020;**75**:2236–70.
- Stone GW, Vahanian AS, Adams DH, Abraham WT, Borer JS, Bax JJ et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 1: clinical trial design principles: a consensus document from the mitral valve academic research consortium. *J Am Coll Cardiol* 2015;**66**:278–307.
- Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *J Am Soc Echocardiogr* 2009;**22**:1–23. quiz 101–2.
- Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2017;**30**:303–71.
- Lancellotti P, Moura L, Pierard LA, Agricola E, Popescu BA, Tribouilloy C, on behalf of the European Association of Echocardiography et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr* 2010;**11**:307–32.
- Goebel B, Heck R, Hamadanchi A, Otto S, Doent T, Jung C et al. Vena contracta area for severity grading in functional and degenerative mitral regurgitation: a transoesophageal 3D colour Doppler analysis in 500 patients. *Eur Heart J Cardiovas Imaging* 2018;**19**:639–46.
- Avenatti E, Mackensen GB, El-Tallawi KC, Reisman M, Gruye L, Barker CM et al. Diagnostic value of 3-dimensional vena contracta area for the quantification of residual mitral regurgitation after MitraClip procedure. *JACC Cardiovasc Interv* 2019;**12**:582–91.
- Dietl A, Prieschenk C, Eckert F, Birner C, Luchner A, Maier LS et al. 3D vena contracta area after MitraClip® procedure: precise quantification of residual mitral regurgitation and identification of prognostic information. *Cardiovasc Ultrasound* 2018;**16**:1.
- Ikenaga H, Yoshida J, Hayashi A, Nagaura T, Yamaguchi S, Rader F et al. Usefulness of intraprocedural pulmonary venous flow for predicting recurrent mitral regurgitation and clinical outcomes after percutaneous mitral valve repair with the MitraClip. *JACC Cardiovasc Interv* 2019;**12**:140–50.
- Corrigan FE, 3rd, Chen JH, Maini A, Lisko JC, Alvarez L, Kamioka N et al. Pulmonary venous waveforms predict rehospitalization and mortality after percutaneous mitral valve repair. *JACC Cardiovasc Imaging* 2019;**12**:1905–13.
- Zoghbi WA, Asch FM, Bruce C, Gillam LD, Grayburn PA, Hahn RT et al. Guidelines for the evaluation of valvular regurgitation after percutaneous valve repair or replacement: a report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2019;**32**:431–75.
- Vieitez JM, Monteagudo JM, Mahia P, Perez L, Lopez T, Marco I et al. New insights of tricuspid regurgitation: a large-scale prospective cohort study. *Eur Heart J Cardiovas Imaging*. 2021;**22**:196–202.
- Muraru D, Guta AC, Ochoa-Jimenez RC, Bartos D, Aruta P, Mihaila S et al. Functional regurgitation of atrioventricular valves and atrial fibrillation: an elusive pathophysiological link deserving further attention. *J Am Soc Echocardiogr* 2020;**33**:42–53.
- Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovas Imaging*. 2017;**18**:1342–43.
- Santoro C, Marco Del Castillo A, Gonzalez-Gomez A, Monteagudo JM, Hinojar R, Lorente A et al. Mid-term outcome of severe tricuspid regurgitation: are there any differences according to mechanism and severity? *Eur Heart J Cardiovas Imaging*. 2019;**20**:1035–42.
- Peri Y, Sadeh B, Sherez C, Hochstadt A, Biner S, Aviram G et al. Quantitative assessment of effective regurgitant orifice: impact on risk stratification, and cut-off for severe and torrential tricuspid regurgitation grade. *Eur Heart J Cardiovas Imaging*. 2020;**21**:768–776.
- Faletra FF, Berrebi A, Pedrazzini G, Leo LA, Paiocchi VL, Cautilli G et al. 3D transesophageal echocardiography: a new imaging tool for assessment of mitral regurgitation and for guiding percutaneous edge-to-edge mitral valve repair. *Progr Cardiovas Dis* 2017;**60**:305–21.
- Freitas-Ferraz AB, Rodés-Cabau J, Junquera Vega L, Beaudoin J, O'Connor K, Turgeon PY et al. Transesophageal echocardiography complications associated with interventional cardiology procedures. *Am Heart J* 2020;**221**: 19–28.
- Fam NP, Samargandy S, Gandhi S, Eckstein J. Intracardiac echocardiography for guidance of transcatheter tricuspid edge-to-edge repair. *EuroIntervention* 2018;**14**: e1004–e5.