SPECIAL ARTICLE

Echocardiographic and Fluoroscopic Fusion Imaging for Procedural Guidance: An Overview and Early Clinical Experience

Jeremy J. Thaden, MD, Saurabh Sanon, MD, Jeffrey B. Geske, MD, Mackram F. Eleid, MD, Niels Nijhof, MSc, Joseph F. Malouf, MD, Charanjit S. Rihal, MD, and Charles J. Bruce, MD, *Rochester, Minnesota; and Best, The Netherlands*

There has been significant growth in the volume and complexity of percutaneous structural heart procedures in the past decade. Increasing procedural complexity and accompanying reliance on multimodality imaging have fueled the development of fusion imaging to facilitate procedural guidance. The first clinically available system capable of echocardiographic and fluoroscopic fusion for real-time guidance of structural heart procedures was approved by the US Food and Drug Administration in 2012. Echocardiographic-fluoroscopic fusion imaging combines the precise catheter and device visualization of fluoroscopy with the soft tissue anatomy and color flow Doppler information afforded by echocardiography in a single image. This allows the interventionalist to perform precise catheter manipulations under fluoroscopy guidance while visualizing critical tissue anatomy provided by echocardiography. However, there are few data available addressing this technology's strengths and limitations in routine clinical practice. The authors provide a critical review of currently available echocardiographic-fluoroscopic fusion imaging for guidance of structural heart interventions to highlight its strengths, limitations, and potential clinical applications and to guide further research into value of this emerging technology. (J Am Soc Echocardiogr 2016;29:503-12.)

Keywords: Fusion imaging, Fluoroscopy, Transesophageal echocardiography, Structural heart disease

Over the past decade, there has been exponential growth in novel percutaneous structural heart interventions developed to treat many valvular and structural heart conditions through a transcatheter approach. Steady growth in the volume of transcatheter aortic valve replacement, along with the introduction of transcatheter mitral valve repair (MitraClip; Abbott Vascular, Santa Clara, CA), left atrial appendage occlusion (Watchman; Boston Scientific, Natick, MA), percutaneous paravalvular leak closure, and a host of other approved and investigational device-based therapies have necessitated more sophisticated imaging guidance not afforded by fluoroscopy alone.

Traditionally, x-ray fluoroscopy with supplemental echocardiography has been used for image guidance. Fluoroscopy offers a wide field of view and excellent visualization of bony structures, catheters, and devices but affords limited visualization of cardiac structural anatomy and adjacent tissues. In contrast, echocardiography has a relatively small field of view, providing limited visualization of catheters and devices, but offers excellent visualization of soft tissue and provides physiologic information using color flow Doppler. Furthermore, echocardiography and fluoroscopy are typically displayed in different orientations, which hinders rapid image interpretation and further contributes to procedural complexity.

The use of cardiac computed tomographic–fluoroscopic fusion imaging and three-dimensional (3D) rotational angiography have recently been described.[1-5] Both of these modalities offer detailed 3D anatomic information. However, unlike echocardiographic-fluoroscopic fusion imaging, they do not provide real-time imaging to account for translational motion of the heart due to respiration, changes in patient positioning, or changes related to the cardiac cycle. Several reports describing the development and early experience with real-time echocardiographic-fluoroscopic fusion imaging have been published,[6-13] but literature outlining practical application of this technology is limited. In this report, we provide a critical review of echocardiographic-fluoroscopic fusion imaging for guidance of structural heart interventions and focus on the technical aspects of image registration, supported imaging modes, potential work flows for several commonly performed procedures, and limitations of the current technology. We believe this is critical to facilitate the safe and efficient incorporation into routine clinical practice and to guide further research into this new technology.

TECHNICAL CONSIDERATIONS AND SOURCES OF IMAGE REGISTRATION ERROR

The first step in fusion imaging is the process of image registration, which involves reorientation of one image (e.g., the

From the Division of Cardiovascular Disease, Mayo Clinic, Rochester, Minnesota (J.J.T., S.S., J.B.G., M.F.E., J.F.M., C.S.R., C.J.B.); and the Philips Healthcare, Best, The Netherlands (N.N.)

Dr. Nijhof is a full-time employee of Philips (Best, The Netherlands) and is responsible for early prototypes and development of the EchoNavigator system.

Reprint requests: Jeremy J. Thaden, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55902 (E-mail: thaden.jeremy@mayo.edu).

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Abbreviations

TEE = Transesophageal echocardiographic

3D = Three-dimensional

2D = Two-dimensional

echocardiographic image) to match the orientation of a second image (e.g., the fluoroscopic image). The currently available platform (EchoNavigator; Philips Healthcare, Best, The Netherlands) is a software-based solution that provides automated registration of two-dimensional (2D) and 3D transesophageal echocardiographic (TEE) images with x-ray fluoroscopy. Because no additional hardware is necessary to fuse the echocardiographic and fluoroscopic images, incorporation into contemporary catheterization laboratories is relatively straightforward, although it does require proprietary echocardiographic and fluoroscopic systems.

Although a full technical review is beyond the scope of this article, image fusion using the current system relies on rapid, automated identification of the TEE probe tip during active fluoroscopy. The electronic and acoustic core of the TEE transducer are housed in a plastic shell at the tip of the probe and have a characteristic x-ray signature, referred to as the x-ray projection, which changes predictably with changes in probe position (translational dimension) and angulation (rotational dimension) (Figure 1). The system continuously follows the probe position and angulation using a 2D-3D correlation algorithm to find the best match between the visualized x-ray projection on fluoroscopy and the predicted x-ray projection on the basis of a template high-resolution C-arm computed tomographic reconstruction.[7,14]

Preclinical validation studies using this technology found median registration error of 2 to 3 mm in the plane of the fluoroscopic image,[7,15] but previous data suggest that there is potential for more substantial error in the direction of the fluoroscopic beam.[14] Echocardiographic-fluoroscopic fusion images rely only on accuracy in the plane of the fluoroscopic image and as such are not affected by this limitation. However, the system also supports placement of annotation points as fiducial markers, which represent points in 3D space and thus require accuracy in all three dimensions (Figure 2). Registration error in the direction of the fluoroscopic beam can be minimized by using multiple fluoroscopic images obtained from different angles at the time of probe registration.[14] The recommended technique for placement of annotation points is discussed later.

A second source of inaccuracy relates to errors in rotational registration. Any error in rotational registration will be magnified as the area of interest moves from the echocardiographic near field to the far field (Figure 2). As an example, a 2° error in rotational registration will result in an error of 1.7 mm at 5 cm of ultrasound depth compared with 3.5 mm at a depth of 10 cm. An early validation study using a phantom heart model demonstrated a mean registration error of 0.8 mm at 5 cm, which increased to 1.4 cm at 10 cm of depth within the ultrasound volume.[14] This source of error can also be minimized by using multiple fluoroscopic images for registration. Further validation of the accuracy of this system in clinical practice and evaluation of potential mechanisms of inaccuracy are needed, with the knowledge that there is increased risk for inaccuracy with increasing distance from the ultrasound transducer.

APPLICATION OF FUSION IMAGING IN THE CLINICAL SETTING

Our early clinical experience with echocardiographic-fluoroscopic fusion imaging includes 34 cases and is summarized in Table 1. We used a Philips iE33 echocardiographic system for the first 22 cases and an EPIQ machine for the remaining 12 cases (Philips Healthcare). This was coupled with a Philips Allura Xper FD20/10 fluoroscopic system (Philips Healthcare). The central processing unit running the fusion imaging software was housed in the catheterization laboratory control room and operated remotely from the procedure room with a wireless mouse. Procedural staff members generally included an interventional cardiologist, a structural heart disease interventional fellow, a structural echocardiographer, an advanced echocardiography fellow, and typical procedural support staff members. In our clinical practice, the fusion imaging system and 3D echocardiographic data sets were controlled primarily by the structural echocardiographer or the advanced echocardiography fellow. This is in contrast to some centers, at which the fusion imaging is controlled by the interventional cardiologist.

Fusion Images

Echocardiographic-fluoroscopic fusion imaging is compatible with 2D echocardiographic imaging with or without color Doppler, simultaneous multiplane, and 3D echocardiographic imaging modes. The fused images are automatically displayed from the perspective of the frontal fluoroscopic C arm. The current system does not support fusion with the lateral C arm when using biplane fluoroscopy.

The system offers several options to display and edit echocardiographic images. Two-dimensional and 3D images can be displayed as they are visualized on the imaging machine ("Echo" view) or from the perspective of the fluoroscopic C arm ("C arm" view). Three-dimensional volumes can be displayed in "Free" view, which allows reorientation and cropping in any plane of interest. Three-dimensional volume data sets can also be displayed as the complete volume of data, which can be cropped in the plane of the fluoroscopic image to display soft tissue anatomy relevant to the procedure (Figure 3A, Video 1; available at www.onlinejase.com), or as a partial-thickness slice that can be moved from near to far in the direction of the fluoroscopic beam (Figure 3B, Video 2; available at www.onlinejase.com). Annotation points (markers), discussed in more detail below, are also displayed on echocardiographic images within the fusion imaging system.

Placement of Annotation Points as Fiducial Markers

The use of annotation points as fiducial markers allows one to identify a point or region of interest in the echocardiographic space and transfer that point to the fluoroscopic space. All imaging modes are supported for the placement of fiducial markers (2D, simultaneous multiplane, and 3D); however, simultaneous multiplane imaging offers rapid and precise localization of regions of interest in 3D space and thus has been the primary modality used in our clinical practice. The transducer should be stationary before placement of annotation points to ensure optimal registration. Although the probe should ideally be "docked" to avoid inadvertent handheld translational motion, we acknowledge that it is frequently not feasible to do this and still maintain adequate esophageal contact.

To create a fiducial marker, one must first register the TEE transducer tip with the fluoroscopic image. This is typically performed with the transducer stationary in the esophagus and with the imaging face of the transducer directed anteriorly. We use three registration angles (45° left anterior oblique, 0°, and 45° right anterior oblique)

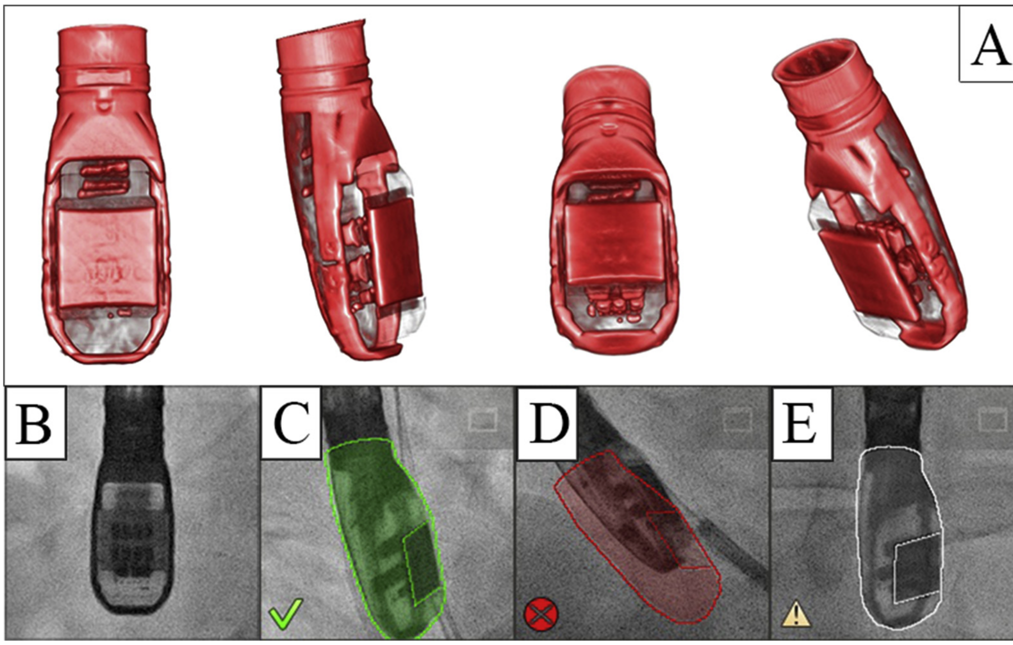

Figure 1 TEE transducer registration status. A 3D reconstruction of the TEE probe tip using a high-resolution C-arm computed tomographic data set **(A)**. During registration, this data set is used as a template and matched to the observed x-ray projection on fluoroscopy **(B)**. The registration status of the probe tip is displayed as a color overlay, with *green* denoting successful registration **(C)**, *red* denoting unsuccessful registration **(D)**, and transparent denoting unknown registration that occurs after fluoroscopy has been inactive for several seconds **(E)**.

to mitigate potential registration error in the direction of the fluoroscopic beam. The transducer tip must be fully in the fluoroscopic view at each angle, and the system will highlight the transducer tip in green when successful registration has occurred (Figure 1). One second or less of active fluoroscopy is typically required at each registration angle. Following successful registration, one must locate the region of interest by echocardiography and place an annotation marker in the echocardiographic space. Once placed, a preliminary annotation marker will appear on the fluoroscopic image. If accurate, this marker is then accepted on the fluoroscopic image, which then "transfers" the marker to the fluoroscopic space. This marker will remain fixed in the fluoroscopic space and will remain accurate regardless of TEE probe position, TEE registration status, or horizontal movement of the procedure table. Vertical (up or down) movement of the table should be minimized because vertical tracking of the table may be less accurate and it is also important to remember that a change in patient position on the procedure table at this stage will render the fiducial markers inaccurate.

We have occasionally observed the echocardiographic annotation points to "drift" during the course of routine clinical practice despite the presence of an accurate fluoroscopic annotation point. Figure 4 demonstrates an example related to inaccurate registration that can occur when the TEE probe is unregistered for an extended period after the initial registration (e.g., following probe movement out of and back into the fluoroscopic view). This causes "resetting" of the TEE probe registration, resulting in the loss of the multiple initial registration points and potential registration error in the direction of the fluoroscopic beam. In this case the fluoroscopic marker remains accurate despite the observed drift in the echocardiographic marker. If an accurate echocardiographic marker is required at this stage, it is recommended that the marker be deleted, and a new marker and registration should be performed. A second potential source of "drift" relates to the static nature of annotation points, which do not respond to device-tissue interaction (e.g., deformation) or translational motion due to respiration or patient positioning; in this case, the annotation marker remains accurate in three dimensional space, but the anatomy changes position during the procedure. Last, small misalignment of 2D echocardiographic images with respect to the anatomy may not be appreciated during the procedure and may appear as "drift" on the echocardiographic image when the annotation marker is out of the echocardiographic imaging plane.

Procedure-Specific Considerations

Transseptal Puncture. Transseptal puncture is a critical step for many structural heart procedures, which often require a precise puncture site location. The addition of a fiducial marker on the live fluoroscopic image facilitates positioning of the transseptal needle in the region of interest, permitting fine adjustments using biplane or 3D echocardiography (Figure 5, Videos 3 and 4; available at www.onlinejase.com). Annotation points also assist with procedural planning to guide coaxial alignment of devices with anatomy such as the left atrial appendage during left atrial appendage occlusion[8] and the left superior pulmonary vein for guidewire passage after initial transseptal access has been obtained.

Left Atrial Appendage Occlusion. Our experience using echocardiographic-fluoroscopic fusion imaging during left atrial appendage occlusion is largely concordant with a recently published case.[8] We often place an annotation point at the site of the transseptal puncture. After access to the left atrium, has been obtained, we use 2D or 3D echocardiographic image overlay to guide cannulation (Figure 6, Videos 5 and 6; available at www.onlinejase.com). With 2D echocardiography, a multiplane angle of 70° to 90° is often sufficient to visualize the anterolateral mitral

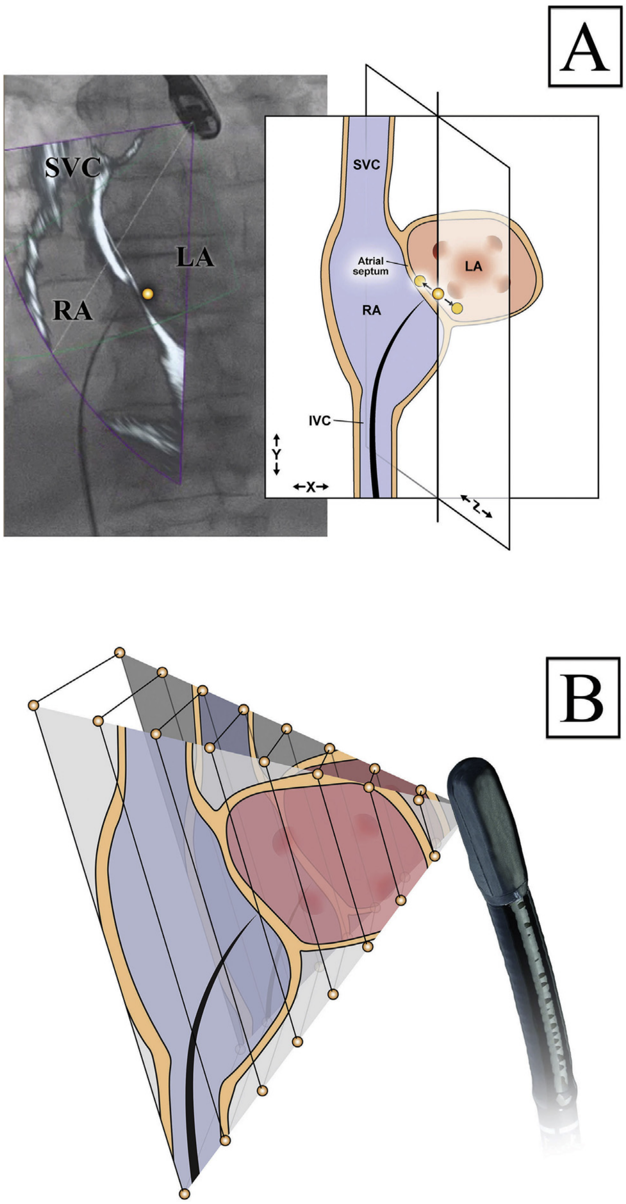

Figure 2 Potential sources of registration inaccuracy. Errors in registration can occur in the translational **(A)** or rotational **(B)** dimensions. Registration is most accurate in the plane of the fluoroscopic image (**A**, X-Y plane), but this method of registration is vulnerable to error in the direction of the fluoroscopic beam (**A**, Z dimension). This error can be mitigated by the use of multiple registration angles. **(B)** An error in rotational registration, whereby the magnitude of the error increases moving from the echocardiographic near field to far field. *IVC*, Inferior vena cava; *LA*, left atrium; *RA*, right atrium; *SVC*, superior vena cava.

annulus, left atrial appendage, and left superior pulmonary vein when viewed from a right anterior oblique position. We have also placed annotation points identifying the left circumflex coronary artery or the most proximal edge of an accessory lobe to help guide appropriate implantation depth before deployment.

Transcatheter Mitral Valve Repair. A single-center experience using echocardiographic-fluoroscopic fusion imaging for transcatheter mitral valve repair has recently been described.[6] At our own center, we typically place fiducial markers at the site of the transseptal puncture and at the orifice of the left superior pulmonary vein, which serve as reference points during the procedure to confirm the guide position across the atrial septum as well as the catheter position in the left superior pulmonary vein.

An important step in the procedure is adjusting the initial trajectory of the clip after entering the left atrium. Clip trajectory is typically visualized with 3D echocardiography, using the "surgeon's view" from the perspective of the posterior left atrium (Figure 7A, Video 7; available at www.onlinejase.com). This view is ideal for visualizing clip arm orientation and for determining the medial-lateral clip trajectory, but determining superior-inferior clip trajectory can be challenging. For visualization of the superior-inferior clip trajectory one can simultaneously display an echocardiographic-fluoroscopic fusion image from a right anterior oblique perspective. Alternatively, fusion imaging using 2D images with color Doppler can be used to help guide clip positioning from a right anterior oblique view (Figure 7B, Video 8; available at www.onlinejase.com).

Table 1 Procedure type and number (n = 34)

Procedure Type	Number of cases
Transcatheter mitral valve repair	13
Paravalvular leak closure	10
Mitral paravalvular leak	6
Aortic paravalvular leak	4
Left atrial appendage occlusion	10
Mitral valve-in-valve	1

Paravalvular Leak Closure. Fusion imaging has the potential to facilitate guidance of mitral paravalvular leak closure, particularly if the leak is small, because it is often not appreciated using 3D surface rendered imaging alone. Fiducial markers can be used to mark the site of regurgitation on the 3D echocardiographic images and the live fluoroscopic images simultaneously (Figure 8, Video 9; available at www.onlinejase.com). In our experience, using fiducial markers to guide aortic paravalvular leak closure is challenging in some cases given the static nature of the annotation point and significant translational motion of the aortic annulus (Video 10; available at www.onlinejase.com). The addition of color flow Doppler imaging (superimposed on the marker) to identify the leak in real time can be a useful surrogate.

FUTURE PERSPECTIVES

Echocardiographic-fluoroscopic fusion imaging supplemented by advances in spatial and temporal resolution of 3D echocardiography will likely influence our approach to guidance of complex structural heart procedures and could serve as an imaging platform for development of future catheter-based beating-heart interventional therapies. As an example, echocardiographic guidance for transcatheter mitral valve repair is essential for procedural success and remains challenging in current clinical practice. Image guidance requires frequent transitions from the atrial septum, mitral apparatus, and pulmonary veins often using a combination of 2D and 3D imaging

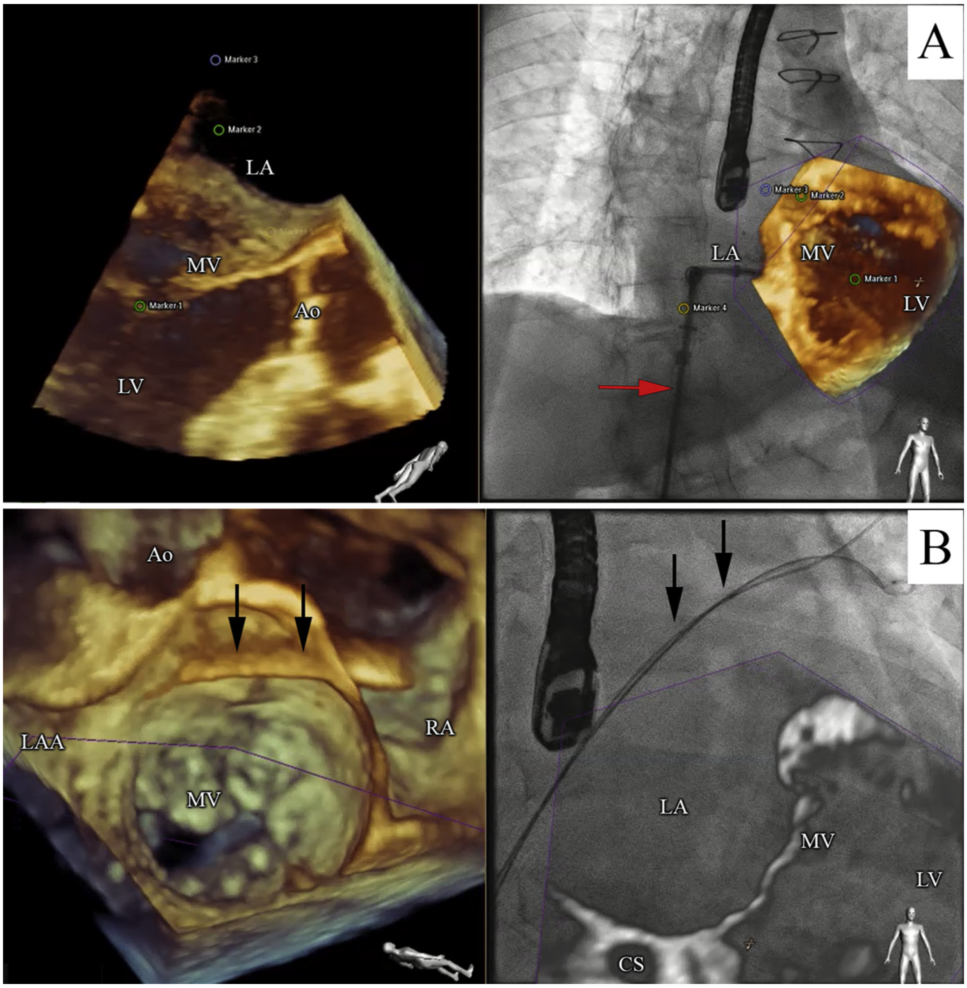

Figure 3 **(A)** A 3D echocardiographic volume is seen on the left, which is cropped to show roughly a long-axis view, which includes the mitral valve (MV), left ventricular outflow tract, and the aortic valve (Ao). The corresponding fusion image on the right shows the entire 3D volume superimposed on the fluoroscopic image, which can be cropped in the plane of the fluoroscopic image to display structures of interest (Video 1; available at www.onlinejase.com). The *purple lines* in the fused image correspond to the boundaries of the 3D echocardiographic volume. A guide catheter used during a transcatheter MV repair (*red arrow*) can be seen in the inferior vena cava and right atrium (RA), eventually traversing the interatrial septum. **(B)** The 3D echocardiographic image on the *left* is cropped and reoriented to display the "surgeon's view." This displays the left atrium (LA) and MV from a posterior perspective in preparation for a transcatheter MV repair. Two guide wires (*black arrows*) can be seen traversing the interatrial septum en route to the left superior pulmonary vein. A partial thickness slice of the 3D volume is displayed on the fused image in the *right panel*. The corresponding location of the partial thickness slice within the 3D volume is denoted by the purple line in the echocardiographic volume on the left. The position of the partial thickness slice can be altered in the plane of the fluoroscopic image (Video 2; available at www.onlinejase.com). *CS*, Coronary sinus; *LAA*, left atrial appendage; *LV*, left ventricle.

modes with and without color flow Doppler. However, with a theoretical 3D volumetric data set that is larger in size and with improved spatial and temporal resolution, much of the critical portion of this procedure could be visualized with minimal probe manipulation (i.e., docking the probe). The left atrium could be visualized from a posterior perspective to guide clip arm orientation and medial-lateral clip trajectory while the guide catheter position is visualized in the atrial septum. With improvements in the spatial resolution of 3D echocardiography, the same 3D volume data set could be simultaneously fused with fluoroscopy to guide leaflet grasping without changing transducer position. A caudal right anterior oblique fluoroscopic position could create a cropping plane orthogonal to the mitral coaptation line that would provide optimal visualization of leaflet grasping. This could also facilitate primary interventionalist-driven imaging. Using echocardiographic-fluoroscopic fusion imaging, interventionalists would have the capability to alter fluoroscopic angles in real time to minimize foreshortening and alter cropping planes.

Despite the numerous potential advantages, additional research and refinements will be important to realize the full potential of this technology. Future developments should focus on improvements in registration speed, system accuracy, and integration of the physiologic and functional data that echocardiography provides. Early efforts have shown the feasibility of identifying the latest site of ventricular activation using 3D speckle-tracking strain and fusing this information with fluoroscopy to guide left ventricular lead placement during resynchronization therapy. Speckle-tracking could also be used to provide automated tissue tracking to overcome the limitation of a "static" fiducial marker.

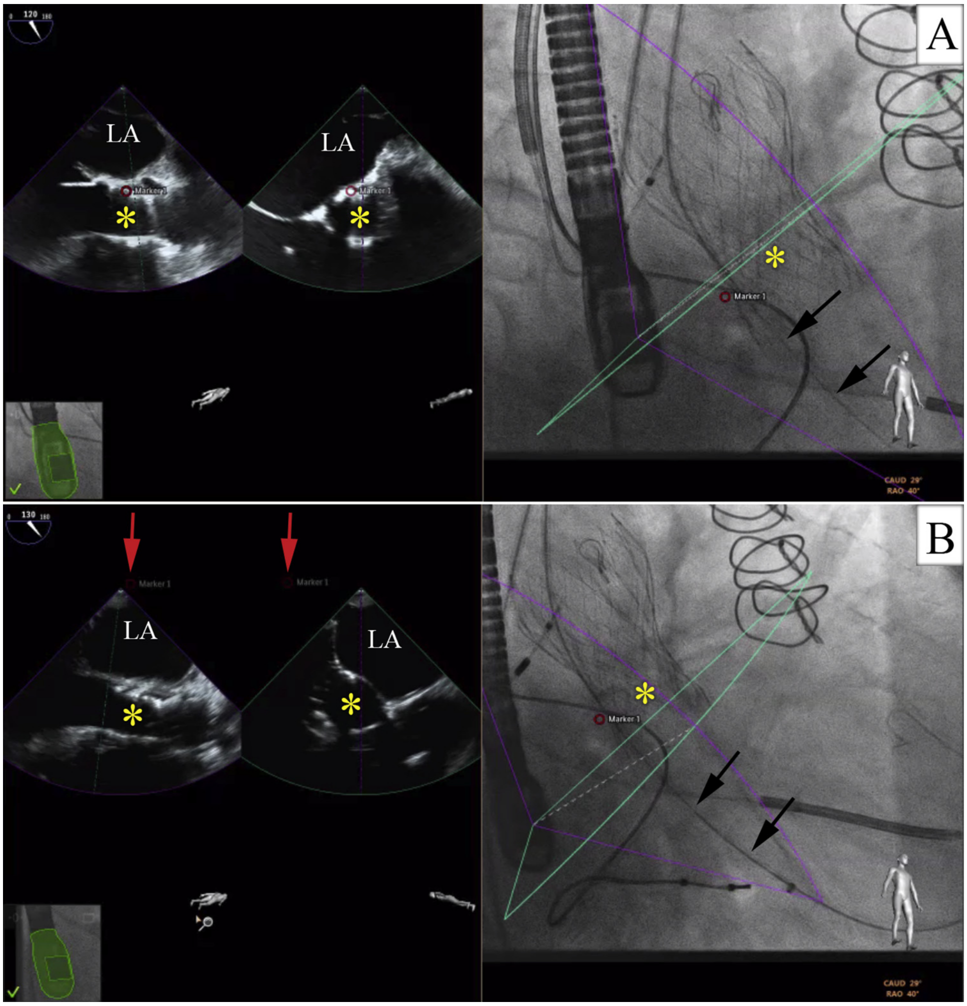

Figure 4 Aortic paravalvular regurgitation: drift of annotation points. **(A)** Simultaneous multiplane echocardiographic images are shown on the left with a fiducial marker denoting a posterior paravalvular leak (*red markers*) in a patient with a prior CoreValve transcatheter aortic valve (*yellow asterisk*). Good correlation is seen between the fiducial marker (*red marker*) and the guidewire (*black arrows*), which is visualized crossing the defect in the fluoroscopic image on the right. The two orthogonal echocardiographic imaging planes are also visualized in the fluoroscopic space outlined in *green* and *purple*, though the image overlay feature is suppressed. **(B)** Following brief transgastric imaging and return to the midesophagus, the fluoroscopic marker remains accurate (*red marker*, *right image*) but the echocardiographic marker (*red arrows*) is now faint and lies posterolateral to the site of the defect by multiplane echocardiographic imaging. This is likely due to a registration error whereby the system interprets the TEE probe position to be closer to the fluoroscopic camera than it actually is. The echocardiographic markers appear faint (*red arrows*) because the system has interpreted them to be outside the plane of imaging. Markers in the echocardiographic space appear brightest when directly in the imaging plane and progressively less bright with increasing distance from the plane of imaging. *LA*, Left atrium.

Limitations

Previous validation studies used an early system prototype,[7,14,15] and there are currently few published data regarding the accuracy of the current platform during routine clinical practice and potential mechanisms of error. Available studies involve only a small number of patients and suggest a mean registration error of 2 to 3 mm. Most of this error is in the direction of the fluoroscopic beam and is generally smaller at shallower imaging depths and larger at increased imaging depths. The degree of accuracy required is highly procedure-specific; recognition that accuracy of annotation markers decreases at increased imaging depths is important, as results may not be sufficient if a high degree of accuracy is required. In general, as with other fusion imaging modalities, at critical portions of procedures (e.g., final positioning of a transcatheter heart valve) it is recommended that the proceduralist rely on a single modality (e.g., echocardiography or fluoroscopy) for positioning and deployment rather than the fusion images, as there is an element of inaccuracy introduced with any fusion imaging.[1,5] It will be critically important moving forward to further evaluate the safety of this technology in routine clinical practice, the accuracy in various clinical scenarios, and the mechanisms of error.

The current system does not support biplane fluoroscopy for placement of fiducial markers, which are displayed only on the frontal fluoroscopic camera. Annotation markers represent a point in 3D space, but this means that one can visualize the marker's position in only two dimensions at any given time depending on the

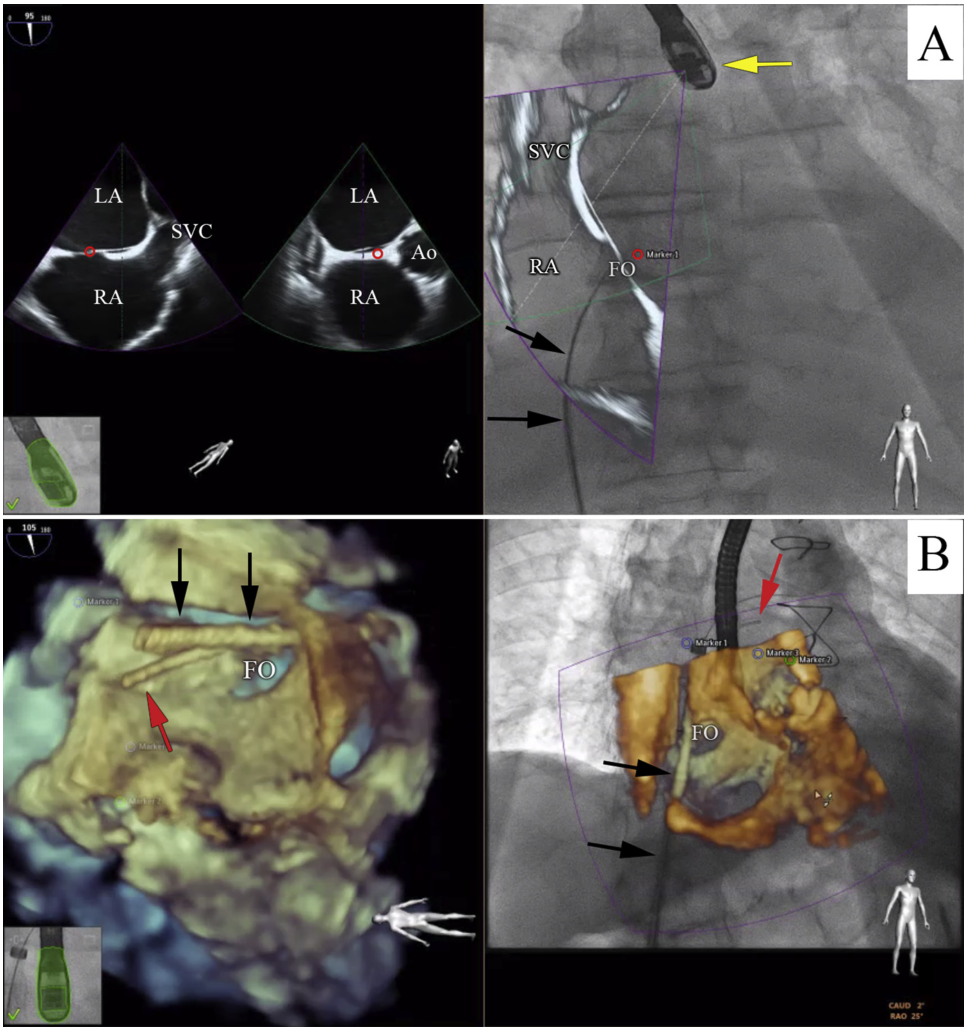

Figure 5 Transseptal puncture. **(A)** A red fiducial marker denotes the optimal site of transseptal puncture in the simultaneous multiplane echocardiographic images on the *left*. Fusion imaging with the bicaval echocardiographic view superimposed on the fluoroscopy is shown on the *right*. The orthogonal echocardiographic imaging plane is also outlined in *green* on the fluoroscopic image and can be superimposed by left-clicking the green wire outline (not shown). The transseptal puncture needle (*black arrows*) and the TEE probe (*yellow arrow*) are also visualized. **(B)** A left atrial view of the atrial septum is seen by 3D echocardiography on the *left*. A large-caliber guide catheter (*black arrows*) and a smaller fluid-filled catheter (*red arrow*) situated in the left superior pulmonary vein are seen crossing the fossa ovalis (FO). In the 3D echocardiographic-fluoroscopic fusion imaging on the *right*, the atrial septum is now viewed from the right atrial side and the location of the guide catheter by 3D echocardiography appears accurately registered with fluoroscopy (*black arrows*). The continuation of the fluid-filled catheter, which is outside the echocardiographic imaging volume, is visualized by fluoroscopy (*red arrow*). *Ao*, Aorta; *LA*, left atrium; *RA*, right atrium; *SVC*, superior vena cava.

angle of the frontal camera. In our clinical practice, we frequently use biplane fluoroscopy during transcatheter structural heart procedures. The ability to simultaneously visualize markers in the frontal and lateral imaging planes would give the interventionalist a complete view of the marker's position in 3D space, and for certain cases (e.g., paravalvular leak closure) this could greatly simplify the procedure.

As with many new devices and technologies, there is a learning curve involved, and in some cases, performing the imaging study while also manipulating the fusion imaging system can be a challenge. In our current clinical practice, we often make use of advanced echocardiography trainees along with specialized structural echocardiographers to more efficiently perform the echocardiographic imaging with simultaneous manipulation of the fusion imaging system. Additional refinements that streamline the work flow could ease integration into busy clinical laboratories and could improve the system's feasibility in nonacademic centers.

Finally, despite the potential benefits of echocardiographic-fluoroscopic fusion imaging, there are very few data on how this technology influences procedural time, radiation exposure, and patient outcomes. This is particularly relevant given associated costs of the system and the requirement for Philips echocardiographic and fluoroscopic systems. As fiscal responsibility and efficient health care delivery become increasingly important, it will be imperative to evaluate whether this new technology adds value compared with the current standard of care.

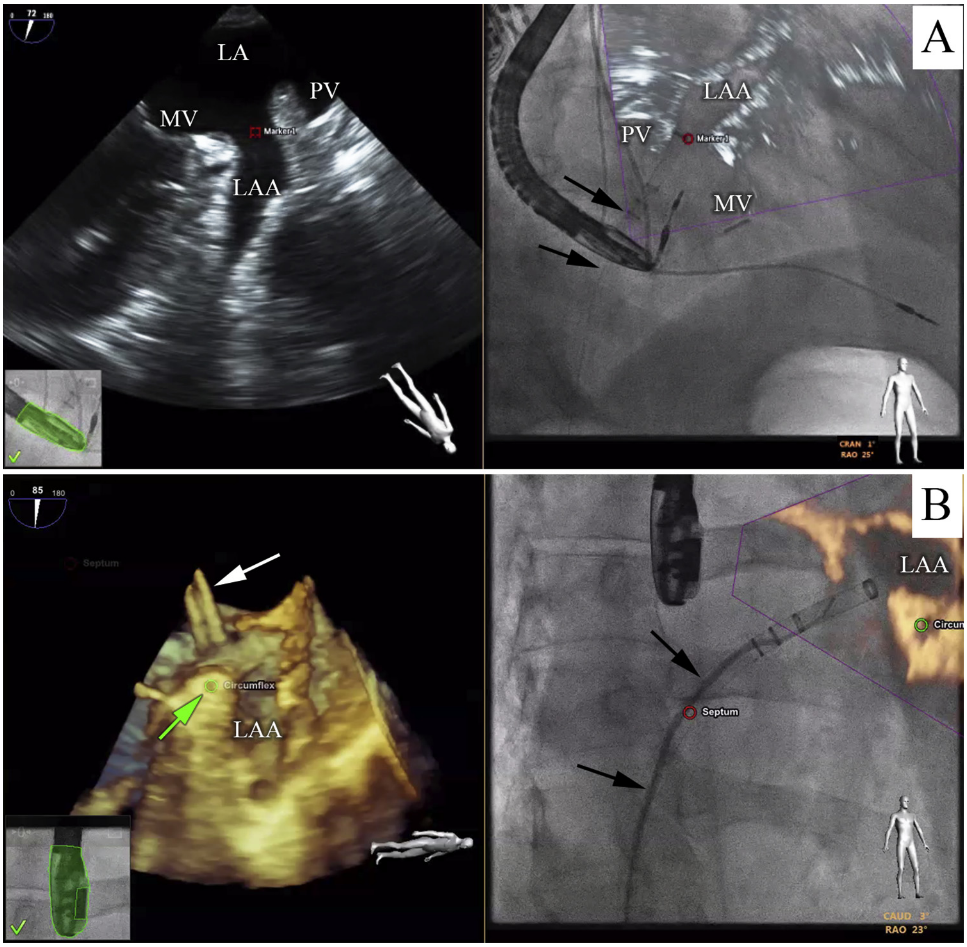

Figure 6 Left atrial appendage (LAA) occlusion. **(A)** A 2D midesophageal view of the LAA at a multiplane angle of 70° is shown on the *left* with a fiducial marker placed at the LAA ostium. The fusion image on the *right* confirms the guide catheter (*black arrows*) position at the ostium of the LAA. The ostium of the *left* superior pulmonary vein (PV) and portion of the anterior mitral valve (MV) leaflet are also visualized. **(B)** A 3D echocardiographic view of the LAA and the tip of the guide catheter (*white arrow*) are shown on the *left*. A *green* fiducial marker (*green arrow*) denotes the circumflex coronary artery. On the *right* a partial thickness slice of the 3D volume is fused with the fluoroscopic image. The guide catheter (*black arrows*) is visualized crossing the atrial septum (*red marker*) with the tip at the ostium of the LAA. *LA*, Left atrium.

CONCLUSIONS

Echocardiographic-fluoroscopic fusion imaging is now possible in the clinical setting, providing automated, real-time fusion images for the guidance of structural heart interventions. This technology provides simultaneous visualization of fine catheter manipulations under fluoroscopic guidance with detailed cardiac structural anatomy and color Doppler hemodynamic information provided by echocardiography. The system also allows the placement of fiducial markers within the echocardiographic space that can be visualized on the live fluoroscopic image. Potential registration error in the direction of the fluoroscopic beam is a limitation that can be mitigated by proper technique to ensure accurate localization of the fiducial markers in three dimensions. Additional studies are needed to better understand the accuracy of the system in routine clinical practice, how it can best be used and whether it can improve outcomes in patients undergoing structural heart procedures.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.echo.2016.01.013.

REFERENCES

1. Kliger C, Jelnin V, Sharma S, Panagopoulos G, Einhorn B, Jumar R, et al. CT angiography-fluoroscopy fusion imaging for percutaneous transapical access. J Am Coll Cardiol Img 2014;7:169-77.
2. Kempfert J, Noettling A, John M, Rastan A, Mohr FW, Walther T. Automatically segmented DynaCT: enhanced imaging during transcatheter aortic valve implantation. J Am Coll Cardiol 2011;58:e211.
3. Knecht S, Wright M, Akrivakis S, Nault I, Matsuo S, Chaudhry GM, et al. Prospective randomized comparison between the conventional

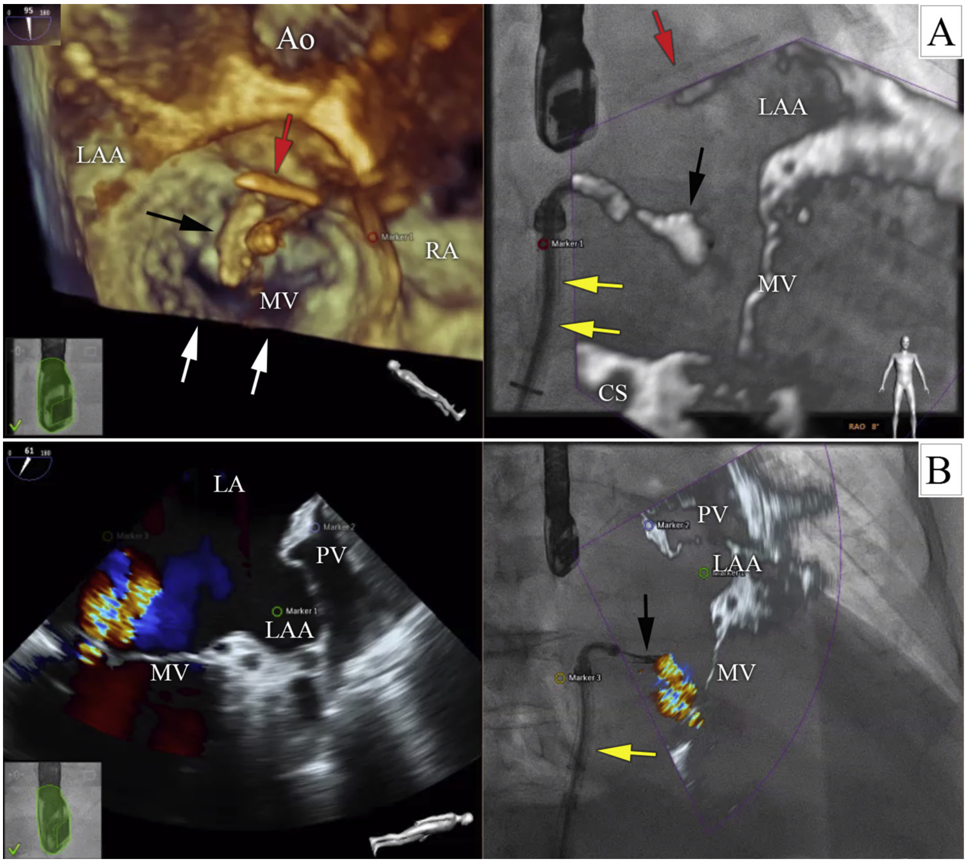

Figure 7 Transcatheter mitral valve (MV) repair. **(A)** A 3D echocardiographic volume viewed from the perspective of the posterior left atrium (LA) (*left image*) with 3D echocardiographic-fluoroscopic fusion imaging (partial-thickness slice, *right image*). Limited acoustic windows resulted in partial truncation of the inferior aspect of the LA and mitral annulus (*white arrows*), but the clip (*black arrow*) is well visualized to assess arm orientation and medial-lateral trajectory. The guide catheter seen by fluoroscopy (*yellow arrows*) on the right lies outside the echocardiographic volume and is not visualized in the echocardiographic image on the *left*. The transseptal puncture site (*red marker*) also lies outside the echocardiographic volume, but a small portion of a catheter lying within the 3D volume (*red arrow*) can be seen traversing the LA en route to the left superior pulmonary vein (PV) and is seen by fluoroscopy on the right (*red arrow*). **(B)** A 2D image with color Doppler identifying the site of mitral regurgitation is seen on the left. The fluoroscopic view shows the guide catheter (*yellow arrow*), transseptal puncture site (*yellow marker*), and the MitraClip (*black arrow*) directed toward the regurgitant jet. *Ao*, Aorta; *CS*, coronary sinus; *LAA*, left atrial appendage; *RA*, right atrium.

electroanatomical system and three-dimensional rotational angiography during catheter ablation for atrial fibrillation. Heart Rhythm 2010;7:459-65.

4. Krishnaswamy A, Tuzcu EM, Kapadia SR. Integration of MDCT and fluoroscopy using C-arm computed tomography to guide structural cardiac interventions in the cardiac catheterization laboratory. Catheter Cardiovasc Interv 2015;85:139-47.
5. Manzke R, Meyer C, Ecabert O, Peters J, Noordhoek NJ, Thiagalingam A, et al. Automatic segmentation of rotational x-ray images for anatomic intra-procedural surface generation in atrial fibrillation ablation procedures. IEEE Trans Med Imaging 2010;29:260-72.
6. Sundermann SH, Biaggi P, Grunenfelder J, Gessat M, Felix C, Bettex D, et al. Safety and feasibility of novel technology fusing echocardiography and fluoroscopy images during MitraClip interventions. EuroIntervention 2014;9:1210-6.
7. Arujuna A, Housden RJ, Ma Y, Rajani R, Gao G, Nijhof N, et al. Novel system for real-time integration of 3-D echocardiography and fluoroscopy for image-guided cardiac interventions: preclinical validation and clinical feasibility evaluation. IEEE J Transl Eng Health Med 2014;2.
8. Gafoor S, Schulz P, Heuer L, Matic P, Franke J, Bertog S, et al. Use of EchoNavigator, a novel echocardiography-fluoroscopy overlay system, for transseptal puncture and left atrial appendage occlusion. J Interv Cardiol 2015;28:215-7.
9. Clegg SD, Chen SJ, Nijhof N, Kim MS, Salcedo EE, Quaife RA, et al. Integrated 3D echo-x ray to optimize image guidance for structural heart intervention. J Am Coll Cardiol Img 2015;8:371-4.
10. Kim MS, Bracken J, Nijhof N, Salcedo EE, Quaife RA, Messenger JC, et al. Integrated 3D Echo-x-ray navigation to predict optimal angiographic deployment projections for TAVR. J Am Coll Cardiol Img 2014;7:847-8.
11. Corti R, Biaggi P, Gaemperli O, Buhler I, Felix C, Bettex D, et al. Integrated x-ray and echocardiography imaging for structural heart interventions. EuroIntervention 2013;9:863-9.

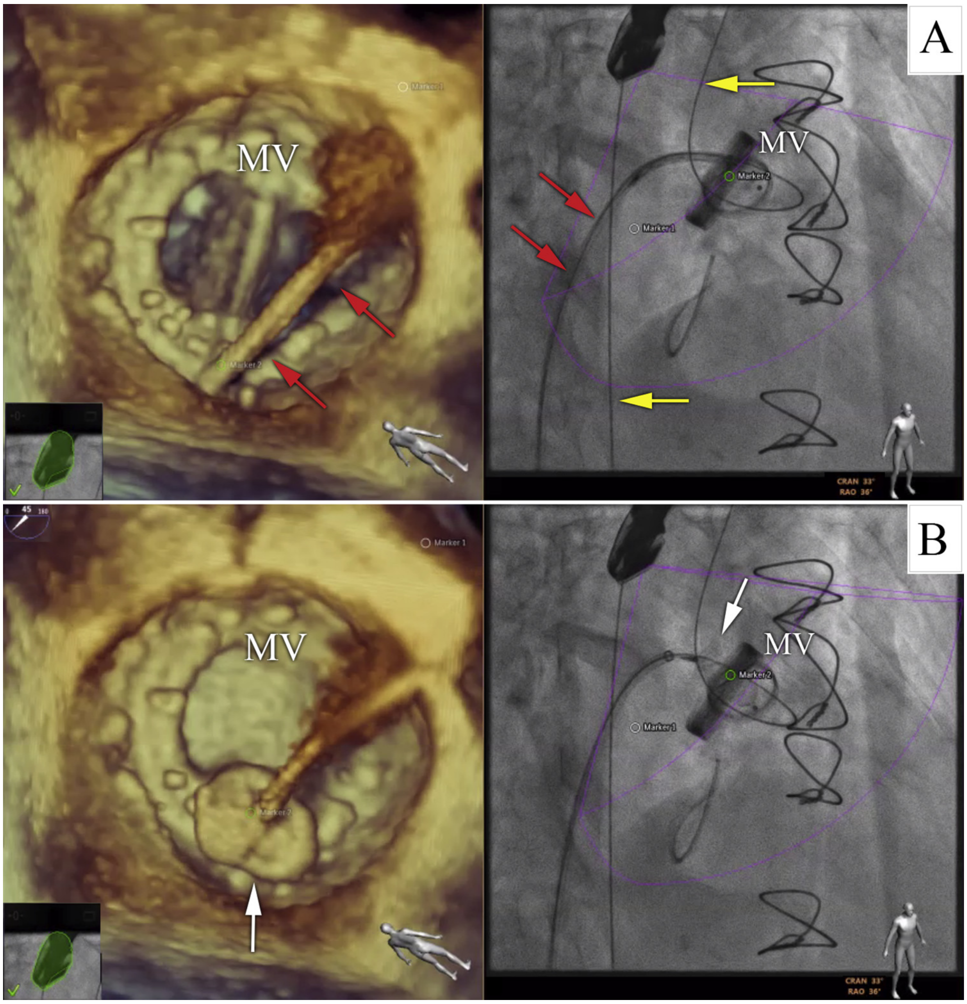

Figure 8 Percutaneous mitral paravalvular leak closure. **(A)** Three-dimensional echocardiography (*left image*) shows a bileaflet mitral mechanical prosthesis (MV) and a guide catheter (*red arrows*) traversing the atrial septum toward the site of paravalvular regurgitation (*green marker*). On the fluoroscopic image (*right image*), the guidewire (*yellow arrows*) is visualized traversing the aortic valve and descending thoracic aorta. The wire outline of the 3D volume in *purple* is visualized on the fluoroscopic image, though fusion imaging is suppressed. Fiducial markers are seen corresponding to the atrial septal puncture site (*white marker*) and site of paravalvular regurgitation (*green marker*). The transseptal puncture was performed slightly posterior and inferior to the original fiducial marker (*white marker*). **(B)** On the left image, an Amplatzer vascular plug (*white arrow*) is seen deployed at the site of paravalvular regurgitation (*green marker*).

12. Biaggi P, Fernandez-Golfin C, Hahn R, Corti R. Hybrid imaging during transcatheter structural heart interventions. Curr Cardiovasc Imaging Rep 2015;8:33.
13. Balzer J, Zeus T, Hellhammer K, Veulemans V, Eschenhagen S, Kehmeier E, et al. Initial clinical experience using the EchoNavigator-system during structural heart disease interventions. World J Cardiol 2015;7:562-70.
14. Gao G, Penney G, Ma Y, Gogin N, Cathier P, Arujuna A, et al. Registration of 3D trans-esophageal echocardiography to X-ray fluoroscopy using image-based probe tracking. Med Image Anal 2012;16:38-49.
15. Housden RJ, Arujuna A, Ma Y, Nijhof N, Gijsbers G, Bullens R, et al. Evaluation of a real-time hybrid three-dimensional echo and X-ray imaging system for guidance of cardiac catheterisation procedures. Med Image Comput Comput Assist Interv 2012;15(Pt 2):25-32.