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REVIEW PAPER

Real-time three-dimensional transoesophageal echocardiography for guidance of non-coronary interventions in the catheter laboratory

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The growing need for less invasive therapies of cardiac disease creates the necessity for improved imaging guidance. Although two-dimensional transthoracic and transoesophageal echocardiography (TEE) have been shown to be essential tools for planning and execution of cardiac interventions, the benefit of three-dimensional TEE for the guidance of interventional procedures still needs to be evaluated. This review aims to describe our first experiences with real-time (RT) three-dimensional TEE for the guidance of percutaneous non-coronary interventions in the catheter laboratory. We used a matrix array TEE probe capable of generating three-dimensional images of cardiac structures in RT. We applied this innovative technique to monitor atrial septal defects or patent foramen ovale closures, valve procedures such as mitral and aortic valve interventions, and electrophysiological procedures. Our first experience using RT three-dimensional TEE for the guidance of percutaneous cardiac interventions in the catheter laboratory demonstrates that this technique is feasible to guide interventions, providing fast and complete information about the underlying pathomorphology, improving spatial orientation, and additionally allowing the online monitoring of the procedure. These benefits may accelerate the learning curve and improve confidence of the interventional cardiologist in order to increase safety, accuracy, and efficacy of interventional cardiac procedures.

Introduction

Percutaneous interventions in the catheter laboratory, such as atrial septal defect (ASD) or patent foramen ovale (PFO) closures, electrophysiological interventions, and in the recent past also interventional valve procedures such as percutaneous mitral and aortic valve repair are usually monitored by fluoroscopy and two-dimensional (2D) transoesophageal echocardiography (TEE).[1–3] In contrast to coronary interventions in which fluoroscopy remains the dominant imaging modality, the evaluation and treatment of structural heart disease require continuous soft-tissue imaging, which cannot be adequately provided by fluoroscopy alone. In these cases, fluoroscopy leads to poor visualization of the target structure, thereby exposing patients to excessive levels of ionizing radiation, which is especially hazardous in young patients with congenital defects. Advanced ultrasound techniques such as 2D TEE are therefore essential for the diagnosis and performance of interventions due to the unique capability to assess cardiac anatomy with reference to the proximity of surrounding structures. However, 2D TEE is limited in its ability to detect the position of a catheter or a device relative to its surrounding environment due to only two spatial dimensions, necessitating several planes in order to mentally reconstruct the anatomical setting. Although several approaches for off-line three-dimensional (3D) reconstruction have been successfully accomplished,[4,5] these images are not available during the intervention and therefore are useless for online monitoring of the procedure. The complex process of data acquisition and processing with off-line reconstruction of sequentially acquired 2D cross-sections have limited this method for daily clinical practice. Significant advances in ultrasound, electronic, and computer technology have enabled the development of a new generation of transoesophageal probes with a new matrix array technique, allowing for 3D presentation of cardiac structures in real time (RT). This innovative new imaging technology has the potential to overcome the main limitations of 2D TEE: it allows

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visualizing the exact cardiac pathomorphology in RT and enables accurate visualization of catheters and devices within its surrounding environment. This review aims to describe our first experiences with RT 3D TEE for the guidance of percutaneous cardiac interventions in the catheter laboratory.

Technical considerations

The 3D TEE probe (X7-2t, 7 MHz, Philips Healthcare, Andover, MA, USA) uses a new matrix-phased array transducer technology with a large number of transducer elements, containing more than 2500 active elements, compared with 128 in conventional phased-array transducers. It is of similar size when compared with a conventional multiplanar 2D TEE probe, measuring 1.5 cm in width, 1.0 cm in height, and 4.5 cm in length, with a cross-sectional area of $\sim 10 \times$ 14 mm. The 3D TEE probe is connected to a commercial 3D-capable echocardiographic system (Philips IE 33, Philips Healthcare), equipped with dedicated software. This TEE system allows all conventional modalities (M-Mode, 2D multiplanar imaging, pulsed- and continuous wave Doppler, colour Doppler). Additionally, the system offers three 3D acquisition modes: RT operator-limited 3D datasets (Live 3D), RT-focused field of view (3D Zoom), and the generation of a complete volume-gated data set (Full volume 3D).

The Live 3D mode displays a pyramidal data set, generating RT 3D images with frame rates between 20 and 26 Hz. Segments of the heart, such as the interatrial septum, may be visualized in 3D, with an immediate spatial orientation of the target structure. The 3D Zoom mode displays a truncated pyramidal data set of variable sizes in both xy- and z-directions (elevation) and is especially useful in guiding the navigation of catheters and interventional devices due to a wider perspective. The Full volume 3D mode provides a pyramidal data set of $\sim 100^\circ \times 100^\circ$, which allows inclusion of a larger cardiac volume. This wide angle mode requires ECG gating and breath-holding, because the wide angle data set is compiled by merging four to seven narrower RT 3D pyramidal scans. The acquired echosectors are available for immediate review after the images have been combined. In addition, the system offers a biplane mode, enabling the 2D imaging of a structure from two different angles. To increase the visual effect of the data sets, the system generates 3D images, using depth-dependent dynamic colorization, according to the spatial perspective of the viewer. These 3D images can also be rotated in any spatial direction on the screen of the ultrasound machine in order to gain the perspective with the most information of the underlying morphology. Moreover, a process known as cropping can be used to cut into the 3D volume to visualize cardiac structures within the pyramidal data set.

Clinical applications of real-time three-dimensional transoesophageal echocardiography for percutaneous interventions

Device closure of interatrial communications

Transcatheter device closure of interatrial communications has become an established technique for the prevention of paradoxical embolism in patients with PFO and an effective treatment alternative to surgery for selected patients with ASDs associated with significant left-to-right shunting.[6–8] Two-dimensional TEE has become an essential and integral tool of the interventional device closure,[1,9] but it is limited in its ability to detect the position of a catheter or a device relative to its surrounding environment due to only two spatial dimensions. Even in experienced operators, numerous cut planes are necessary in order to mentally reconstruct the anatomical setting. Recently, the application of RT 3D transthoracic echocardiography was shown to be feasible for guiding ASD closures in infants from a subcostal echo window[10,11] and also demonstrated a decrease in fluoroscopy time.[12] In adults, image quality of transthoracic techniques is often not sufficient for appropriate evaluation of interatrial communications, especially during interventions. RT 3D TEE provides a novel imaging modality for the guidance of ASDs and PFO closures, giving fast and complete information about the appropriate position of the device in its surrounding environment.[13,14] In our laboratory, we have performed ASD and PFO closure in over 50 patients using a combination of fluoroscopic, 2D TEE, and RT 3D TEE imaging.

Figure 1A shows a 3D TEE image of the ASD, displaying an en-face view from the left atrium. The size and shape of the defect including the rim of the interatrial septum are displayed on-line, allowing the assessment of the complete circumference of the ASD. *Figure 1B* demonstrates the setting of the guiding sheath passing through the ASD before deployment of the left atrial device. The delivery system centrally passes through the ASD orthogonally, which can be depicted with only a single 3D perspective. After unfolding the left atrial disc (*Figure 1C*), spatial orientation of the device as well as distance and relation of disc size to defect size can easily be assessed with 3D TEE, as shown in *Figure 1D*. Note the high spatial resolution showing the wire mesh of the occluder disc. After unfolding the right atrial disc, exact positioning of the device has to be ensured prior to definite release by unscrewing the disc from the delivery system. The 3D TEE imaging technique (*Figure 1E*) enables to exactly visualize on-line the correct position of the occluder and its relation to the interatrial septum as well as to other adjacent cardiac structures such as the mitral and tricuspid valves and the coronary sinus, preventing mismatch of the device relative to the ASD size and residual shunting. In this mode, the 3D data set can be cropped and rotated to visualize the device from both the left and the right atrial perspectives (*Figure 1F*) to ensure the correct positioning of the device. The greatest advantage of 3D echocardiography may be seen in its use for immediate pre-release and post-deployment evaluation of occluder devices.[5] This is a critically important function of any mode of ultrasound guidance for interatrial defect closure as inadequate visualization can lead to residual leaks, device embolization, interference of the rim with surrounding structures, and potential malpositioning of the device potentiating the risk for device erosion into the aorta and the roof of the atria.

The value of RT 3D TEE to prevent malpositioning of the device is shown in *Figures 2* and *3*. *Figure 2* demonstrates the device closure of an ASD. In this patient, balloon-sizing of the defect under fluoroscopic control demonstrated that the size of a 27 mm Amplatzer occluder would close the defect. The RT 3D TEE image in *Figure 2A* demonstrates that the device is too small for the size of the ASD, resulting

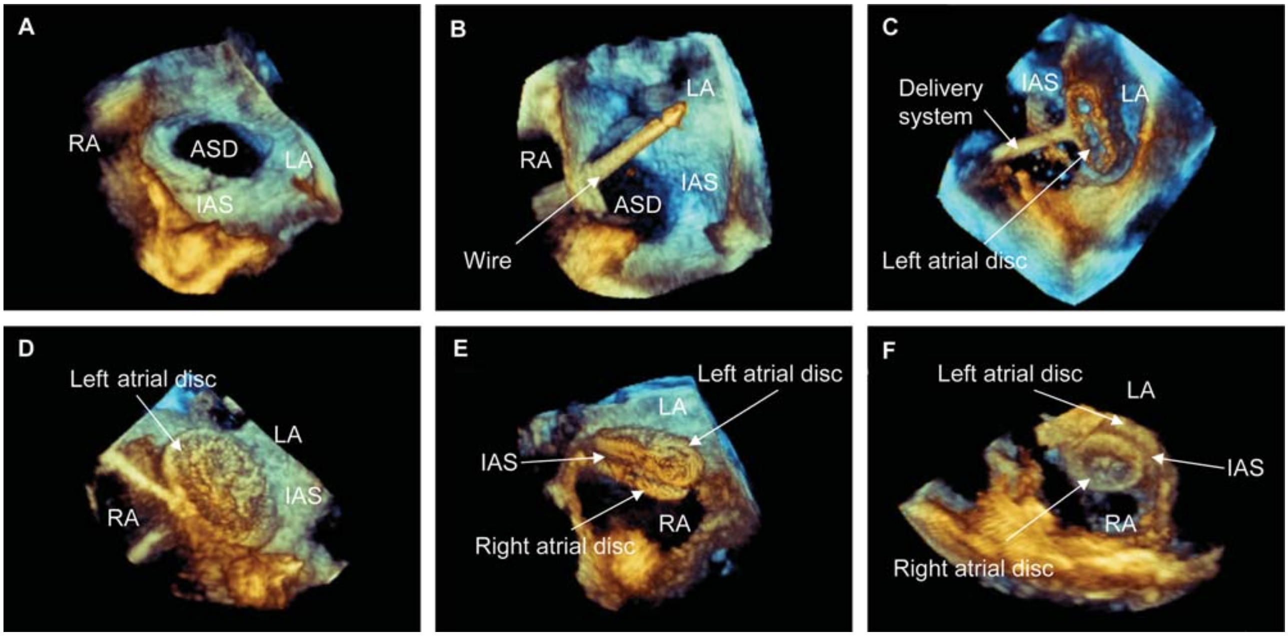

Figure 1 (*A–F*) Monitoring of atrial septal defect closure (ASD, atrial septal defect; LA, left atrium; RA, right atrium; IAS, interatrial septum).

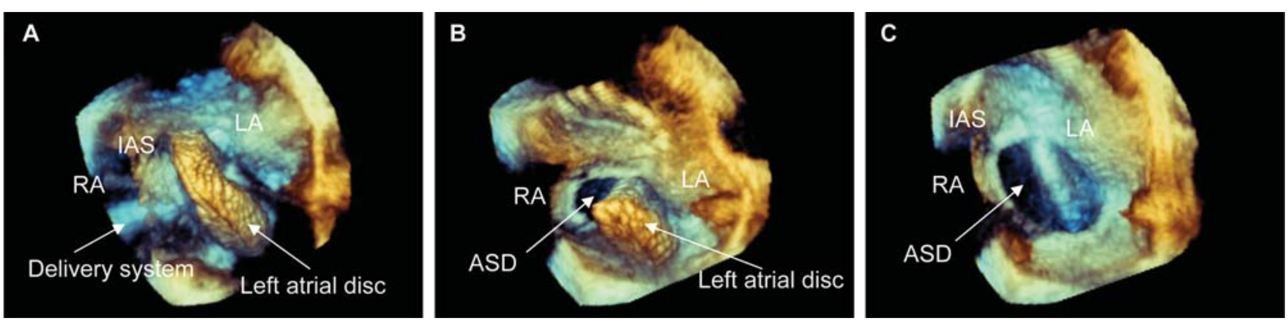

Figure 2 (*A–C*) Mismatch between Amplatzer occluder and atrial septal defect (ASD, atrial septal defect; LA, left atrium; RA, right atrium; IAS, interatrial septum).

in mismatch and instability of the left atrial disc, slipping through the ASD into the right atrium (*Figure 2B* and *C*). This patient had to be transferred to the cardiovascular surgeons for operative repair of the defect.

PFO closure can be performed successfully without any ultrasound guidance[15] or without the use of fluoroscopy.[16] Either way is possible, but the use of only one imaging modality is subject to experienced centres only. The combination of two imaging modalities facilitates the intervention for the interventional cardiologist, especially by adding a third dimension using RT 3D TEE.[17] Operators experienced with PFO closure have learnt that a wide array of PFO anatomies exist, and as a result, any given device fails to consistently perform well in the real patient setting, underscoring the importance of echocardiographic imaging guidance.[18] The following figures show an example of a PFO closing procedure under RT 3D TEE guidance. *Figure 3A* demonstrates the passage of the delivery system through an open foramen ovale. Note how the catheter stretches the PFO, clearly visualizing the tentering of the channel within the interatrial septum. The next step after passing the PFO is the guidance of the catheter into the pulmonary vein for improved stability during passage of the delivery system through the PFO. Often, the catheter finds its way into the left atrial appendage, which might be hazardous in the context of penetrating the appendage and causing complications such as tamponade of the pericardium. *Figure 3B* gives a unique view of the left atrial appendage with the delivery system inside. Virtually seeing the system in the wrong position before unfolding the left-sided disc of the device underscores the advantages of RT 3D TEE for increasing the safety of the intervention. *Figure 3C* gives an en-face view of the left atrial appendage and the pulmonary vein, where the catheter has now successfully been placed for good catheter back-up during the intervention. *Figure 3D* shows the unfolding and the pull-back of the left atrial disc towards the interatrial septum, accurately monitoring the correct position of disc and its relation to the interatrial septum and the PFO. The RT 3D TEE technique allows for complete insight into the left atrium and its surrounding structures for confident deployment of the left atrial disc and also for deployment of the right atrial disc, as shown in *Figure 3E*. The possibility of twisting the 3D image around its own axis to gain views from both the left and the right atria implicates more confidence to the interventionalist performing the closing procedure. *Figure 3F* demonstrates the correct position of the both discs with a single 3D

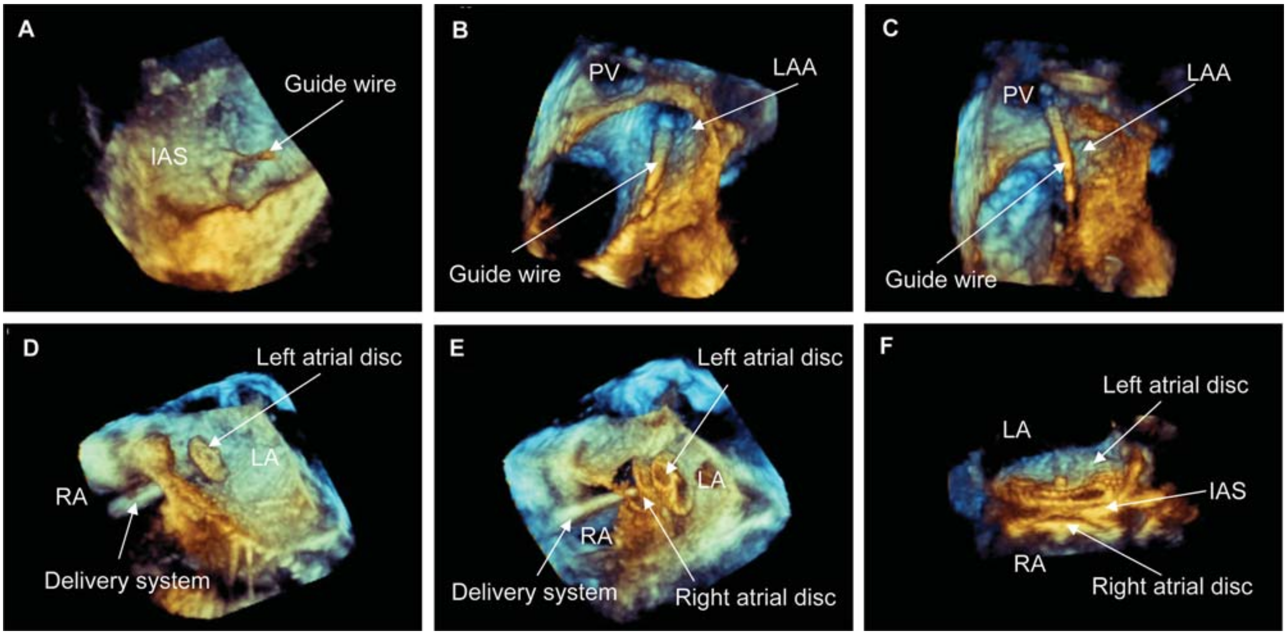

Figure 3 (*A–F*) Monitoring of patent foramen ovale closure (PFO, patent foramen ovale; LA, left atrium; LAA, left atrial appendage; PV, pulmonary vein; IAS, interatrial septum).

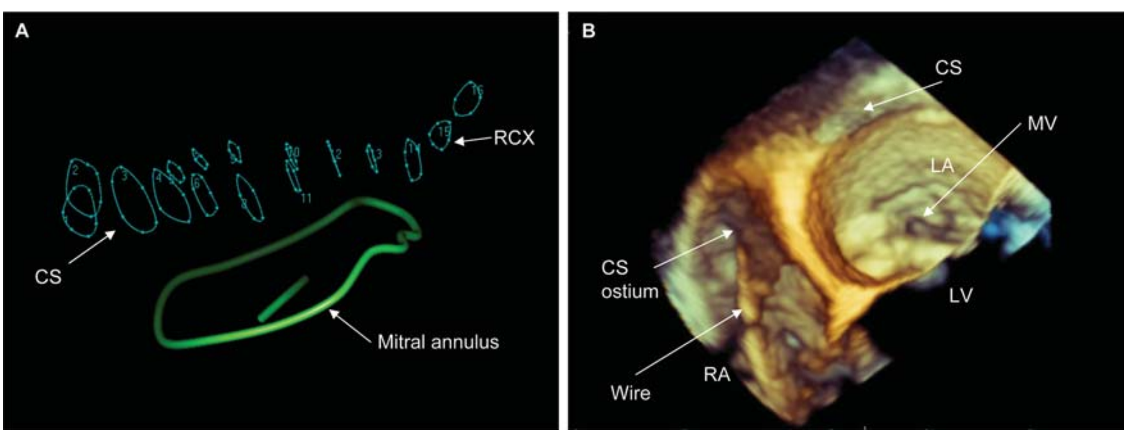

Figure 4 (*A*) Reconstructed image (TomTec Imaging Systems®) of the mitral valve with depiction of the mitral ring in relation to the coronary sinus. (B) Intubation of the coronary sinus (CS, coronary sinus; RCX, Ramus circumflex; LA, left atrium; RA, right atrium; LV, left ventricle; MV, mitral valve; CS, coronary sinus.

perspective after the final release of the device, encompassing the interatrial septum adequately.

Overall, the potential value of RT 3D TEE for interventional closure of interatrial defects includes improved visualization of the size and the shape of the defect, as well as quantification of the number of defects promoting optimal device sizing and selection, and improved guidance of the closing procedure for improved post-implantation assessment to prevent suboptimal device sizing and positioning.

Percutaneous mitral valve interventions

Although surgical mitral valve repair is the current standard treatment for ischaemic mitral regurgitation, the high morbidity and mortality associated with the surgical procedure limit its applications in patients with ischaemic heart disease and reduced left ventricular function.[19] Many patients with severe mitral regurgitation are denied or refused mitral valve surgery. A less invasive procedure with possibly fewer potential complications may thus be attractive for patients with severe mitral regurgitation. Recently, percutaneous catheter-based approaches for mitral valve interventions have been developed, using either the Viacor® device for mitral valve annuloplasty over the coronary sinus or the MitraClip® device for direct clipping of the mitral valve. The anatomic proximity of the coronary sinus to the mitral annulus led to the hypothesis that mitral annuloplasty could be performed percutaneously by placing a device in the coronary sinus.[20] Because of its easy accessibility and close relationship to the posterior mitral annulus, alterations of the coronary sinus geometry with percutaneous devices may translate to displacement of the posterior annulus and correct mitral leaflet coaptation.[21] Another technique for the reduction of mitral regurgitation is related to the surgical Alfieri approach. A percutaneous method to create the same type of repair

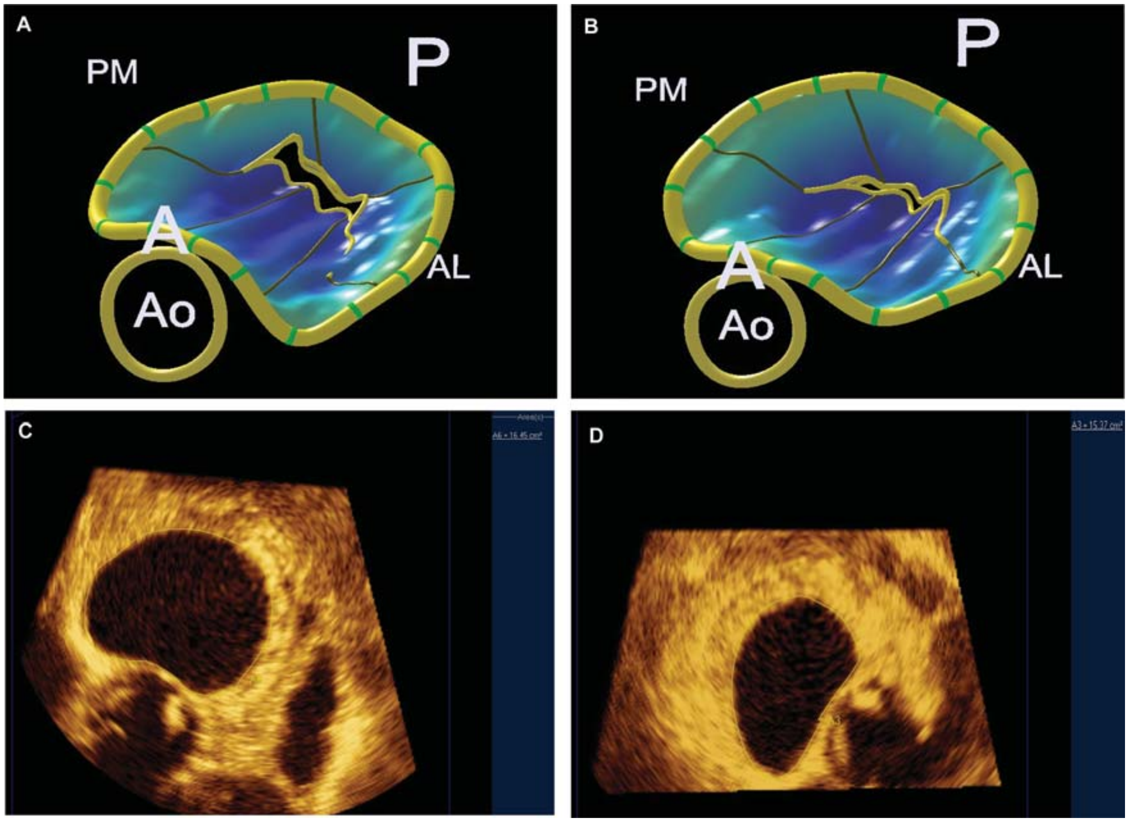

Figure 5 (*A–D*) Reconstructed image (Qlab 7.0®, Philips Healthcare) of the mitral valve annulus and the mitral regurgitation orifice area before (*A*) and after (*B*) annuloplasty (A, anterior; P, posterior; AL, anterolateral; PM, posteromedial; Ao, aorta). Mitral valve area before (*A*) and after (*B*) annuloplasty, documenting a reduction of the mitral valve area from 1645 to 1537 mm^2.

was developed recently. A transseptal puncture is used to deliver a clip device that grasps the mitral leaflet edges to approximate the middle scallops of the mitral leaflets and to create a double orifice with improved leaflet coaptation.[2] In order to sufficiently plan and accomplish such interventions, a 3D view of the mitral valve and the coronary sinus is highly desirable.

Based on acquired 3D images, post-processing software products (TomTec® Imaging systems) can be used to reconstruct the mitral valve annulus and the coronary sinus (*Figure 4A*). Note the 3D volume rendered reconstruction of the coronary sinus around the mitral valve annulus. This may help to improve planning of mitral valve annuloplasty procedures and to monitor such interventions. *Figure 4B* depicts a view from the right atrium into the coronary sinus. Note the correct position of the exchange wire in the origin of the coronary sinus. Essentially, the 3D data set can be rotated with respect to the best view upon the orifice of the coronary sinus in RT, thus aiding the interventionalist to adapt to the position of the catheter under TEE guidance. In order to document the success of the annuloplasty procedure, the rendered 3D image can be used to exactly quantify measurements of the mitral valve and the mitral valve annulus using dedicated software (Qlab 7.0®, Philips Healthcare). With this technique, the mitral valve and its annulus can be characterized with regard to the perimeter, the width of the annulus, and the anterior-to-posterior and the anterolateral-to-posteromedial diameter. More important, the extent of the mitral valve regurgitant area can be visualized before (*Figure 5A*) and after annuloplasty (*Figure 5B*). Note the deformation of the mitral valve annulus, and the decrease in the orifice area of the regurgitant mitral valve, as demonstrated in *Figure 5C* and *D*.

Precise steering of the MitraClip® device during edge-to-edge mitral valve repair is essential for exact positioning of the clip in order to grasp both mitral leaflets for sufficient coaptation and reduction of mitral regurgitation. The clip has to be perpendicular to the coaptation line and horizontal to the mitral valve annulus. This can be accomplished by using different reference positions of the TEE transducer for generating 2D images or by using the 2D biplane image mode, enabling the presentation of the device from two different angles at the same time. These have to be integrated into a 3D mental representation. RT 3D TEE gives an en-face view of the mitral valve with immediate presentation of the delivery system in its exact position in the space of the left atrium after transseptal puncture of the interatrial septum, as can be clearly seen in *Figure 6A*. By rotating the 3D image and after cropping into the dataset, both the perpendicular and the horizontal position of the clip system can easily be assessed as shown in *Figure 6B*. Movement of the delivery system and both clip arms can be controlled in RT during placement of the device by generating a 3D image of the left atrium (*Figure 6C*). After retraction of the delivery sheath from the left atrium, size and shape of the artificial ASD can be demonstrated, as presented in *Figure 6D*. Note the exact position of the transseptal puncture, right in the middle of the interatrial septum, with sufficient distance to the roof of

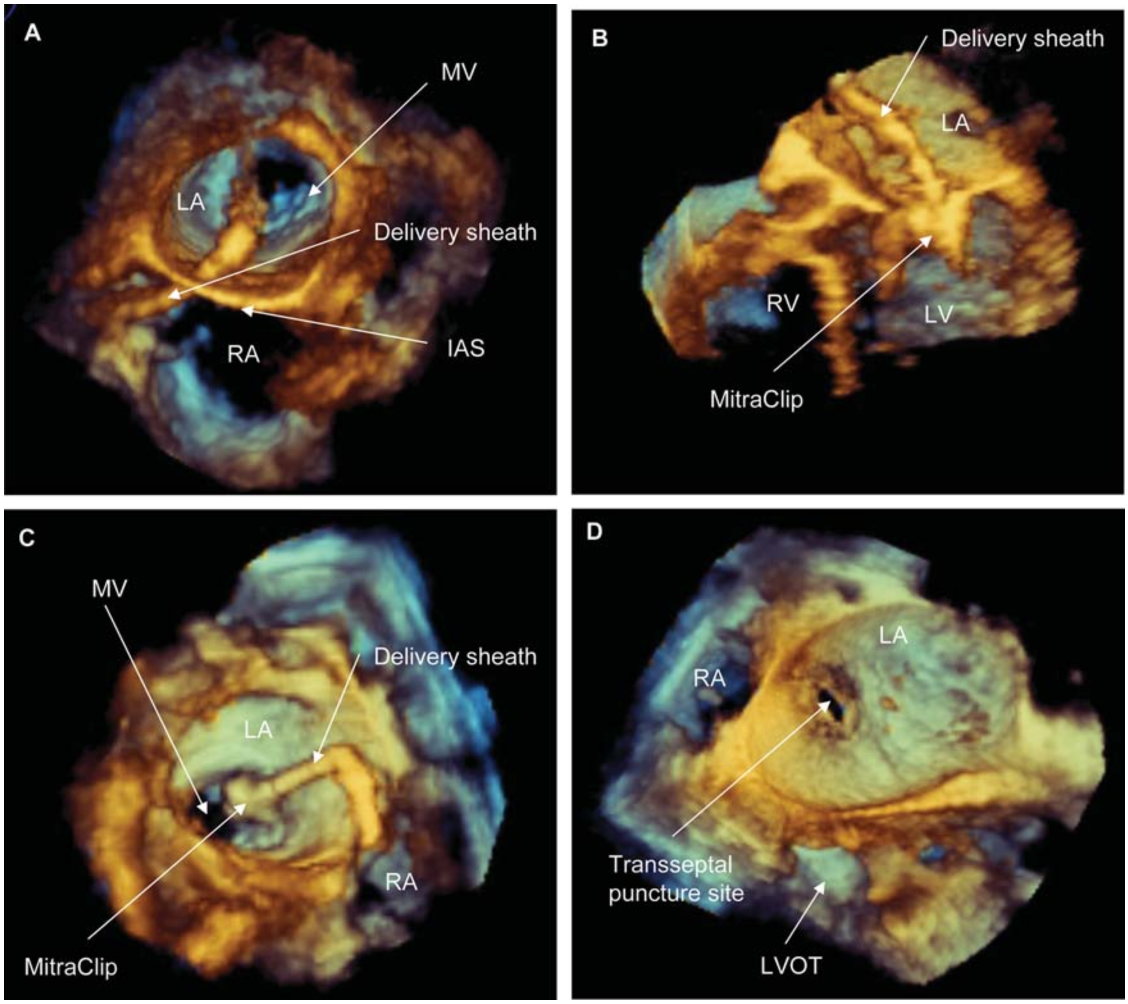

Figure 6 (*A–D*) Monitoring of a mitral valve intervention using the MitraClip® system (LA, left atrium; RA, right atrium; IAS, interatrial septum; MV, mitral valve; LV, left ventricle; LVOT, left ventricular outflow tract).

the left atrium and the left ventricular outflow tract (LVOT) with the aorta.

Taken together, the use of RT 3D TEE for the guidance of mitral valve interventions allows for adequate visualization of the mitral valve and its surrounding structures for precise placement of devices in the coronary sinus during annuloplasty procedures and during edge-to-edge repair of the mitral valve. The excellent spatial orientation of both atria and the metal valve are important benefits of the technique for planning and performing such interventions.

Percutaneous aortic valve interventions

Percutaneous treatment of aortic valve disease has been performed since the 1980s using balloon valvuloplasty with different opinions, considering its lack of efficacy and the risks involved.[22] Recently, the combination of percutaneous balloon valvuloplasty followed by the implantation of a stent-based valve prothesis (CoreValve®) for the treatment of aortic stenosis has been shown to be feasible in high-risk patients.[23] *Figure 7A* shows a 3D image of the aortic valve seen from a 60° angle, giving a spatial impression of the aortic valve and its surrounding structures. *Figure 7B* gives a nice 3D view of the LVOT. Once again the advantage of the 3D view upon the aortic valve, the LVOT, and its surrounding structures is underscored. Before the device is deployed, a balloon valvuloplasty with a 23 mm balloon under rapid pacing was performed before device implantation. After the aortic stent is released from the delivery system, the artificial aortic valve prosthesis can be clearly visualized, as shown in *Figure 7C*. *Figure 7D* shows a 3D image of the artificial aortic valve prosthesis in the LVOT, clearly demonstrating free movement of all prosthetic leaflets inside the aortic stent. The narrowing of the stent at the orifice of the coronary arteries can also be seen very accurately. An important consideration during performance of aortic stenting using the CoreValve system is the position of the device inside the LVOT. Unprecise positioning can lead to severe aortic regurgitation, especially when the device has been drawn back too much into the aorta. In contrast, malpositioning of the device too much inside the left ventricle might lead to restricted movement of the anterior leaflet of the mitral valve. The relation of the anterior leaflet of the mitral valve to the LVOT can be depicted with high precision using RT 3D TEE, showing an en-face or surgical view of the mitral valve. This is important for the positioning of the self-expanding aortic stent before final implantation, as shown in *Figure 8A*. After deployment of the device into the LVOT, the anterior leaflet of the mitral valve is somehow constrained in its movement, which can

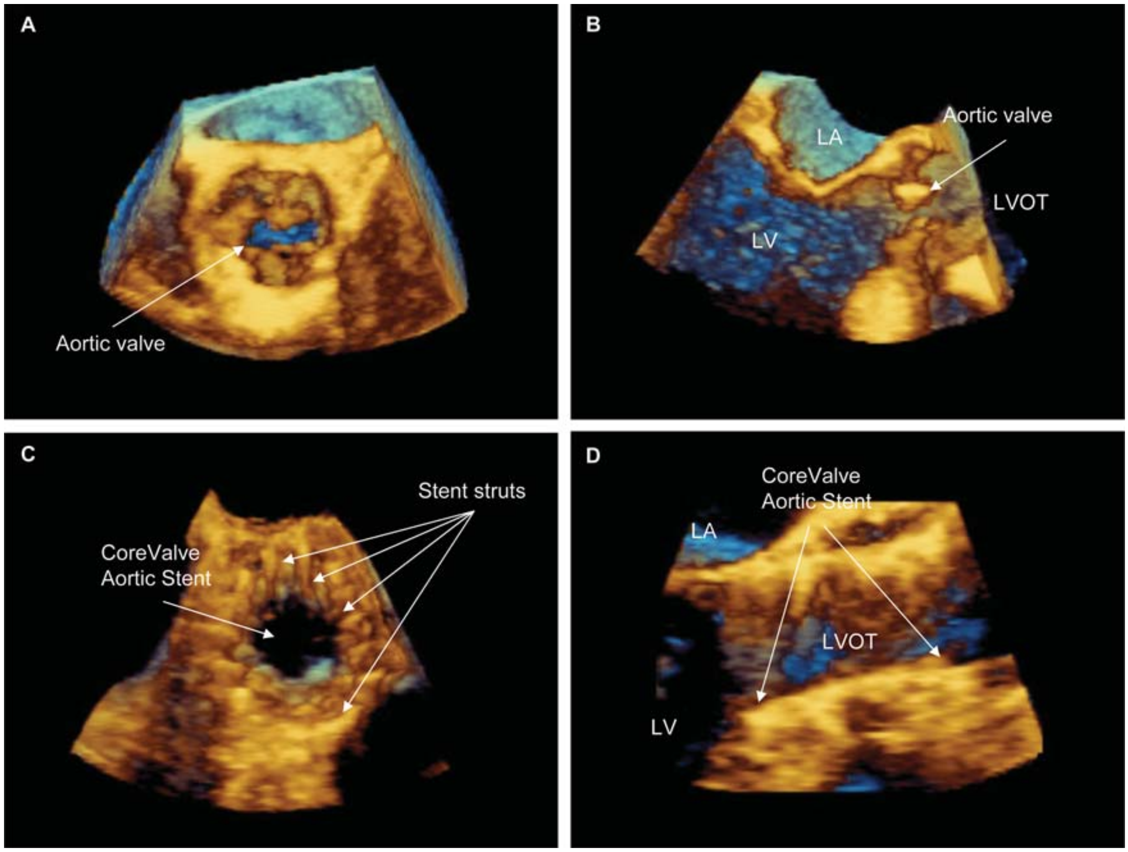

Figure 7 (*A–D*) Monitoring the implantation of an aortic stent (CoreValve®, LA, left atrium; RA, right atrium; LV, left ventricle; LVOT, left ventricular outflow tract).

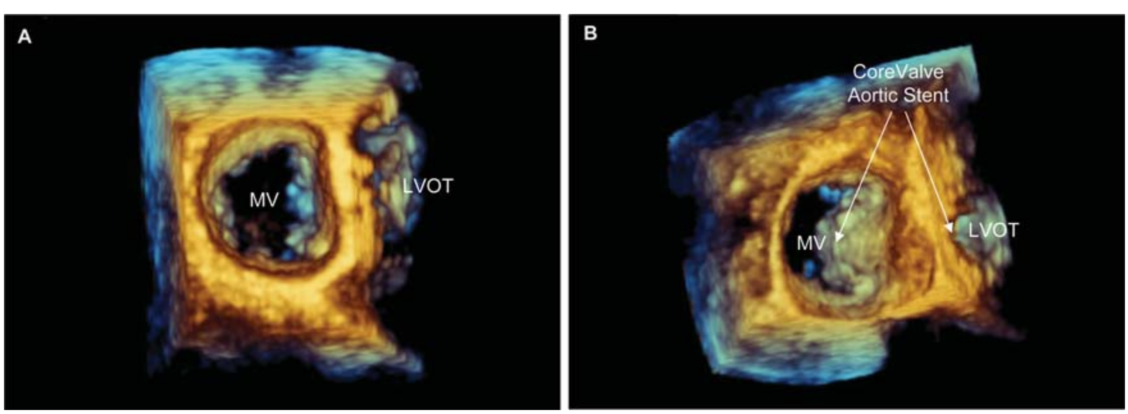

Figure 8 Surgical view of the mitral valve in diastole before (*A*) and after (*B*) implantation of an aortic stent.

be depicted with a single 3D perspective shown in *Figure 8B*. In this case, the aortic stent should be transferred further into the LVOT before final release.

Electrophysiological procedures

There is increasing interests in the utility of TEE for the guidance of electrophysiological procedures. Navigation of the catheter for electrophysiological procedures has been performed thus far using fluoroscopy. This technique lacks soft tissue contrast and adequate visualization of the target region inside the heart, especially during ablation of atrial fibrillation in the left atrium. Electroanatomical mapping systems such as CARTO using electromagnetic sensor localization have become widely adopted for complicated procedures.[24] In addition, 2D intracardiac echo systems have been used for the guidance of electrophysiological interventions, thus obtaining only a 2D image of cardiac structures during the procedure. The value of 3D anatomic information in electrophysiological procedures has been demonstrated by non-RT reconstructed 3D intracardiac ultrasound imaging.[25] This method is limited by its invasive nature, using large sheaths with possible bleeding complications. RT 3D TEE may address these challenges acquiring high-quality 3D visualization of the atria, pulmonary veins, and the mitral valve annulus less invasively.[26,27] The addition

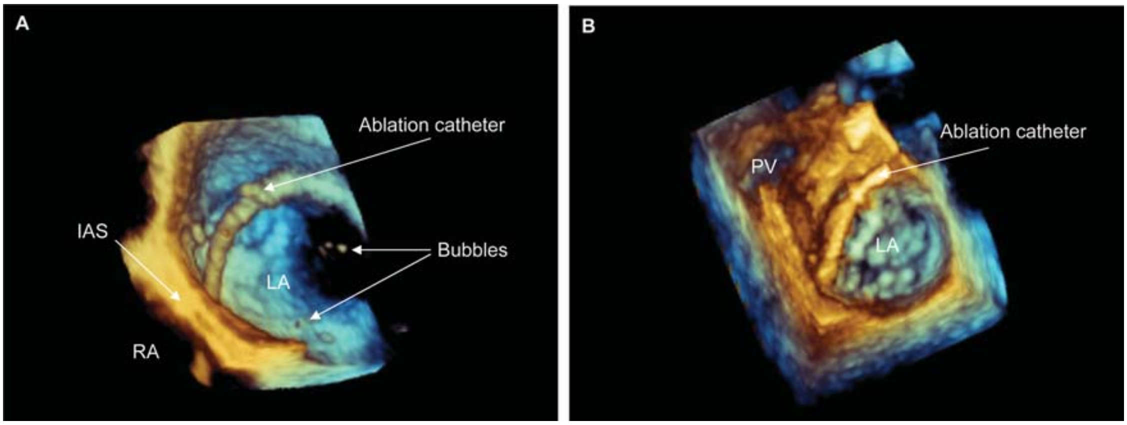

Figure 9 (*A* and *B*) Monitoring of an ablation procedure after transseptal puncture (LA, left atrium; MV, mitral valve; PV, pulmonary vein; IAS, interatrial septum).

of the third dimension is also useful during transseptal puncture in patients receiving left atrial electrophysiological procedures such as ablation of fibrillation.[28,29] This corroborates with our own findings, as demonstrated in *Figure 9A*.

Figure 9A shows a 3D image of an ablation catheter coming from the right atrium into the left atrium after transseptal puncture of the interatrial septum. Due to the unique view of the atrial septum, which defines morphology and relation of the septum to contiguous cardiac structures, safe transseptal puncture under accurate 3D TEE imaging guidance is feasible. *Figure 9B* gives a view of the pulmonary vein ostium, making it possible to virtually look inside the left upper pulmonary vein. Note how the catheter is rinsed during each electrical stimulation, forming 3D bubbles in the left atrium from the catheter tip positioned at the pulmonary vein ostium. This figure gives an en-face view of the mitral valve during systole, clearly depicting the precise position of the catheter tip along the mitral valve annulus.

Current limitations

RT 3D TEE represents a technological solution for many drawbacks of conventional 2D TEE and 3D off-line reconstruction techniques. Despite its documented clinical value, it is not devoid of limitations. One limitation is the fact that in its current phase of development, it slightly prolongs the TEE probe exposure time, most likely due to the learning curve while establishing this new technique in clinical practice. This is also corroborated by a recent study performed by Sugeng *et al.*[30] Furthermore, the technique is still limited by a relatively low temporal resolution (38–50 ms) when compared with conventional 2D TEE with a temporal resolution of $<$10 ms, which in certain clinical situations might be a practical limitation. Similarly, spatial resolution is also worse to that provided by high-end 2D systems. Additionally, on-line measurement of 3D distances and volumes has not yet been implemented. Current measurements have to be made off-line using dedicated software. Finally, the high costs of the equipment, including the transducer, the 3D-capable echo system, and the dedicated software products, may be limiting factors for a number of echo laboratories. Nevertheless, it is unlikely that these limitations will outweigh the potential of this novel imaging technique. RT 3D TEE is an innovative imaging modality that is complementary and supplementary, but not compensatory to 2D imaging.

Conclusions and future directions

The most important goal of any imaging modality suitable for the guidance of cardiac interventions is accuracy in performing the procedure and prevention of complications. As identified in this review, RT 3D TEE is feasible and safe for guiding non-coronary cardiac interventions in the catheter laboratory in humans. This review aims to describe our first experience with this technique during interventions in the catheter laboratory, such as ASD and PFO closures, revalving procedures of the aortic and the mitral valves and in electrophysiological procedures.

RT 3D TEE features a novel imaging technique to guide interventions in the catheter laboratory, providing fast and complete information about the underlying pathomorphology, improving spatial orientation, and additionally allowing the online monitoring of the procedure. These advantages over 2D TEE, intracardiac echocardiography, and in parts over fluoroscopy may accelerate decision process during interventions, reduce fluoroscopy time, and increase procedural safety and efficacy in a short- and long-term perspective. Our first experiences using this new technique in the catheter laboratory may open new avenues, enabling the performance of interventional procedures with unfolding, delivery, and implantation of devices without fluoroscopic control, only using RT 3D TEE. Taken together, these benefits may accelerate the learning curve and improve confidence of the interventional cardiologist in order to increase safety, accuracy, and efficacy of the procedure. With further enhancements in image quality and display techniques, RT 3D TEE has great potential for serving as an essential tool for visualizing minimally invasive and catheter-based therapies within the heart. It may also reduce radiation exposure from fluoroscopic guidance and also potentially shorten procedure time during interventions.

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Conflict of interest: none declared.

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