Evaluating the morphology of the left atrial appendage by a transesophageal echocardiographic 3-dimensional printed model

Hongning Song, MD\textsuperscript{a}, Qing Zhou, MD\textsuperscript{b,∗}, Lan Zhang, MD\textsuperscript{a}, Qing Deng, MD\textsuperscript{a}, Yijia Wang, MD\textsuperscript{a}, Bo Hu, MD\textsuperscript{a}, Tuantuan Tan, MD\textsuperscript{a}, Jinling Chen, MD\textsuperscript{a}, Yiteng Pan, MD\textsuperscript{b}, Fazhi He, MD\textsuperscript{b}

Abstract

The novel 3-dimensional printing (3DP) technique has shown its ability to assist personalized cardiac intervention therapy. This study aimed to determine the feasibility of 3D-printed left atrial appendage (LAA) models based on 3D transesophageal echocardiography (3D TEE) data and their application value in treating LAA occlusions.

Eighteen patients with transcatheter LAA occlusion, and preprocedure 3D TEE and cardiac computed tomography were enrolled. 3D TEE volumetric data of the LAA were acquired and postprocessed for 3DP. Two types of 3D models of the LAA (ie, hard chamber model and flexible wall model) were printed by a 3D printer. The morphological classification and lobe identification of the LAA were assessed by the 3D chamber model, and LAA dimensions were measured via the 3D wall model. Additionally, a simulation operative rehearsal was performed on the 3D models in cases of challenging LAA morphology for the purpose of understanding the interactions between the device and the model.

Three-dimensional TEE volumetric data of the LAA were successfully reprocessed and printed as 3D LAA chamber models and 3D LAA wall models in all patients. The consistency of the morphological classifications of the LAA based on 3D models and cardiac computed tomography was 0.92 (\(P<.01\)). The differences between the LAA ostium dimensions and depth measured using the 3D models were not significant from those measured on 3D TEE (\(P>.05\)). A simulation occlusion was successfully performed on the 3D model of the 2 challenging cases and compared with the real procedure.

The echocardiographic 3DP technique is feasible and accurate in reflecting the spatial morphology of the LAA, which may be promising for the personalized planning of transcatheter LAA occlusion.

\textbf{Abbreviations:} 2D TEE = 2-dimensional transesophageal echocardiography, 3D printing = 3-dimensional printing, 3D TEE = 3-dimensional transesophageal echocardiography, CHA2DS2-VASC = congestive heart failure, hypertension, age \(\geq 75\) (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74, female, CT = computed tomography, CT-VR = computed tomography volume rendering, DICOM = Digital Imaging and Communications in Medicine, GVI = gray value inverted, LA = left atrium, LAA = left atrial appendage, NOAC = novel oral anticoagulation, OAC = oral anticoagulation.

\textbf{Keywords:} 3D printing, left atrial appendage, 3-dimensional transesophageal echocardiography

1. Introduction

Atrial fibrillation (AF), the most common cardiac arrhythmia in China and western countries, is highly associated with the increased risk of cerebral stroke, sudden death, heart failure, and impaired quality of life, and also poor exercise capacity.\[1\] The management of AF, especially AF-related stroke prevention, is critical for the patients’ outcome. Oral anticoagulation (OAC) is widely used for the conventional treatment of stroke prevention; however, it triggers bleeding events and contraindications in some cases. Although the novel OAC (NOAC) was considered to be more reliable and superior than conventional vitamin K antagonists in patients initially diagnosed with AF, its application still involves great caution.\[2,3\] As an effective alteration therapy of OAC, catheter-based left atrial appendage (LAA) occlusion, a promising nonpharmacological approach, has been recommended in the latest released guideline of European Society of Cardiology (ESC).\[4\]

Left atrial appendage occlusion is experience-dependent, technical-demanding, and is highly associated with risks of occlusion-related complications, especially in LAAs with complex morphology.\[5,6\] Moreover, the regular occlusion may not be feasible in LAAs with specific morphologies. Recently, 3-dimensional printing (3DP) technology has been introduced to cardiovascular intervention and surgery. It is a rapid prototyping technology that can transform medical images into a vivid physical model, which allows better understanding on complicated cardiac anatomy and personalized preprocedure planning.\[7,8\]

Although cardiac computed tomography (CT) can provide the full-view spatial morphology of the LAA and served as the dominant data source of cardiac 3DP,\[9\] echocardiography
actually has been more clinically used for the monitoring of periocclusion.\textsuperscript{10} Echocardiography is also of great value in long-term screening of the cardiac structure and the function of patients with AF or with a high risk of AF (eg, the aged and professional athletes with strenuous endurance exercise).\textsuperscript{11–13}

The limitation of the conventional transesophageal echocardiography (TEE) is that it fails to provide a full-view outline image of the LAA. Therefore, this study aimed to develop a 3DP technique based on 3D TEE full-volume dataset of the LAA, and explore the feasibility and accuracy of 3DP model to depict the morphologic features of the LAA. Also, we addressed the methods on how to use the model to guide transcatheter LAA closure.

1.1. Study population

In this retrospective study, we screened 23 patients with nonvalvular AF who received transcatheter LAA occlusions at Renmin Hospital of Wuhan University from April 2014 to December 2015, and also had preprocedure 3D TEE and cardiac CT raw data in our database. All patients had a CHA2DS2-VASc (congestive heart failure, hypertension, age ≥75 (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74, female) score of ≥2 (1 point was assigned for patients who were female with congestive heart failure and/or hypertension, and age between 65 and 74, diabetes mellitus, and vascular disease; 2 points were assigned for patients presenting with stroke or transient ischemic attack and age ≥75) and were unable to undergo oral anticoagulant therapy. The patients were excluded if they had a history of other arrhythmia, coronary heart disease, cardiomyopathy, or organic heart diseases. After reviewing the 3D TEE dataset and CT images, 2 cases were excluded due to acquired 3D TEE image were over 12 volumetric frames per second (VPS), resulting in a lower spatial resolution of echo dataset. Three cases were excluded because of dislocation and poor splicing of the CT images. Finally, we enrolled 18 patients in this study, consisting of 10 males and 8 females, aged 55 to 82 years (66.72 ± 7.72 years); 14 had persistent AFs, and the remaining 4 had paroxysmal AFs.

Ten patients in the study received the LAmbre system (Lifetech Scientific Co., Shenzhen, China) for LAA closure, and the other 8 patients had the Lefort device (Shanghai Shape Memory Alloy Co., Ltd, Shanghai, China). The LAmbre system consisted of an occlusion umbrella inside the appendage and a sealing disk outside the appendage. The following 2 types of the LAmbre occlusion systems are available: a regular system, which is suitable for most LAAs, and a special type called the “small-umbrella with large-seal disk” type, which is designed for nonsingle lobed LAAs. Herein, 9 regular LAmbre systems were used, and the special LAmbre was only used 1 time. The other device, a Lefort occlusion plug, is a single umbrella-shaped device, consisting of a nickel-titanium alloy metal stent and a flow barrier that accomplishes occlusion by plug-in and expansion.

All patients were informed of the benefits and risks associated with the procedure before LAA closure and signed an informed consent form. The study protocols were approved by the Institutional Review Board of Wuhan University.

2. Materials and methods

2.1. 3D echocardiographic raw data acquisition of the LAA

Three-dimensional TEE was performed with a GE Vivid E9 XD cardiac ultrasound platform (GE Vingmed Ultrasound AS, Horten, Norway) and a 3D TEE probe 6VT-D (3.0–8.0 MHz). All patients were monitored via a synchronized electrocardiogram (ECG) and were examined in the left lateral and supine positions after fasting for more than 6 hours. The 3D TEE probe was placed in the middle esophagus to acquire full-volume 3D images of the LAA.

Three-dimensional TEE raw data acquisition was followed by conventional 2D TEE. The 3D TEE imaging parameters were set as optimized conditions to ensure the quality of the images, which allowed successful postprocessing of the upcoming dataset. Once clear 2D images of the LAA were acquired, a “3D zoom” tool was applied to place the LAA into the sample box in the 90° plane. The size of the 3D zoom sample box was fixed to include the whole LAA and some adjacent structures, and the imaging frame rate was set to be 8 to 12 VPS to increase the spatial resolution. The overall gain was adjusted to a relatively lower level to minimize the noise in the LAA chamber. If the 3D images reviewed were of good quality and clarity, 5 consecutive cardiac cycles of the LAA dataset at full volume, using a single beat pattern, were stored. All of the datasets were transferred to an EchoPac workstation and stored in the Digital Imaging and Communications in Medicine (DICOM) format.

2.2. Postprocessing of 3D TEE volumetric raw data and the 3D model printing of the LAA

Three-dimensional TEE images were replayed and the volumetric frames with the largest LAA diameters were exported into the postprocessing software (Mimics17.0; Materialise, Leuven, Belgium) with the DICOM files. The data were postprocessed by gray value inverted (GVI) imaging and threshold value segmentation. The LAA chambers (blood pool) were displayed as high gray scale values (white), and the walls were displayed as low gray scale values (black) after being processed with GVI. An optimal threshold value was carefully set as the value of high coincidence between the blood cavity border and the endocardium. The maximum threshold value was 254, and minimum values were between 110 and 150, depending on the details of the different cases. The LAA chamber and the adjacent left atrium chamber mask were acquired afterward. In addition to the threshold segmentation, manual interactive segmentation was then applied to remove the tissue noise signal and the adjacent structures; as a result, a 3D LAA chamber volume mask was extracted from the raw data.

Based on the chamber mask, a new mask representing the LAA wall could be created by extending the area by 1 to 2 mm, followed by extraction of the original LAA chamber background. The above 1 volume masks of the LAA were saved as Standard Tessellation Language (STL) files and printed by an Objet Eden 500V 3D printer in the form of the following 2 models: the cardiac chamber model and the cardiac wall model (Fig. 1).

The 3D cardiac chamber model was printed by a hard material of photosensitive resins and was used for the general morphologic evaluation of the LAA, including determining the morphological classification of the LAA; and deciding if the structure of the LAA was complex and challengeable for the occlusion procedure.

The cardiac wall model was printed with a flexible, rubber-like material (Tango Plus Material, Shore hardness 26–28° A) and was applied to measure the ostial dimension and the depth of the LAA, which were the key parameters for device selection. In addition, a procedure simulation for device implantation could be performed on the 3D cardiac wall model.
2.3. Accuracy of the 3D-printed cardiac chamber model of the LAA

To evaluate the accuracy of the 3D printed cardiac chamber model, including whether it could depict the morphologic characters of the LAA in an intuitive and objective manner, we examined the cardiac CT volume rendered imaging (CT-VR) as the morphologic assessment reference.

A 64-multidetector computed tomographer (GE Healthcare, VA) was used for the CT scans. All patients had scans ranging from the level of tracheal bifurcation to 5 cm below the diaphragm. The CT contrast agent was Ultravist and the CT parameters were set as follows: retrospect ECG gating, a tube voltage of 120 kV, a tube current of 300 to 650 mA, a scanning layer thickness of 5 mm, and a reconstruction thickness of 0.625 mm. CT DICOM images with a 75% phase were exported from a GE ADW 4.6 workstation, and the Mimics innovation suite 17.0 was used for segmentation to acquire the LAA volume rendered mask.

The classification of general LAA morphology was performed according to the previous description.14 LAAs were classified into 4 morphological groups: (1) windsock LAA, which is an LAA with a dominant lobe of sufficient length as the primary structure with secondary or tertiary lobes arising from the dominant lobe; (2) chicken wing LAA, which is an LAA with an obvious bend in the proximal part of the dominant lobe or folding back of the LAA; (3) cauliflower LAA, which is an LAA that has a limited overall length with more complex internal characteristics; and (4) cactus LAA, which is an LAA with a dominant central lobe with secondary lobes extending from the central lobe in both superior and inferior directions. The LAAs of the 18 patients were evaluated, and morphological classifications were determined by 3D-printed cardiac chamber models and CT-VR based on the criteria described above. In addition, the number of lobes of LAAs observed in the 3D-printed model and CT images were recorded as single lobe, bi-lobe, and multi-lobe, according to the definition as an outpouching of the LAA with a width and length of ≥1 cm.13

According to previous clinical occlusion experiences,10,16 if the 3D printed model displayed the following morphologic characters, we considered them "challenged LAAs" for device implantation: a bi-lobed LAA with similarly sized lobes and a relatively high muscle ridge near the ostium; an LAA with some anatomic structures in the landing zone, which could interfere with the release of the device, for example, a significant secondary lobe originating proximal to the main anchor lobe or thick crest inside; or an LAA with larger ostial dimensions and smaller landing zone dimensions and less depth availability. The challenged cases were recorded for the further device implantation tests.

2.4. Accuracy of the 3D-printed cardiac wall model of the LAA

To confirm that the 3D cardiac wall model can accurately depict the ostial dimensions and the depth of the LAA, we compared the maximal and minimal ostial dimensions and the depth of the LAA obtained on models with electronic Vernier calipers to standard dimension measurements made on 3D TEE by 2 experienced readers.

Unlike 2D TEE, the axial view of the LAA ostium was reconstructed by the Flexi Slice mode under 3D TEE to clearly
display the cross-section of the LAA ostium. The maximal and minimal dimensions could be obtained for comparison. The depth of the LAA was defined as the distance between the midpoint of the ostium to the tip of the LAA.

Regarding the measurements on the 3D-printed cardiac wall model, the visual transition plane was considered to be the LAA ostial plane. We attempted to maintain the same plane as in the 3D TEE measurement. The maximal and the minimal ostial dimensions were measured, and the depth of the LAA was the largest dimension of the model that the tip of the Vernier calipers could access (Fig. 2).

2.5. Simulation operative device implantation on 3D models in challenging cases

Based on the 3D model, if an LAA demonstrated a complex structure and the challenges of occlusion, as previously indicated, a simulated device implantation would be performed on the 3D cardiac wall model to reproduce the real operation. Additionally, the actual on-site results of the occlusion were reviewed as a reference for understanding and evaluating the practices on the 3D models.

A sample device (same type and size as the actual device in the patient) was manually implanted into the 3D model using a sheath. Once the device was released into the model, the device release and potentially unacceptable peri-device leakage (a gap emerged between the device and the model) were evaluated. In addition, the device height relative to the ostium plane was visualized. We could also softly drag the implanted device to test stability. The performance of the 3D model was recorded for comparison with the actual operation results.

2.6. Observer variability

Intra and interobserver variability of the 3D printing data processing and measurements were assessed in 5 randomly selected subjects by 2 experienced readers. Regarding the interobserver variability, the same volume echo frame of each subject was processed by 2 different observers using the same data-processing protocol and printed independently. The 2 observers were blinded to each other and to the clinical details of the data. As for intraobserver reproducibility, 1 of the observers analyzed the data 1 week later, and they were blinded to the final results of the first analysis and the clinical details of the data.

2.7. Statistical analysis

SPSS 17.0 (SPSS, Inc., Chicago, IL) and MedCalc (11.0.1.0, Mariakerke, Belgium) were used for statistical analyses. Continuous data are expressed as the mean ± standard deviation (SD), and categorical data as frequencies. A paired t test was used to compare the differences in measurements between the 3D printed model and 3D TEE. Differences in measurements between the imaging modalities are recorded as biases ± the

Figure 2. LAA measurement on 3D TEE images and on the 3-dimensional (3D)-printed wall model. LAA measurement comprising ostial dimensions and the depth on 3D TEE (A–C), and on the 3D-printed wall model (D–F). In 3D TEE, the left circumflex coronary artery was considered to be the anatomic mark to reconstruct the axial view of the LAA ostium (A). D1 represented the maximal diameter of the ostium, and D2 was the minimal dimension that was perpendicular to D1 (B). (C) Depth of the LAA. Regarding the ostium plane on the 3D model, the internal transition point was first decided and then the other point was set at a position lower than the model margin (1–2 cm), which was similar to the 3D TEE measurement method (D). The Vernier caliper was placed on the ostium plane to measure D1 and D2 (E), and then the measured value was recorded in the model as the depth of the LAA model (F). LAA = left atrial appendage, TEE = transesophageal echocardiography.
levels of agreement (LOA) (2 SD), as determined by a Bland-Altman plot. The agreement of the morphological classification by the 3D model and the cardiac CT scan was analyzed by the Kappa test, which was weighted according to the frequency of LAA morphological types. Inter and intraobserver agreements between the measurements of the LAA dimensions and the morphological evaluations were determined based on intraclass correlation coefficients (ICCs). $P < .05$ was considered statistically significant.

3. Results

3.1. 3D-printed models

The 3D volumetric raw data of all 18 patients were successfully postprocessed, and the 3D digital model for printing was generated. The 3D models were printed out as 2 modes: cardiac chamber model and cardiac wall model, at a 1:1 ratio (Fig. 3). Segmentation time including threshold segmentation and interactive segmentation was approximately 15 to 25 minutes for each case. Other postprocessing procedures, such as smoothing, required 8 to 12 minutes. The model printing time was approximately 3 to 5 hours.

The demographic information and the evaluation of LAA morphology by 3D model and the LAA occlusion details of on-site and 6-month follow-up by TTE of all 18 patients were listed in Table 1.

3.2. Accuracy of 3D-printed models

The LAA morphological classification observed in echo 3D-printed models consisted of a chicken wing in 6 cases, a windsock in 8 cases, a cauliflower in 3 cases, and a cactus in 1 case. These 4 types were also observed by CT-VR, with a chicken wing identified in 6 cases, a windsock in 7 cases, a cauliflower in 3 cases, and a cactus in 2 cases. In 1 case, the morphological type...
observed by the echo 3D-printed models was a windsock, whereas CT-VR determined the type to be a cactus. The Kappa value between these 2 methods was 0.919.

Left atrial appendages with a single lobe, double lobe, or multiple lobes were observed by 3D models in 7, 7, and 4 cases, respectively, and by CT-VR in 6, 7, and 5 cases, respectively. In 1 case, the LAA was defined as a single lobe LAA by the printed model and as a double lobe LAA by CT scans. In another case, the LAA was defined as a double-lobe LAA by the 3D model and as a multi-lobe LAA by CT scans. The Kappa value between these 2 methods was 0.831.

The maximum and minimum ostial dimensions and the depth of LAAs measured in 3D-printed cardiac wall models demonstrated no significant difference with the 3D TEE measurement (Table 1). Agreement was verified by a Bland-Altman plot, which demonstrated that the limits of agreement of measurements between 3DP and 3D TEE regarding the maximum and minimum ostial dimensions and the depth were (−2.1 mm, 2.9 mm), (−2.5 mm, 2.6 mm), and (−2.3 mm, 2.8 mm), respectively, and all of the data points fell within the mean difference ± LOA (Fig. 4).

### Table 1
The clinical information of 18 patients with LAAO.

| Number | Age | M/F | DOAF, y | CHA2DS2-VASC score | LAA morphology by 3DP | Challenge LAA | LAAO time, min | Device type/numbers | On-site LAAO evaluation | Follow-up 6 mos |
|--------|-----|-----|---------|--------------------|-----------------------|---------------|-----------------|---------------------|-----------------------|-----------------|
| 1      | 73  | F   | 0.5     | 5                  | Wind sock             | No            | 50              | LAmbré regular / 1  | Leak (0.2 cm)        | None            |
| 2      | 58  | M   | 0.5     | 2                  | Cauliflower           | Yes           | 63              | LAmbré special / 1 | Leak (0.3 cm)        | None            |
| 3      | 55  | M   | 3       | 3                  | Wind sock             | No            | 60              | LAmbré regular / 1  | Leak (0.2 cm), PE  | PE              |
| 4      | 68  | M   | 0.5     | 6                  | Wind sock             | No            | 55              | LAmbré regular / 1  | None                | None            |
| 5      | 60  | M   | 1       | 4                  | Wind sock             | No            | 60              | LAmbré regular / 1  | None                | None            |
| 6      | 66  | M   | 10      | 2                  | Wind sock             | No            | 73              | LAmbré regular / 1  | None                | None            |
| 7      | 71  | M   | 10      | 3                  | Wind sock             | No            | 70              | LAmbré regular / 1  | None                | None            |
| 8      | 80  | M   | 1       | 5                  | Chicken wing          | No            | 82              | LAmbré regular / 1  | None                | None            |
| 9      | 62  | F   | 2       | 5                  | Chicken wing          | No            | 70              | LAmbré regular / 1  | Leak (0.2 cm)        | None            |
| 10     | 64  | M   | 2       | 2                  | Wind sock             | No            | 60              | LAmbré regular / 1  | Leak (0.2 cm)        | None            |
| 11     | 71  | F   | 1       | 5                  | Cauliflower           | Yes           | 95              | Lefort / 2          | None                | PE              |
| 12     | 82  | F   | 10      | 5                  | Wind sock             | No            | 40              | Lefort / 1          | Leak (0.2 cm), PE  | PE              |
| 13     | 65  | F   | 1       | 5                  | Chicken wing          | No            | 60              | Lefort / 1          | Leak (0.2 cm)        | None            |
| 14     | 70  | F   | 10      | 6                  | Chicken wing          | No            | 55              | Lefort / 1          | PE                  | None            |
| 15     | 74  | F   | 3       | 4                  | Chicken wing          | No            | 60              | Lefort / 1          | None                | None            |
| 16     | 61  | F   | 10      | 4                  | Cactus                | No            | 60              | Lefort / 1          | None                | None            |
| 17     | 55  | M   | 3       | 2                  | Chicken wing          | No            | 55              | Lefort / 1          | None                | None            |
| 18     | 66  | F   | 14      | 3                  | Wind sock             | No            | 50              | Lefort / 1          | None                | None            |

CHA2DS2-VASC = congestive heart failure, hypertension, age ≥75 (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74, female, DOAF = duration of atrial fibrillation, LAAO = left atrial appendage occlusion.

3.3. Inter and intraobserver variations

The interobserver ICCs for the 3D-printed models based on estimates of the maximum and minimum diameters of the LAA ostia and the depth and morphological type of the LAA were 0.92, 0.91, 0.88, and 0.80, respectively. The intraobserver ICCs for the 3D-printed models based on estimates of the maximum and minimum diameters, the depth, and the morphological type of the LAA were 0.94, 0.92, 0.92, and 1.0, respectively.

3.4. Simulation operative device implantation in 3D models in challenging cases

We obtained 2 challenging LAAs, according to the morphologic assessment based on 3D models. The first case was classified as a cauliflower LAA with a second lobe near the ostium and many trabeculations inside the LAA. The landing zone diameter of the dominant lobe was 11 mm, and the depth was 18 mm as measured using the 3D model, whereas the dimension of outer ostium that required sealing was 24 mm. Considering the issue of complete coverage of the lobe near the ostium, we firstly tried a...
regular LAmbre device (32 mm), which failed to thoroughly release due to the limited available space inside the LAA. Then, we implanted a special LAmbre device (30/16 mm seal disk size/occlusion disk size) that was actually used in the procedure. The device was well-positioned in the model and fully covered the ostium, and the released device in the model was similar to the actual operative condition.

The second case was a bi-lobed cauliflower-type LAA with 2 oriﬁces separated by a thick muscular crest very close to the ostium. The ostial dimensions of each lobe measured using the 3D model were 13 and 16 mm, respectively. Our ﬁrst test used a 30-mm Lefort device. As expected in the interventional rehearsals, the single occlusion plans failed due to incomplete coverage of the LAA orifice, with obvious leakage and 8-mm protrusion of the device, which implied the instability of the device. Afterward, we performed a double device closure practice, in accordance with the real operation. The lower lobe was occluded with a 24-mm Lefort device and a second Lefort device (21 mm) in the superior lobe. There was no gap between the device and the model, and the upper device was minimally displayed beyond the ostium. With complete coverage and a satisfactory tug test during the practice, the test of double device occlusion was considered to be a reproducible operation (Fig. 5).

4. Discussion
The major ﬁndings of this study were as follows: stereo models of 3DP of LAAs could be quickly produced via GVI postprocessing based on commercially available 3D TEE full volumetric images; and echocardiographic 3DP chamber models can accurately depict the morphologic features of the LAAs in detail, and the 3D wall model could be used to evaluate the performance of the device implantation. The combination of these 2 models strongly supports the personalized occlusion planning before procedures.

4.1. Signiﬁcance and feasibility of echocardiographic 3DP of the LAA
The structure and function of left atrium (LA) were abnormal in AF patients, despite size of the (LA) was normal or not. Echocardiographic assessment of the structure and function of LA can provide incremental information for the management of AF. Conventional echocardiographic parameters, such as LA size (volume) obtained by M-mode and the mitral valve obtained by pulse wave Doppler, can reﬂect the structure and the pressure of LA. Tissue Doppler imaging, strain imaging, and the novel speckle tracking imaging (STI) were all validated for their feasibility of fast assessing the LA function accurately. Although
there are still some pitfalls of these echocardiographic techniques, for example, the flow spectral parameters were affected by age and heart rate, and the current available analysis software for strain imaging and STI were designed for left ventricle instead of LA which could impair the analysis reproducibility.\textsuperscript{[13]} Echocardiography is still generally used to evaluate the cardiac function and structure of AF patients in daily clinical working. Besides, it is considered as the most valuable imaging modality to assess the structural features of LA and LAA, especially for the AF patients receiving interventional procedures.

In terms of interventional LAA occlusion in AF patients, the novel 3DP technique has been introduced to support challenging closure in cases with complex anatomy, thus ensuring the procedural safety.\textsuperscript{[18]} Since 3D printing was firstly applied to medical domains, CT and magnetic resonance (MR) have been the dominant data source for 3DP.\textsuperscript{[7,19]} However, some researchers suggested that cardiac CT should be only used in those patients in cases of a LA ostia of greater than 26 mm and there is a complex anatomical structure beyond TEE assessment.\textsuperscript{[20]} In addition, CT has the potential risks of radiation, allergic reactions to the contrast agent, and the inability to be carried out in the catheter unit. On the contrary, TEE was more convenient and valuable for detecting thrombi in the LAA, providing anatomic information about the LAA (such as its shape, ostial size, and depth), and guiding sheath and device during the operation.\textsuperscript{[21,22]} Therefore, in this study, we developed a novel raw data-processing technique that could generate a stereo digital model based on clinical routinely acquired TEE images. This method would support echocardiography as a single imaging modality that could provide detailed assessment of both morphology and function of the LAA, and it does not bring extra medical imaging costs as well.

Currently, both 3D echocardiographic hardware and advanced postprocessing software allow the possibility of reconstruction of a 3D-rendered image of cardiac structures, which is the foundation of 3DP. In conventional echocardiography, the endocardium is clearly imaged, whereas the epicardium and adjacent extra cardiac tissue are not imaged in high quality. The cardiac structure, with both sides facing a noise-free blood pool, such as intracardiac defects and valve, was described in Olivier et al’s study\textsuperscript{[23]} and could be 3D-printed directly from an acquired 3D-echo dataset without special postprocessing. However, for other structures, such as the LAA, with only 1 side facing the blood pool, whereas the other side is epicardium, 3DP is difficult to conduct directly. To solve this problem, we postprocessed the 3D TEE volumetric data using GVI imaging. The GVI mode removed the signal from the epicardium, kept the chamber information, and thus displayed the LAA chamber instead of the LAA wall. This method allowed us to generate an LAA 3D volume-rendered image, similar to CT volume-rendered imaging, which was the basis of the 3DP of the LAA.

4.2. Accuracy of the echo 3DP model of the LAA

Major concerns about 3DP included whether the model can precisely reflect the LAA anatomy and how much the model varied from the original raw data, along the reproducibility of data processing as well.

During the experiments, we believed that the accuracy of the model would be affected by every step of the entire process, from image acquisition to final printing, although mainly by the 3D dataset acquisition and data segmentation, especially threshold segmentation. The parameters must be very rigorous. Firstly, a high-quality 3D dataset was essential for the following segmentation and 3DP. A qualified image should have a completely dark blood pool with a bright endocardium and minimal artifacts and noise, which would be accomplished by regulating the overall gain, time gain compensation (TGC), probe frequency, harmonic status, and the size of the sample box. Secondly, the threshold segmentation was the key step in mapping the LAA cavity. An optimal threshold value should be set as the value can cause high coincidence between the blood cavity border and the endocardium. If an incorrect threshold was used, the mask of the segmented LAA would be anamorphic, and the printed model would be fuzzy. In addition, the interactive segmentation would also affect the accuracy of the LAA mask to a certain degree. Interactive segmentation was applied to remove the uninvolved adjacent part of the heart.\textsuperscript{[24]} Thus, it needs to be cautiously decided whether the region removed was target of interest or not when segmentation blurred a portion of the target area. An accurate STL file for 3DP can be obtained if the above processes were well-executed.

The variations of the 3D data acquisition and observation are concerned. In this study, all the TEEs were performed by 1 physician using the same echocardiographic instrument and the probe. The 3D TEE imaging parameter settings were set as the same gain, depth, and frame rates for the purpose of keeping the consistency of data acquisition. On the contrary, we had acceptable inter and intraobserver variations of LAA measurement of 3D TEE in both qualitative and quantitative assessments, which showed similar efficiency as Deutsch research in which both the wall motion grading and area ejection fraction of left ventricle acquired from intraoperative TEE had sufficiency inter and intraobserver reproducibility of evaluating left ventricular function.\textsuperscript{[25]} In our study, among the 18 patients, the morphology classifications of 17 patients determined by 3D cardiac chamber models highly agreed with those obtained by CT-VR. The consistency Kappa value was 0.919. Additionally, the maximal and minimal dimensions of the LAA ostium and the depth measured by the 3D models had no significant difference from the 3D TEE, and good agreement was shown between the 3D model measurement and 3D TEE, which demonstrated that based on the imaging parameters set in our study and data-processing protocol, our 3D model was highly coincident with the original dataset and could provide accurate morphologic classification of the LAA for clinical use.

We had only 1 case of conflicting judgment of the morphologic classification, which occurred in an LAA that was identified as a windsock LAA with the 3D model, whereas the CT model identified it as a cactus LAA, and 2 cases of lobe identification conflicts. This result might have occurred because the 3D-TEE spatial resolution is relatively limited in the far acoustic field, which corresponds to the distal and tip of the LAA in the images, when compared with the acoustic middle field corresponding to the ostium and landing zone of the LAA. In addition, the disagreement occurred in a single lobe to a bi-lobe and a bi-lobe to a multi-lobe, rather than a single lobe to a multi-lobe, and the anatomic definition of windsock and cactus are similar in some respects, which indicated that the disagreement between the 3D model and CT was not significant.

4.3. Benefit of the 2 modes of 3D models

The few currently published studies on the application of the LAA 3D model in challenging LAA occlusion cases demonstrated that they used a model that allowed for approximate morphologic
observations and preprocedural rehearsals.\textsuperscript{[9,11]} In this study, we printed out 2 modes of the 3D model, which aimed to explore the potential practical value of various 3D models.

We firstly considered the value of 3D chamber model in the advantageous display of the LAA morphologic details, which were not provided by conventional 2D TEE or even 3D TEE. The chamber model was printed as a crystalline, hard material that exhibited the general spatial shape, and terminal small lobular morphologic details of the LAA, including the numbers of lobes, orientation of secondary or tertiary branches, binding portions of the main lobe and the bending angle, and any great pectinate muscles near the landing zone as well. This model is very helpful for clinic doctors and fellows to obtain a thorough understanding of the anatomy. Secondly, the model fabricated by this material can be kept long-term, making it very useful for daily clinical training, especially for fellows and better communications with patients. In addition, to produce this solid 3D chamber model, there was no need for extra data acquisition or data processing.

The value of the flexible 3D-printed wall model was the device sizing and the ability for operation simulation practices in cases with complex morphologic LAA. The model allows access to the interventional sheath and the release of the various commercially available devices. Thus, it would be possible to decide an optimal device by repeated implantation tests on the model. The compression of the device and the gap between the device and the model, which indicates the potential of peridevice leakage, could also be visualized and assessed. Therefore, we believe that various 3D models can play individual roles in the actual clinical activities, and the combinations of these 2 models would be ideal for LAA closure.

4.4. Clinical prospect of LAA closure rehearsal on 3DP model

In this study, we performed 2 practices to mimic the real operation on the 3D model in 2 challenging cases to understand the way the device interacted with the flexible 3D model and to prepare for future preprocedural rehearsals in difficult cases. Besides the above mentioned decision of device and possible leakage, the simulation on 3D model could display the height of device protruding beyond the LAA ostium which indicated the instability of the device. In addition, the thickness of the internal muscular crest in the landing zone could be visualized and whether the distance from the orifice of the LAA to the top of crest was sufficient for the landing of a closure device could be tested as well. Moreover, the number of the devices required for a safety complete occlusion could be identified by rehearsal, such as double device strategy shown in the present study.

Consequently, with the assistance of 3DP, it would be expected that the detailed occlusion for ordinary patients and personalized occlusion for special cases could be accomplished with increased one-time operating success and free from closure complications. The 3DP technique would be helpful for patient-specific device design and production in the near future.

4.5. Limitations

The study was a tentative study of TEE-derived 3D-printed models applied to the cardiovascular area. The 3D model in this study only included the LAA itself; however, for the purpose of mimicking the LAA occlusion, the idea model should include all the structures in the operating path, such as the atrial septum, the left atrium, the left superior pulmonary vein, and the mitral valve. Although we used flexible materials to print the model, it did not completely represent the in vivo conditions; therefore, the compression ratio of the device in the model was not identical to that in vivo. Further studies should create a whole heart model and find simulated cardiac tissue materials to establish a better 3D model for interventional and surgical preprocedural practice.

5. Conclusions

The echocardiographic 3DP method in this study was feasible and capable of generating LAA model from 3D TEE volumetric dataset. Various 3D models can play various roles in clinical activities. 3DP technique is a promising candidate for LAA morphologic evaluation and interventions LAA occlusion, which is featured by easy data acquisition, accuracy of postprocessing, and the ability to simulate operation.

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