Three-dimensional echocardiography and structural heart interventions

This article looks at the role of three-dimensional echocardiography in the anatomical assessment of cardiac structures, how this complements standard methods of assessing structural cardiac lesions and the advantages of three-dimensional echocardiography in peri-procedural guidance in the cardiac catheterization laboratory.

Since the initial description of three-dimensional echocardiography (3D echo) over 40 years ago, there have been a number of considerable advances in technology (Dekker et al, 1974). The use of 3D echo in clinical practice was initially limited by the availability of live (real-time) imaging. The first generation 3D echo probes required gated acquisitions with static rendering of images – a laborious time-consuming process. Today, 3D echo probes allow real-time imaging with excellent image resolution. Recently available 3D real-time colour Doppler imaging, along with the ability to perform direct measurements from the 3D images, continues to support the growth of this imaging modality in clinical practice.

Clinical applications of 3D echocardiography

3D echo offers an unrivalled appreciation of the cardiac structures and spatial orientation to neighbouring structures. This has two major consequences. First, through this understanding new concepts and anatomical phenotypes continue to be revealed, e.g. the importance of deep clefts within the mitral valve associated with mitral regurgitation (Ring et al, 2013) or of a prominent Eustachian ridge within the right atrium when attempting percutaneous closure of a patent foramen ovale (Rana et al, 2010a). Second, the ability to image the heart live in three dimensions has pivotal implications for guiding percutaneous interventions on the beating heart in the cardiac catheterization laboratory.

The growth of cardiac interventions, surgical and catheter based, has been mirrored by advances in cardiac imaging. The expanding spectrum of structural heart interventions includes heart valve disease therapies (e.g. MitraClip for severe mitral regurgitation, surgical mitral valve repair, transcatheter aortic valve replacement, paraprosthetic valvular leak closure), atrial septum device closure (patent foramen ovale and secundum atrial septum defect closure) and left atrial appendage occlusion to name but a few.

Two-dimensional echocardiography and fluoroscopy imaging remain essential in this arena. Increasingly, 3D echo plays a pivotal role through initial assessment and diagnosis, peri-procedural guidance and during follow up. Real-time 3D echo has brought with it a new era, where the reality of cardiac structures in the beating heart can be appreciated as never before. This article describes current clinical applications of 3D echo and its key contributions in a number of cardiac structures and their intervention.

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Mitral valve interventions

Surgical mitral valve repair

Mitral valve repair techniques have continued to evolve and European Cardiology Society Heart Valve Guidelines (Vahanian et al, 2012) support mitral valve repair for severe mitral regurgitation as a first line whenever feasible. Evidence supports preservation of the native mitral valve and its subvalvular apparatus since it carries lower perioperative mortality, with improved survival and lower long-term morbidity, than mitral valve replacement. Postoperative left ventricular function appears to be an important determinant, where avoiding disruption of mitral valve annulus continuity with papillary muscles and the left ventricle is a critical factor. The occurrence of symptoms already indicates an altered prognosis. Thus, even in asymptomatic patients, mitral valve repair may be considered when the likelihood of a successful repair is high.

Determining the optimal time of intervention is based on clear understanding of the complexity of the valve lesion. This is where 3D echo assessment is advantageous. Current approaches to mitral valve morphology assessment include two-dimensional (2D) transoesophageal echocardiography imaging, along with direct inspection of the valve anatomy at the time of surgery (by arresting the heart and emptying it of blood and examining flaccid mitral valve leaflets); although crucial, these have their limitations. 3D transoesophageal echocardiography has allowed surgeons to understand in more detail the behaviour of the mitral valve lesions (Salcedo et al, 2009) and refine their approach to mitral valve repair.

3D echo confers a number of advantages. The view of the mitral valve from the left atrium is referred to as the surgeon's view. During cardiac surgery the mitral valve is typically accessed through an incision in the atrial septum, exposing the left atrium with direct visualization of the left atrial aspect on the mitral valve. 3D echo therefore improves dialogue between surgeon and cardiologist. A detailed morphology assessment is possible through live 3D imaging of the mitral valve, where the mitral valve can be seen in its entirety; the two leaflets, the annulus and the complete line

where the two leaflets meet (coaptation line) can be viewed as the valve opens and closes. This bird's eye view gives an appreciation of the valve, its surrounding structures and their interactions. A precise segment by segment analysis of the valve, along its line of coaptation (Rana et al, 2010b), is possible using on-line software. A simple protocol has been devised to allow rapid assessment, taking no more than a few minutes (Rana et al, 2010b). 3D colour Doppler acquisition gives the ability to understand the impact of particular anatomical abnormalities by superimposing the regurgitant colour Doppler jet. Further refinement of the technique through advanced software enables measurements of the valve annulus dimensions, prolapsing tissue size, area and volume along with other useful valve parameters.

Pivotal information gained includes understanding the true extent of segment(s) involvement in mitral valve prolapse (*Figures 1* and *2*). The appreciation that there is a deep cleft within the valve leaflet corresponding to the location of the primary regurgitant jet guides the type of repair needed (*Figure 3*).

Figure 1. Surgical view of the mitral valve. The anterior (segments A1, A2, A3) and posterior (segments P1, P2, P3) leaflets are visualized in their entirety. There is anterior leaflet prolapse in the region of A2. A ruptured chord is seen (*). AV = aortic valve; LAA = left atrial appendage.

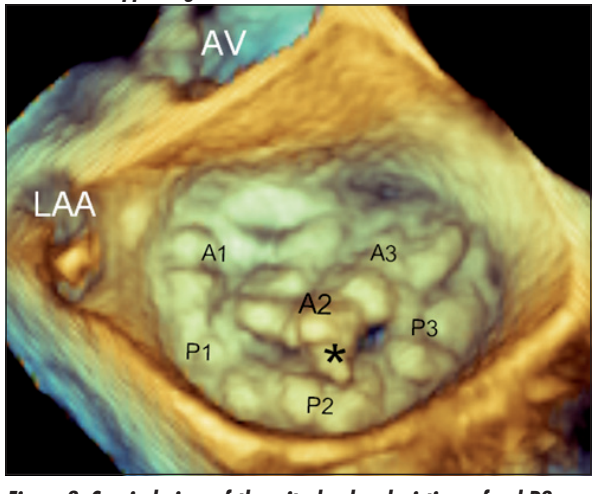
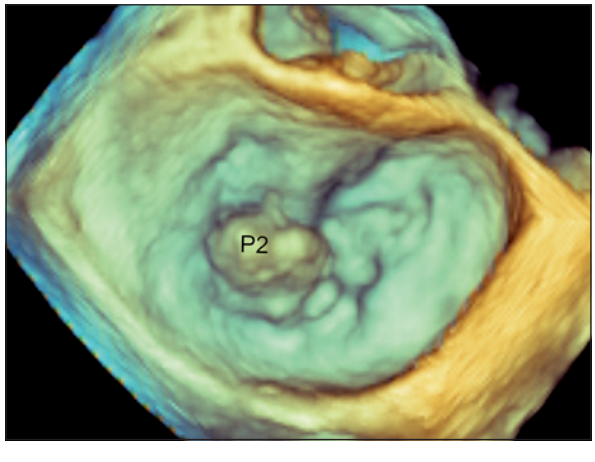


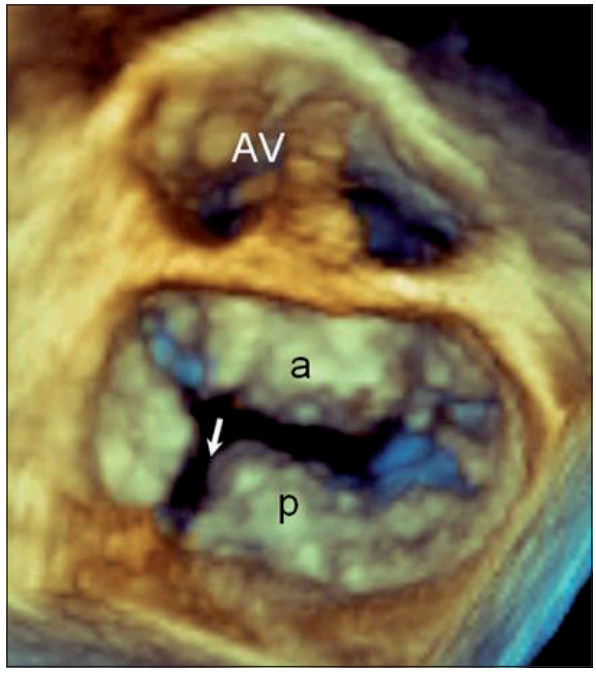
Figure 2. Surgical view of the mitral valve depicting a focal P2 prolapse associated with chordal rupture.



Through such imaging our understanding of the mechanics of the mitral valve structure in health and disease, and the structures it interacts with – left ventricle and atrium – continue to provide new insights into new therapies such as developing mitral valve annuloplasty rings for new mitral valve repair techniques (Khabbaz et al, 2013). The long-held belief that left atrial enlargement per se was not responsible for functional mitral regurgitation has been challenged (Gertz et al, 2011). Recent 3D echo analysis has provided insights into the possible mechanism of 'atrial' mitral regurgitation through a description of mitral valve area enlargement, reduced leaflet coaptation and resultant mitral regurgitation in the absence of left ventricular dilatation (Ring et al, 2014).

3D echo quantification of mitral regurgitation is another evolving technique. A key quantitative parameter of mitral regurgitation severity is effective regurgitant orifice area (Lancellotti et al, 2013). However, this parameter relies on geometric assumptions based on a circular orifice, as measured with 2D colour Doppler. 3D echo allows direct measurement of the region of flow convergence and has shown promise (Grady et al, 2011). The technique remains to be validated in larger studies and limitations in software have restricted its use in routine clinical practice. Although volumetric 3D measures are under development, a direct visualization of the regurgitant orifice is both possible and clinically useful. A surrogate measure of effective regurgitant orifice area is the vena contracta width, a direct measure of the physiological regurgitant orifice (i.e. the narrowest portion of the regurgitant jet). Limitations in this 2D parameter include a non-circular

Figure 3. Surgical view of the mitral valve depicting an abnormally deep cleft between P1 and P2 associated with severe mitral regurgitation. a = anterior mitral valve leaflet; AV = aortic valve; p = posterior mitral valve leaflet.



orifice. 3D colour allows true alignment to the en face view of the regurgitant orifice and hence vena contracta, which can then be directly traced through planimetry.

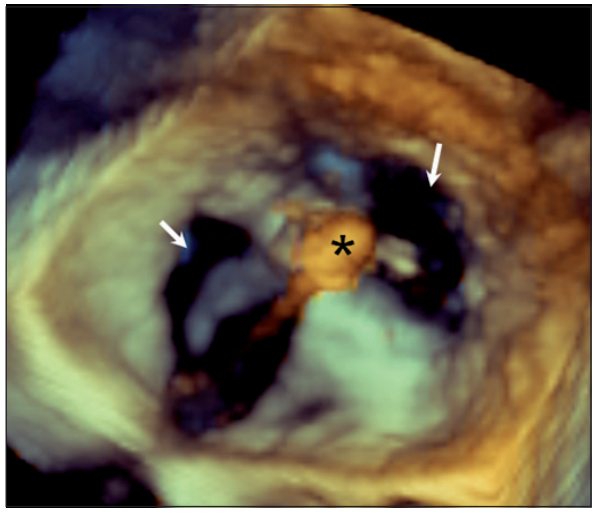
Several studies have validated this technique with high sensitivity and specificity (Zeng et al, 2011), demonstrating its greater accuracy compared to corresponding 2D measurements, and shown this measure to be comparable to cardiac magnetic resonance quantification methods (Marsan et al, 2009). This assessment is particularly useful in quantifying lesions with an irregular or complex orifice, such as functional mitral regurgitation where the orifice is elliptical, or in the setting of a paravalvular leak where the defect is irregular and assumes a serpiginous course around the outer edge of the sewing ring of a valve prosthesis.

Percutaneous mitral valve repair

Percutaneous techniques of mitral valve repair have seen the arrival of several device types. However, one device – the MitraClip – is proving promising and has entered the clinical arena. EVEREST I and II trials showed the feasibility (Feldman et al, 2005) and non-inferiority, but superior safety (Feldman et al, 2011) of this technique compared to surgical repair or replacement, in a highly selected group of patients. This treatment is currently reserved for patients with severe mitral regurgitation and poor left ventricular function who are deemed too high risk for surgery, where optimal medical therapy has failed to control symptoms. A number of anatomical characteristics must be met in order to qualify for this innovative therapy.

The concept is based on the surgical Alfieri stitch, a technique where sutures bring together the central portion of the two mitral valve leaflets, creating a double orifice. A metallic clip, designed to grasp the moving leaflets thus replicating this concept, can be deployed through a percutaneous route (*Figure 4*). The mitral valve is accessed via the femoral vein and right atrium with entry into the left atrium via a trans-septal puncture. The technique is heavily echo-imaging dependent and 3D echo is emerging as a pivotal tool in guiding the procedure (Faletra et al, 2013), through optimal and safe trans-septal puncture, to positioning the catheter over the correct portion of the mitral valve orifice to allow leaflets to be captured within the mitral clip.

Figure 4. Surgical view of mitral valve, showing the MitraClip device attached to the central portion of the mitral valve leaflets at P2/A2 (*). A double orifice results (two white arrows).



Assessment of the mitral valve morphology and severity of regurgitation using 3D echo has added value in patient selection pre- and post-procedure evaluation. This procedure beautifully illustrates the advantages of real-time 3D echo imaging in procedure guidance. 3D echo can depict the left atrium in its entirety with simultaneous views of the atrial septum and mitral valve. Using this view the catheter position within the left atrium and its relationship to the mitral valve is monitored in real time. 3D imaging allows precise manoeuvring of the catheter within the left atrium and across the mitral valve orifice. Correct alignment of the clip to the valve can be performed using another 3D modality – X-plane. This allows display of simultaneous 2D orthogonal planes so avoids repeatedly having to move back and forth between views to understand the clip's spatial orientation before attempting capture of the two leaflets. 3D imaging increases the accuracy and time taken to perform such a procedure, and improves safety.

Percutaneous paravalvular leak closure

In the last two decades advances in cardiac surgical techniques have significantly improved surgical outcomes. An aging population and greater life expectancy has increased the prevalence of heart valve disease and consequent valve replacement surgery. Leaks around the valve sewing ring often result from distortion of the valve annulus through heavy fibrosis or calcification, suture technique or shape and size of the prosthesis. The incidence of paravalvular leak is thought be 2–10% (Hammermeister et al, 2000). Minor paravalvular leaks are often clinically insignificant and problems only arise in a relatively small proportion of patients. The patient usually presents with progressive breathlessness and heart failure as a result of volume overload, in the setting of a severe leak, or as a result of haemolytic anaemia. The latter may occur with a less severe leak, where the smaller defect results in a high velocity jet driving mechanical destruction of red blood cells.

Such patients often have multiple comorbidities where redo cardiac surgery presents a higher surgical risk and may not necessarily guarantee success, particularly in mitral valve surgery because of the annular anatomy. Percutaneous closure of the leaks may be preferred. The reported incidence of major complications is 8.7% (Kumar et al, 2013) and includes bleeding, device embolization, exacerbation of haemolysis through residual leak, emergency surgery and death. However, risks can be significantly reduced through careful assessment and patient selection. 3D echo has a crucial role in identifying the leak(s), their exact location, size and shape of the defect and catheter guidance during the procedure (*Figures 5* and *6*). Accurate depiction of the anatomy can improve outcomes through reduced procedure times, and improved device type and size selection.

Atrial septum interventions

Repairing a defect (i.e. secundum atrial septal defect or patent foramen ovale in cardioembolic stroke) of the atrial septum often involves younger patients. Percutaneous closure is the preferred method if the anatomy is suitable, since it is less invasive with low complication rates, rapid recovery times and early hospital discharge.

3D echo has increased our understanding of complex atrial septum anatomy. 2D imaging requires careful mental reconstruction of such defects, which necessitates considerable experience (Rana et al, 2010c). However, despite experience it is evident that limitations remain. 3D echo has depicted previously undefined anatomical variations (Rana et al, 2010b). In the author's experience, a better appreciation of the 3D defect shape and its spatial relationships to surrounding structures during percutaneous device closure has improved closure rates (*Figures 7* and *8*). The Eustachian ridge has been defined by 3D echo to be an important anatomical structure within the right atrium (Rana et al, 2010b). It has the potential to interfere with optimal device positioning with risk of large residual shunts (*Figure 9*). Similarly, accurate measurements of the entrance (right atrium) and exit (left atrium) of the patent foramen ovale and its tunnel length aid device selection (*Figure 10*). If the atrial septum is aneurysmal then 3D imaging allows a panoramic view with instant understanding of how defects within the fossa ovalis (septum primum tissue) relate to the aneurysm. Further, how the defect(s) behave once it has been crossed by a guidewire can only be fully appreciated with real-time 3D imaging.

Figure 5. Surgical view from left atrium, showing a bileaflet mechanical mitral valve prosthesis. A cardiac catheter (*) is seen to cross the inter-atrial septum (IAS) and transverse the left atrium towards the left atrial appendage (LAA), and disappear alongside the mitral prosthesis as it enters a paravalvular defect into the left ventricle.

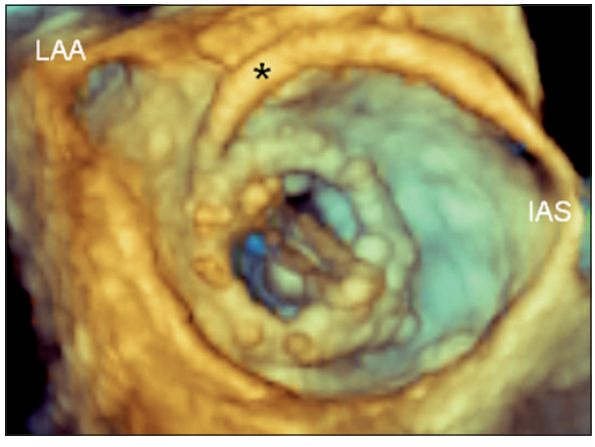
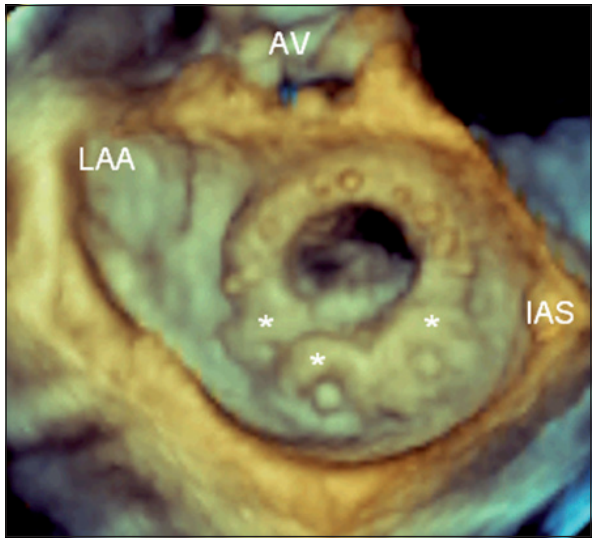


Figure 6. Surgical view of a mitral valve bioprosthesis, with three paravalvular devices seen deployed around the posterior mitral annulus. AV = aortic valve; IAS = inter-atrial septum; LAA = left atrial appendage.



Left atrial appendage occlusion

Atrial fibrillation constitutes a significant health burden, increasing in prevalence with age – 2–3% of people aged <65 years are affected, increasing to 8–9% in octogenarians. The incidence of stroke caused by atrial fibrillation

Figure 7. View of the atrial septum seen from the left atrium. Two moderate sized secundum atrial septal defects, measuring 11 mm and 10 mm, are identified clearly with an instant appreciation of the rims of each defect, their spatial relations to each other and surrounding structures. MV = mitral valve; RUPV = right upper pulmonary vein.

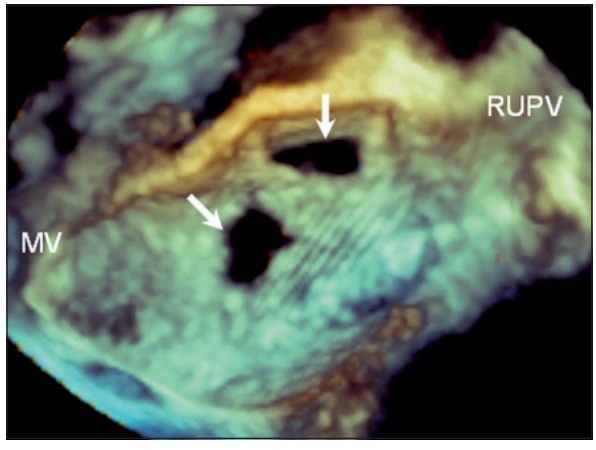
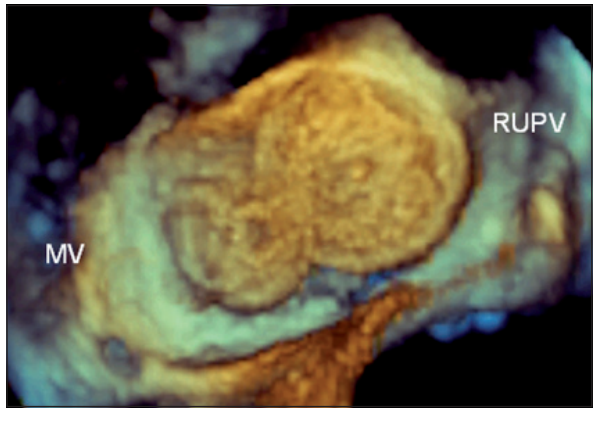


Figure 8. Similar view as in* Figure 7*, now the two defects have been closed with two separate atrial septum device occluders. MV = mitral valve; RUPV = right upper pulmonary vein.



raises steeply from 1.5% in those under 60 years to more than 20% in those aged 80–89 years (Roger et al, 2011). Stroke resulting from a cardiac source, and particularly atrial fibrillation, is often larger resulting in more severe cerebral deficit and higher morbidity and mortality. Currently, the most effective treatment for stroke prevention in atrial fibrillation is oral anticoagulation. Unfortunately a significant number of individuals, approximately 30%, never receive anticoagulation therapy through a number of relative and absolute contraindications (Nieuwlaat et al, 2005).

Figure 9. View of the right atrium and the atrial septum. The fossa ovalis can be visualized with a guide wire (*) running from the inferior vena cava (IVC) and transversing the fossa ovalis, and then disappearing at its superior border into a patent foramen ovale. A large Eustachian ridge (black dotted lines) is seen to attach to the superior border of the fossa ovalis and partially obscures its anterior portion. CS = coronary sinus; SVC = superior vena cava.

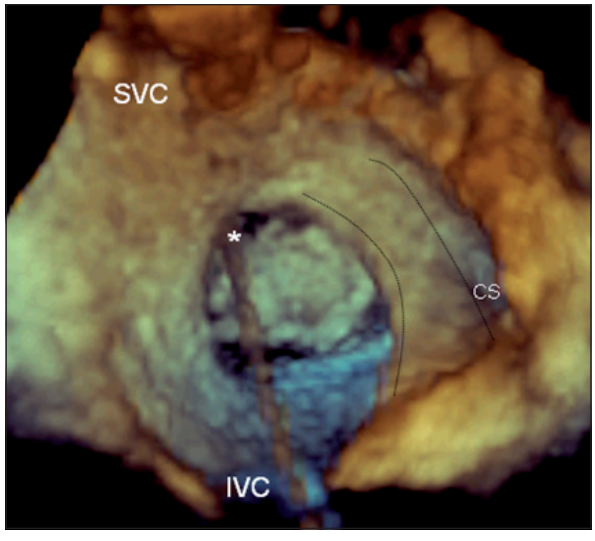
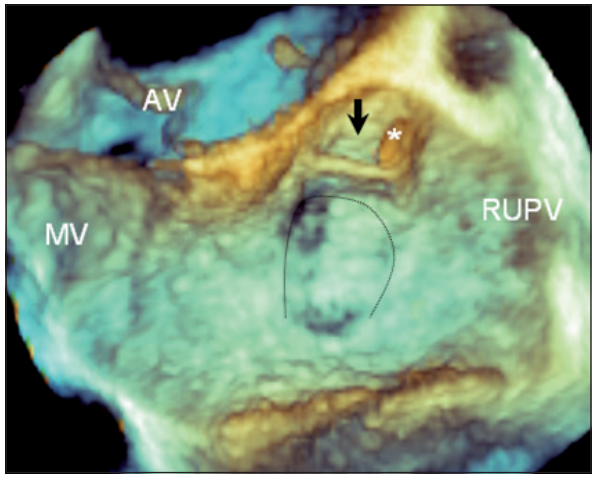


Figure 10. Left atrial view of the atrial septum. The guide wire continues through the patent foramen ovale (black arrow) and is seen to exit into the left atrium (*). The position of the fossa ovalis in relation to the opening of the patent foramen ovale is depicted by the black dotted line. AV = aortic valve; MV = mitral valve; RUPV = right upper pulmonary vein.



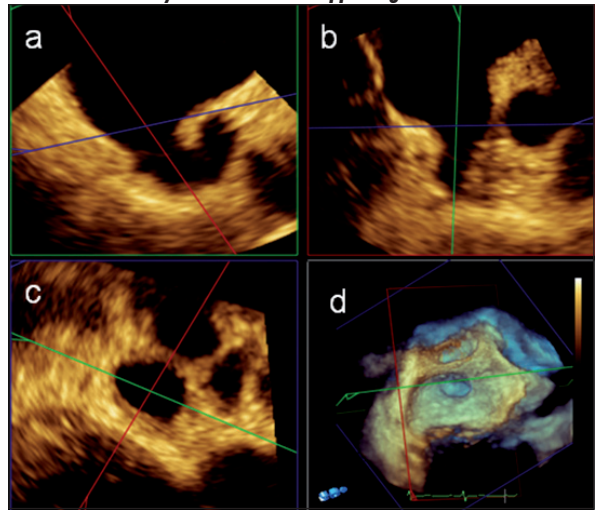
In non-valvular atrial fibrillation, echo studies have confirmed 90% of the thrombus seen in the heart to be located in the left atrial appendage; hence, the rationale to exclude the left atrial appendage from the circulation to lower the risk of stroke. A percutaneous approach to left atrial appendage occlusion has been validated. The randomized clinical trial PROTECT AF found a left atrial appendage occlusion device to be non-inferior to warfarin therapy (Holmes et al, 2009). Four-year follow-up data demonstrated left atrial appendage occlusion to be statistically superior to warfarin stroke prevention (Reddy et al, 2013). The European Society of Cardiology guidelines state that left atrial appendage occlusion may be considered in patients with a high stroke risk and contraindications to long-term oral anticoagulation (Camm et al, 2012).

Left atrium appendage occlusion procedure is performed antegrade, via the femoral vein and trans-septal puncture to gain entry into the left atrium. The left atrial appendage anatomy is very variable. 2D imaging provides standardized views to measure its orifice and depth for sizing the occlusion device. However, 3D echo provides additional detail of the overall shape, any complex anatomy such as 'accessory lobes', which may be a potential source of clot formation if not adequately covered, its position in relation to the catheters and the device angle during deployment. 3D echo improves sizing of the left atrial appendage for optimal device selection and ensures the position of the device is optimized (*Figures 11* and *12*).

Conclusions

The ability to view the beating heart in real time has revolutionized our ability to assess cardiac morphology. New anatomical phenotypes responsible for disease (e.g. the existence of deep clefts in the mitral valve) or poten-

Figure 11. Philips QLab Software depicting the left atrial appendage. a and b. Long axis planes – at least two lobes exist. c. This accurately depicts the true orifice of the appendage and measurement can be taken for device sizing. d. The three-dimensional image dataset, from which orthogonal views in three planes can be used to assess the anatomy of the left atrial appendage in detail.



tial complications during device placement (e.g. a prominent Eustachian ridge associated with the atrial septum) are being realized through 3D echo imaging. Improved confidence in describing the morphology and accurate sizing of a defect (e.g. an atrial septal defect or paravalvular leak), coupled with live imaging during the procedure to precisely guide wire and catheter positioning and device deployment, have all facilitated the rapid growth in structural heart interventions. An exciting future lies ahead as technological advances continue. **BJHM**

Conflict of interest: none.

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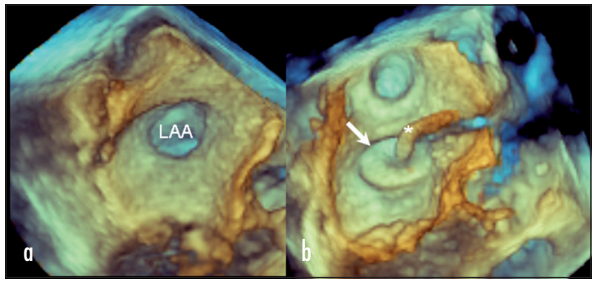
Figure 12. Views of the left atrial appendage (LAA) before and after occlusion. a. The orifice of the appendage; (b) the same appendage after deployment of a closure device (white arrow). The cable on which the device was deployed is still attached (*).



KEY POINTS

- The continued development of real time three-dimensional imaging has revolutionized our ability to understand cardiac anatomy.
- New anatomical phenotypes responsible for disease or potential complications during device placement are being realized through three-dimensional echocardiographic imaging.
- Key cardiac structures which lend themselves to three-dimensional transoesophageal echocardiography are the mitral valve, the atrial septum and the left atrial appendage.
- Three-dimensional transoesophageal echocardiography has many advantages in guiding cardiac interventions and has facilitated development of techniques, reducing procedure times and improving safety.