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The Value of 3D Printing Models of Left Atrial Appendage Using Real-Time 3D Transesophageal Echocardiographic Data in Left Atrial Appendage Occlusion: Applications toward an Era of Truly Personalized Medicine

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For editorial comment see p. 249

Key Words
Real-time 3D transesophageal echocardiography · 3D printing · Left atrial appendage occlusion

Abstract
Aims and Objectives: The objective of this study was to assess the clinical feasibility of generating 3D printing models of left atrial appendage (LAA) using real-time 3D transesophageal echocardiogram (TEE) data for preoperative reference of LAA occlusion. ***Background:*** Percutaneous LAA occlusion can effectively prevent patients with atrial fibrillation from stroke. However, the anatomical structure of LAA is so complicated that adequate information of its structure is essential for successful LAA occlusion. Emerging 3D printing technology has the demonstrated potential to structure more accurately than conventional imaging modalities by creating tangible patient-specific models. Typically, 3D printing data sets are acquired from CT and MRI, which may involve intravenous contrast, sedation, and ionizing radiation. It has been reported that 3D models of LAA were successfully created by the data acquired from CT. However, 3D printing of the LAA using real-time 3D TEE data has not yet been explored. ***Methods:*** Acquisition of 3D transesophageal echocardiographic data from 8 patients with atrial fibrillation was performed using the Philips EPIQ7 ultrasound system. Raw echocardiographic image data were opened in Philips QLAB and converted to 'Cartesian DICOM' format and imported into Mimics® software to create 3D models of LAA, which were printed using a rubber-like material. The printed 3D models were then used for preoperative reference and procedural simulation in LAA occlusion. ***Results:*** We successfully printed LAAs of 8 patients. Each LAA costs approximately CNY 800–1,000 and the total process takes 16–17 h. Seven of the 8 Watchman devices predicted by preprocedural 2D TEE images were of the same sizes as those placed in the real operation. Interestingly, 3D printing models were highly reflective of the shape and size of LAAs, and all device sizes predicted by the 3D printing model were fully consistent with those placed in the real operation. Also, the 3D printed model could predict operating difficulty and the presence of a peridevice leak. ***Conclusions:*** 3D printing of the LAA using real-time 3D transesophageal echocardiographic data has a perfect and rapid application in LAA occlusion to assist with physician planning and decision making.

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Introduction

Atrial fibrillation, the most frequently encountered cardiac arrhythmia in clinical practice, is an important cause of ischemic stroke [1, 2]. Considering that more than 90% of thrombi are located in the left atrial appendage (LAA) in patients with nonvalvular atrial fibrillation, percutaneous LAA occlusion can effectively prevent patients with atrial fibrillation from stroke, and is especially suitable for patients with a high risk of cardioembolic stroke but contraindicated for oral anticoagulation [3–5]. However, the anatomical structure of LAA is so complicated [6] that adequate information of its structure is essential for successful LAA occlusion.

Generally, multidetector CT, MRI and transesophageal echocardiogram (TEE) are the most accurate noninvasive imaging modalities used to define LAA anatomy and topographic relationships [7, 8]. Although these multiple different 3D imaging modalities allow us to create a volumetric data set and then manipulate and crop it from different perspectives to focus on the area of interest, one must question its effectiveness when a 3D structure is projected onto a 2D screen. Individuals vary in the strength of their visuospatial skills, meaning that 3D images on a 2D screen presented to a group of colleagues may not be interpreted in the same way by all.

3D printing technology has significantly advanced in the past 10 years [9], and has been used in various biomedical applications. The use of 3D printed cardiac models eliminates this possibility and leaves no aspect of the spatial relationships to the imagination, which can be invaluable in patients with a complex anatomy [10–12]. It has been reported that 3D models of LAA were successfully created by the data acquired from CT [13]. However, 3D printing of LAA using real-time 3D TEE data has not yet been explored. TEE provides several advantages over cardiac MRI and CT: it is portable, is readily available, possesses a high temporal resolution, involves no radiation, and can be done without sedation or with conscious sedation when indicated [14–18]. At present, TEE is routinely performed preoperatively, intraoperatively and during follow-up for LAA occlusion; therefore, using echocardiographic data for 3D printing of LAA will bring forth a new level of accessibility in the clinic.

Our aim here was to utilize real-time 3D TEE data in conjunction with image segmentation software (Mimics® software) for the 3D printing of LAA models, and to compare the measurements derived from those models with corresponding measurements from conventional 2D echocardiographic images.

Methods

Acquisition of 3D TEE Data

3D TEE data from 8 patients with a history of persistent atrial fibrillation and a CHA_2DS_2-VASc score ≥2, HAS-BLED score ≥3 and intolerance of anticoagulation was acquired. The experimental protocol was approved by the Research Ethics Committee of Southern Medical University, China, and written informed consent was obtained from all of the subjects. Participant recruitment was conducted from September 2015 to December 2015, and follow-up participant recruitment will continue until December 2016. 3D echocardiography image acquisition was performed using the Philips EPIQ7 ultrasound system. The high-quality selected data were initially exported in digital imaging for communication in medicine (DICOM) format, after which the data must be opened in Philips QLAB. Within QLAB there is a function to enable the ‘Cartesian DICOM’ export, an option that is not possible directly from the EPIQ7 machine.

Extraction of the Chosen Region of Interest Termed ‘Segmentation’

The Cartesian DICOM echocardiography data set was imported into dedicated postprocessing software (Mimics®) and processed to reduce imaging noise and isolate the area of the LAA. A threshold tool allows the user to set a range of values from the data to be retained while ignoring data that fall outside of that range. Therefore, the LAA was segmented from the data via thresholding and interactive editing operations. Once segmentation was completed, a 3D reconstruction model was rendered for visualization and measurements. The Mimics® software was then utilized to smooth the surface of the anatomy and ensure that it was suitable for 3D printing before exporting in the stereolithography (or STL) format.

LAA 3D Models

The processed data saved in the STL format that was 3D printable was then exported to the Stratasys Objet 30 Pro 3D printer, and a rubber-like material was used for printing the LAA.

3D Models for Preoperative Reference and Procedural Simulation in LAA Occlusion

The maximum diameter and depth of each of the LAAs (n = 8) were measured from the 2D TEE images to predict the dimensions of the device. The optimal size of the Watchman device was selected through simulating the surgical procedure using a 3D printed model in vitro. Finally, a comparison was made between the Watchman devices predicted by 2D TEE or 3D printing models and those actually placed intraoperatively.

Results

In this study, the echocardiographic data (fig. 1) of LAA from 8 patients with a history of persistent atrial fibrillation were successfully segmented and converted to the STL format (fig. 2). A 3D LAA model was then printed within 16 h using a 3D printer. All the 8 echocardiographic data sets were successfully segmented, and a 3D

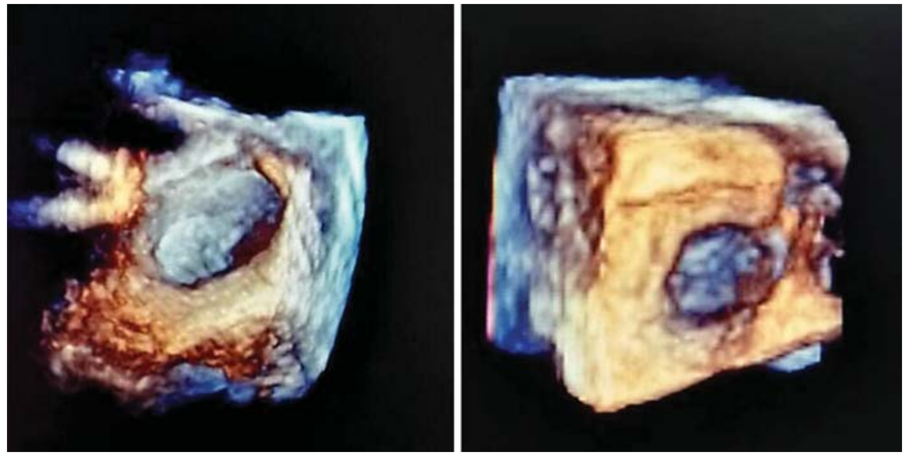

Fig. 1. A 3D echocardiographic image of LAA was acquired from patient atrial fibrillation.

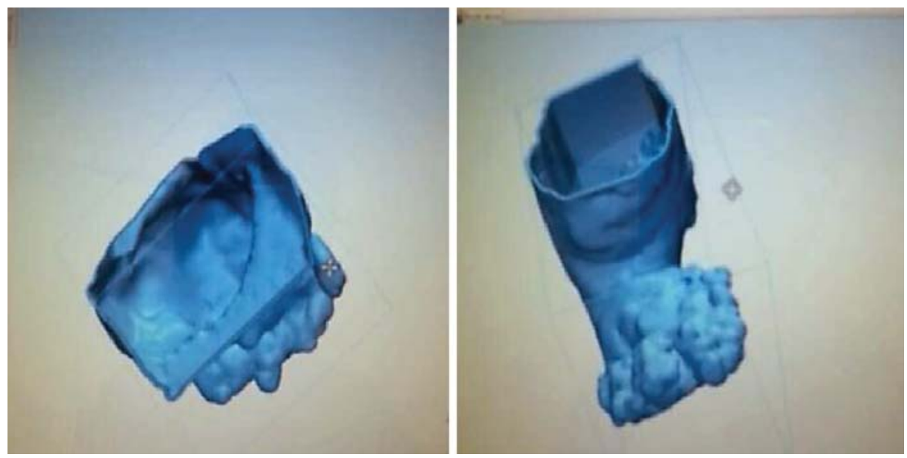

Fig. 2. The 3D transesophageal echocardiographic data were converted to a 3D reconstruction image suitable for 3D printing by Mimics® software.

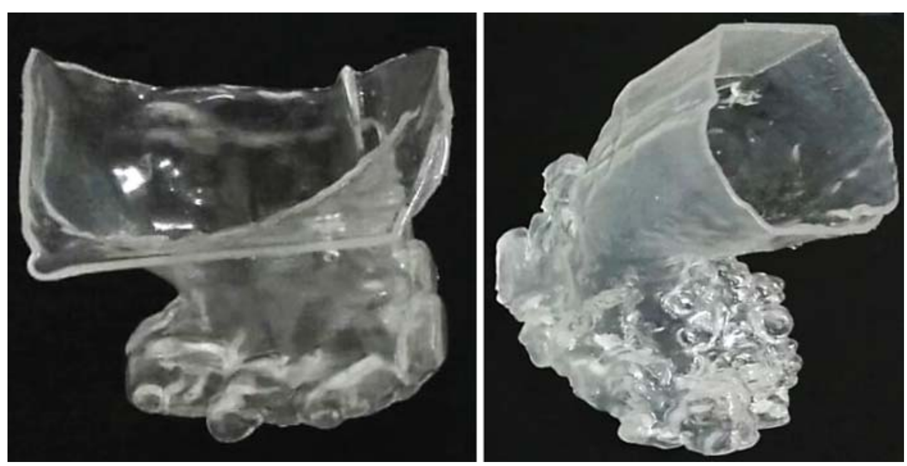

Fig. 3. The 3D printed LAA model was created using the 3D reconstruction image data.

digital image and printed models were created (fig. 3). The maximum diameter and depth of each of the LAAs (n = 8) were measured from the 2D conventional TEE images (fig. 4), predicting the size of the Watchman devices. The optimal size of the Watchman device can be selected through simulating the surgical procedure using the 3D printed model, which can be compared with those placed in the real operation.

Seven of the 8 Watchman devices predicted by preprocedural 2D TEE images were of the same sizes as those

Color version available online

Fig. 4. The maximum diameter and depth of the LAA were measured by the 2D conventional transesophageal echocardiographic image.

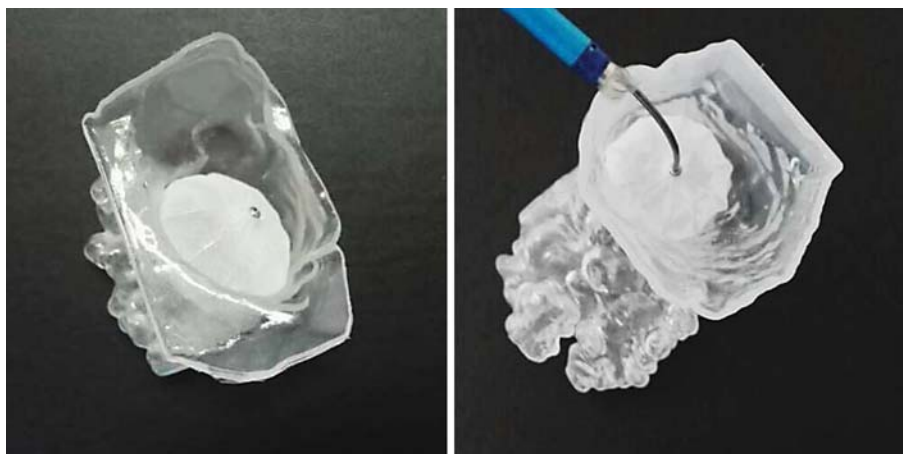

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Fig. 5. The Watchman device was placed within the patient-specific 3D printed models.

placed in the real operation (table 1). In the only case in which 2D TEE images failed to accurately predict the device size, the LAA had a wide oval ostium, a shallow depth and a cauliflower shape. The preprocedural 2D TEE images predicted a diameter of 27 mm, meaning a 30-mm device was expected to be deployed. However, the 3D printed model demonstrated that the thick musculi pectinati divided the LAA tip into two lobes, with the anterior lobe smaller and the posterior one bigger. The 3D printed model can simulate the surgical procedure in the following ways. The first involves using the pigtail catheter to guide the outer sheath into the posterior lobe, using the advanced Watchman Delivery System, and releasing the occluder. A gap of about 6–7 mm was found in the place where the occluder adjoined the pulmonary vein, meaning the LAA could not be fully closed by the occluder. The alternative approach reselected the position and guided the outer sheath into the anterior lobe until the sheath approximated the LAA tip. The Watchman Delivery System retracted and released the occluder. This time, the gap was largely narrowed, but the 30-mm occluder only caused a slight compression and had poor stability. Employing a third technique, a 33-mm occluder was selected and released along the same axis. This time the occluder was stable. The 33-mm occluder needed a deeper space, but the musculi pectinati between the posterior and anterior lobe obstructed the occluder feet. The occluder was therefore not fully distended, leaving a 3-mm gap. According to the results of the simulated operations, it was recommended that the 33-mm occluder be axially placed in the anterior lobe. It was estimated that there would be a 2- to 3-mm gap at the inferior margin. The 3D printed model was made of gelatin with characteristics different from those of the cardiac myocardium. The device barb could be pierced into the cardiac myocardium to anchor the occluder, but it could not enter the gelatin model. Considering this, the 30-mm occluder was first tested in real surgery. The results were consistent with the predictions made by the 3D printed model. The 30-mm occluder placed in the posterior lobe axially left a 7-mm

Table 1. The recommended size of the Watchman device by different preoperative assessment measures, and the finally selected size and peridevice leak after placement in the real operation

LAA No.	Recommended by 3D printed models, mm	Measured by 2D TEE, mm	Recommended by 2D TEE, mm	LAA occlusion finally selected, mm	Peridevice leak, mm
1	27	23	27	27	–
2	33	27	30	33	3
3	24	20	24	24	–
4	24	20	24	24	–
5	21	19	21	21	–
6	27	23	27	27	–
7	24	22	24	24	–
8	27	23	27	27	–

peridevice leak. If released axially in the anterior lobe, the occluder would have fallen out of the LAA. Again, a 33-mm occluder along the same axis was selected. After being released, the occluder was stable and in a good position, but there was a peridevice leak of about 3 mm at the inferior margin. However, since 3 mm is within the acceptable range, the surgery was ended.

To summarize, all device sizes predicted by the 3D printing model were fully consistent with those placed in the real operation (fig. 5). Also, the 3D printed model could predict the operating difficulty and the presence of a peridevice leak.

Discussion

The anatomical structure of an LAA is so complex that getting sufficient information about its structure has become crucial to the success of LAA occlusion, guidance of preoperative planning, intraoperative assessment and follow-up. Typically, the most accurate noninvasive imaging modalities, including MRCT, MRI, and TEE, are used to define the LAA anatomy and topographic relationships. The feasibility of these current devices are high. Studies have reported LAA measurements based on mean TEE-like multidetector row computed tomography (or MDCT). MDCT LAA diameter estimation resulted in feasibilities of 93.9, 97 and 99.0% for the Watchman, the ACP and for either one of the two devices, respectively. However, the imaging data can only be appreciated on a 2D screen, resulting in a lack of tangibility. Besides, the inner diameter of the LAA could vary if measured by different doctors or on different planes. With the help of advanced software and hardware, especially with the development of 3D reconstructions, the images have been considerably improved. Under 2D or 3D imaging, the position and size of the Watchman device placed intraoperatively may differ from that in the preoperative assessment. Therefore, printing out the replica of a patient's anatomy is necessary.

LAA anatomy is complicated and it is hard to quantify the interaction between the device and the appendage even with advanced imaging techniques. The position in which to release the device was determined by multiple factors, including the morphology, diameter, depth, and lobulation of the LAA and the distribution of the musculi pectinati. In most cases, 2D TEE alone can accurately predict the occluder size and its position. However, more attempts are necessary when it comes to complex LAA. Consequently, the duration of the operation will be prolonged and more contrast and X-rays will be utilized, exposing the patient to greater risks. A 3D printed model can reduce the duration of the operation and the use of contrast agents and X-rays. Overall, we have accumulated the following experience. (1) Using the 3D printed model to simulate the release of the appendage occluder to determine the device size and the axis of placement is of great importance to the judgment of results. (2) With the printed appendage, the subtle structure of the musculi pectinati is tangible, which is considerably conducive for us to predict the influence of the musculi pectinati on the occluder.

It is also worth pointing out that the inner diameter of the occluder will reduce by 8–25% due to the fact that the LAA is oval shaped and the occluder is round. In this way, the LAA and the occluder will fit closely together. Gelatin was selected as the printing material for models in this study because this material makes the model flexible and resilient. Thus, the gelatin model is more in line with the requirements of the simulated operation.

In this study, the 3D printed models of LAA were created using data from 3D TEEs of 8 patients. Seven of the 8 Watchman devices predicted by preprocedural 2D TEE images were of the same sizes as those placed in the real operation. All of the device sizes predicted by the 3D printing model were fully consistent with those placed in the real operation. Most importantly, the 3D printed model could predict the operating difficulty and the presence of peridevice leak and its relevant causes.

Regarding peridevice leaks, residual peridevice flow into the LAA after percutaneous closure with the Watchman device was common. TEE follow-up revealed that 32% of implanted patients had at least some degree of peridevice flow at 12 months. The hazard ratio of the primary efficacy endpoint per 1 mm larger peridevice flow was 0.84 [19]. Cardiac-CT follow-up detected any persistent LAA contrast filling in 62% of patients, but the leak sizes were small (1.5 ± 1.4 mm). TEE follow-up revealed peridevice flow in 36% of patients (jet sizes ≤4 mm). Also, they were almost exclusively localized at the posterior portion of the LAA orifice (>90%) [20]. There are reports that residual peridevice flow is not associated with an increased risk of thromboembolism. However, this finding should be interpreted with caution as the low event rate decreases the confidence of this conclusion [19]. On the one hand, a peridevice leak could enhance thrombus formation and embolization of thrombi around the device into the circulation, while on the other hand the relatively small size of these leaks may preclude clinically relevant embolizations. Therefore, the clinical significance of small leaks after LAA closure is unclear.

Conclusion

3D printing of the LAA using 3D TEE data can help interventional cardiologists simulate operative procedures prior to LAA occlusion and choose the right size and position at which to release the occluder with consideration of various factors, including the diameter, depth and lobulation of the 3D printed models. More complex cases (e.g. a wide, flat shape of the LAA, multiple lobes and thick musculi pectinati) will all affect the release of the occluder. The 3D model is superior to 2D imaging in that the former can predict operating difficulty and complications (e.g. an unstable occluder and peridevice leak). Therefore, creating 3D models with the use of 3D TEE data for LAA occlusion is more desirable and shows great promise.

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