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ORIGINAL RESEARCH - CLINICAL

A Novel Puncturable Atrial Septal Defect Occluder

The Results of Preclinical Experiment and First-in-Human Study

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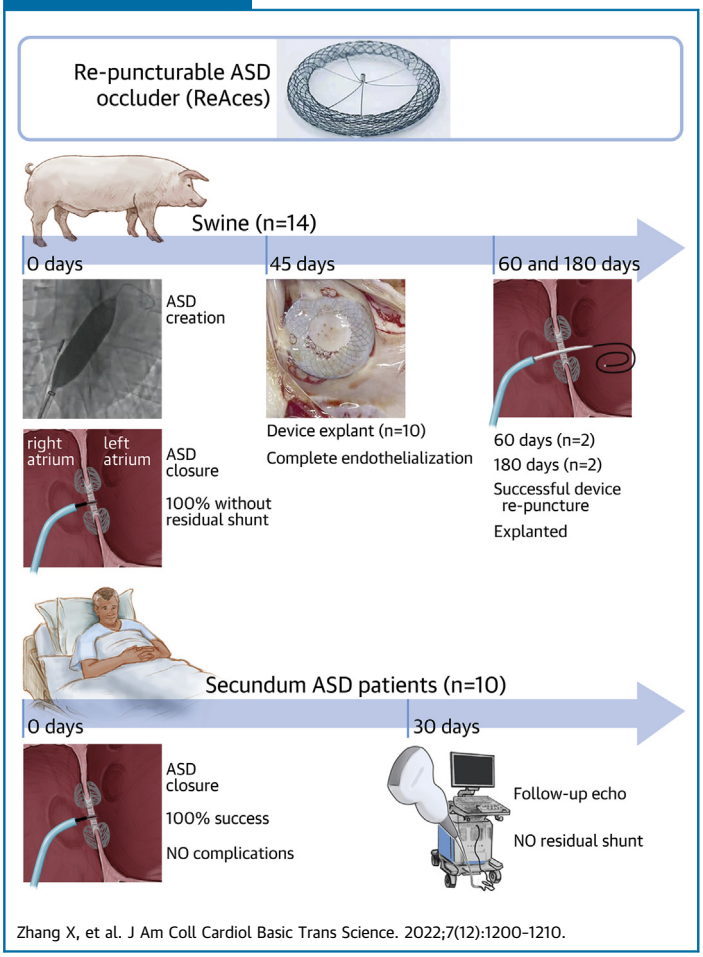
VISUAL ABSTRACT



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HIGHLIGHTS

- **In the presence of an ASD occluder, the subsequent puncture of the atrial septum for such patients may be challenging, and this important route for left-sided interventional procedures correspondingly is limited.**
- **The ReAces device is a novel transcatheter ASD occluder, which is designed for easily puncturing and crossing the atrial septum when a left-sided interventional procedure is needed.**
- **The animal experiment and first-in-human study show that it is safe and effective to use the ReAces device for closure of ASD and that puncturing and crossing the device with a large catheter is feasible and simple.**

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SUMMARY

ReAces is a novel puncturable transcatheter atrial septal defect occluder. The device success rate was 100% (n = 14 of 14) in the animal experiment. Four swine successfully received puncture of the device 60 days after implantation of the device. The acute procedure success rate in the 10 patients was 100%. Transthoracic echocardiography examination showed that the devices were well positioned with no residual shunt, and the area of central portion of occluder was substantially thin. It is safe and effective to use ReAces for closure of secundum atrial septal defect, and puncture the atrial septum at the portion of the device is feasible.

ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defect

AF = atrial fibrillation

CTA = computed tomography angiography

ICE = intracardiac echocardiography

PET = polyethylene terephthalate

TTE = transthoracic echocardiography

Atrial septal defect (ASD) is one of the most common types of congenital heart diseases, of which 80% are secundum ASD. Transcatheter device closure is the preferred treatment for secundum ASD.[1] Currently, the core materials of ASD occluders used in clinical practices are devices containing 2 disks and 1 waist that are woven with the nickel-titanium wire. The closure by such occluders could isolate the left and right atria by multilayer metal meshes and barrier films. Most patients undergoing ASD closure are relatively young, and the long-term rate of complication with atrial fibrillation (AF) and mitral regurgitation is as high as 20%.[2,3] These complications are generally treated with transcatheter intervention, such as radiofrequency ablation, left atrial appendage occlusion, and transcatheter edge-to-edge mitral valve repair.[4-6] These techniques of transcatheter intervention all require transfemoral catheterization through the atrial septum to access the left atrium for the treatment procedures. However, in the presence of an ASD occluder, the subsequent puncture of the atrial septum for such patients may be challenging, and this important route for left-sided interventional procedures is correspondingly limited. A novel puncturable transcatheter ASD occluder, the ReAces device (Hanyu Medical Technology), was recently developed. Here, we report the short-term findings of this medical device in animal models and first-in-human studies.

METHODS

DEVICE DESIGN. The ReAces device is a puncturable ASD occluder. The main part of the ReAces device is made of memory nickel-titanium wire, which is a framework consisting of the left disc, right disc, and waist connecting the 2 discs. The central hole through the framework is equipped with the polyethylene terephthalate (PET) membrane without metal mesh, which blocks the blood flow. The overall morphology of the occluder remains the 2 disks and 1 waist structure of conventional occluders to maintain stability. The diameter of the central hole is equal to the diameter of the waist, in which only few nickel-titanium connecting wires are used to connect the right disk to interconnecting piece. The interconnecting piece is connected to the delivery steel cable to allow the connection between occluder and delivery system. The central hole is covered by PET membrane, which ensures the effectiveness of occlusion and also allows the puncture or delivery of a large-diameter sheath catheter through the central hole very easily. The salient characteristics of the puncturable occluder design are shown in **Figure 1**. The diameter of the waist is considered as the size of occluder, which has 19 different sizes ranging from 8 to 44 mm, and the diameter of 2 adjacent occluders has a range of 2 mm. The diameters of the right and left discs are 8 to 10 mm larger and 10 to 14 mm larger, respectively, than the diameter of waist. The size of the delivery catheter for the device ranges from 12F to 16F, according to the size of the occluder.

ANIMAL EXPERIMENT. Animal model. Fourteen adult swine (Yorkshire pigs) were used in this study between January 2021 and February 2021, of which 64% (n = 9 of 14) were male, and the mean body weight of the swine was 47.9 ± 3.8 kg (range 41-52 kg). Ceftriaxone (1 g) was intramuscularly injected before and once per day for 3 days after the

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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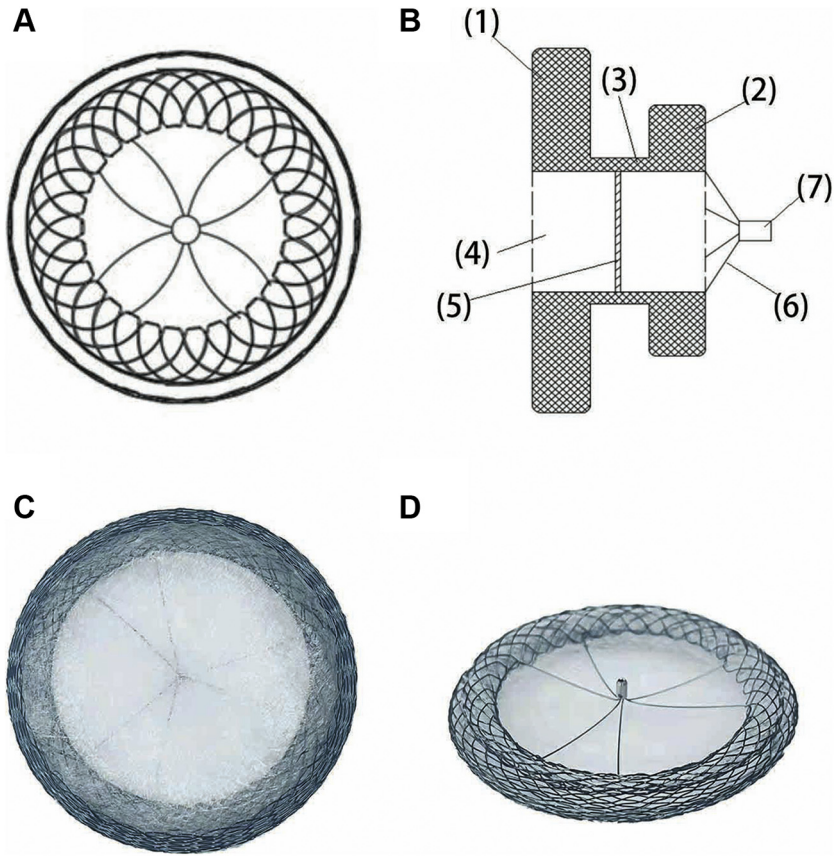
FIGURE 1 The Schematic Diagrams and Actual Pictures of the ReAces Device



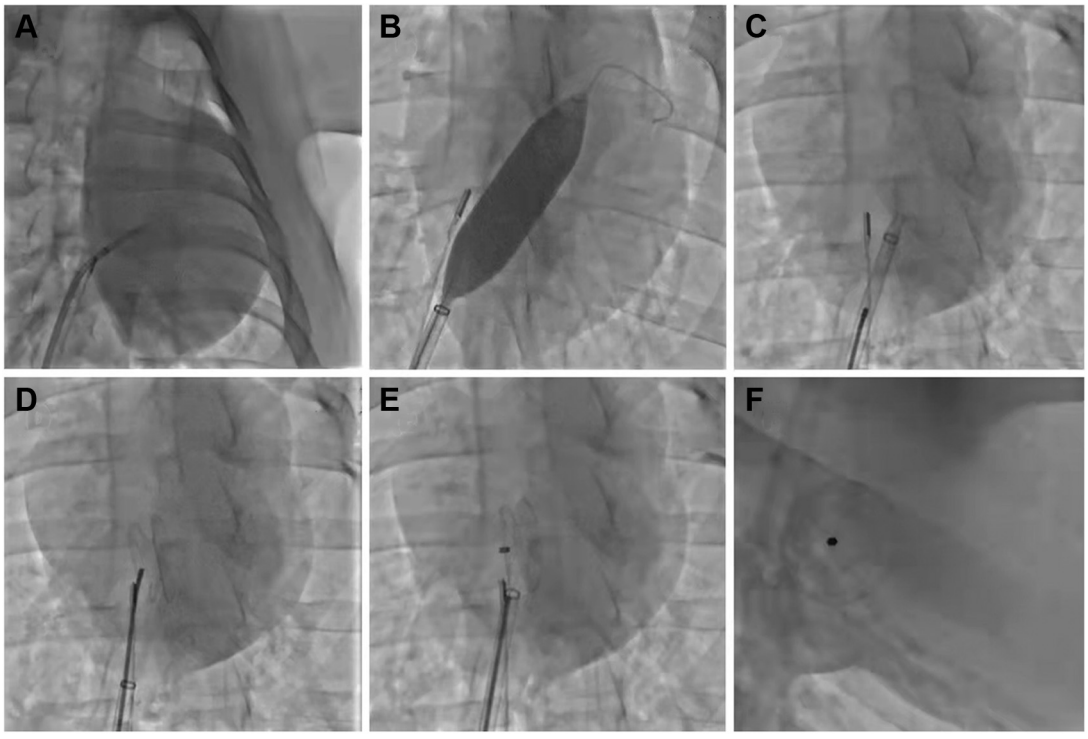
(A) A schematic diagram top view of the device. **(B)** A schematic diagram section view of the device, including the **(1)** left disc, **(2)** right disc, **(3)** waist, **(4)** central hole, **(5)** polyethylene terephthalate membrane, **(6)** nickel-titanium connecting wire, and **(7)** interconnecting piece. **(C)** Left atrial side view of the actual device. **(D)** Right atrial side view of the actual device.

procedure. Aspirin (100 mg/d) was used for the animals until the experiment ended. All animals received humane care in compliance with the 2011 Guide for the Care and Use of Laboratory Animals.

Animal procedure. The procedure was performed under general anesthesia. Anesthesia was induced by intramuscularly injecting 6 mg/kg of tiletamine and zolazepam (Virbac), and then, was maintained with isoflurane. The right femoral vein was punctured as the route for atrial septal puncture, and the left femoral vein was punctured as the route for intracardiac echocardiography (ICE). The atrial septal puncture was performed under the guidance of ICE and fluoroscopy, and a 20 × 40 mm Z-MED II balloon (NuMED) was used to continuously dilate the atrial septum for 10 seconds at 4 atm after the puncture succeeded. After the balloon was removed, ICE examinations showed the ASD. The color Doppler ultrasound was used to show the shunt flow and measure the diameter of shunt flow. The defect diameter was defined as the maximal shunt diameter measurement. A ReAces device with the waist diameter 6 mm larger than the defect diameter was selected for the ASD closure. Figure 2 shows the procedures of the ASD animal model establishment and closure of the ASD with the puncturable device.

The atrial septal repuncture at the center portion of the device was performed 60 days or 180 days after ReAces implantation. The right femoral vein was used for access, and the common Brockenbrough needle and Swartz sheath were used for repuncture, under the guidance of epicardial echocardiography and fluoroscopy. Subsequently, a 14-F sheath was delivered to cross the occluder and then went into the left atrium. Figure 3 shows the procedures of atrial septal repuncture performed 60 days after ReAces implantation, as well as the echocardiography evaluation of the remaining defect after repuncture.

FIGURE 2 Fluoroscopy-Guided Atrial Septal Defect Creation and Subsequent Closure With the ReAces Device in Animal



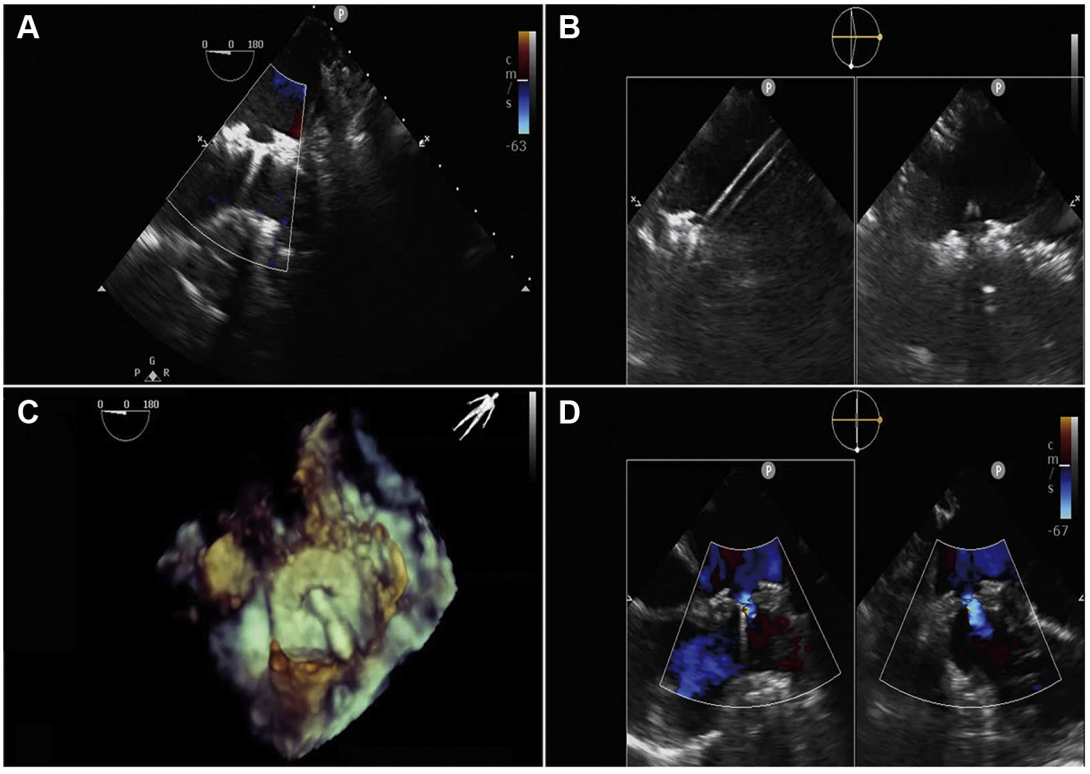
(A) The trailing end of a 0.014-inch percutaneous transluminal coronary angioplasty wire was successfully inserted through the atrial septum and accessed the left atrium under the support of an atrial septal puncture sheath. **(B)** A balloon was used for atrial septal dilation under the support of a 0.035-inch super-stiff guidewire. **(C)** The left disc was deployed and the delivery sheath was withdrawn until the left disc apposed the atrial septum. **(D)** The right disc was deployed. **(E, F)** The delivery system was separated from the occluder and the device deployed.

Evaluation protocol. The definition of device success was that after separation of the delivery system from the occluder and successful deployment the occluder remained in a stable position at the atrial septum and that ICE examination showed no sign of residual atrial septal shunt. Adverse events included death, pericardial tamponade, malignant arrhythmia, infection, device migration, and occluder-related thrombosis or embolization during the operation or follow-up. Transthoracic echocardiography (TTE) was performed 45 days after the operation. The device success rate, closure rate at 45 days, and incidence of adverse events were assessed.

Four pigs underwent atrial septal repuncture at the device portion after the implantation of the device and were subsequently explanted. The other 10 swine were explanted 45 days after ASD closure. The left and right atria were cut open to assess the position of occluder, as well as the influences on adjacent structures, endothelialization of the device surface, thrombosis, and residual defect after atrial septal repuncture. The thickness of the center hole of the occluder was measured. For the 4 pigs that underwent atrial septal repuncture, epicardial echocardiography was performed to evaluate the shunt at atrial septal-level shunt after repuncture; in addition, the time from the insertion of a puncture needle to successful insertion of a 14-F sheath through the atrial septum to the left atrium, as well as the success rate of repuncture, were recorded.

FIRST-IN-HUMAN STUDY. Study design. In this prospective, single-center, explorative clinical study, 10 patients with secundum ASD were included from the Fudan University Affiliated Zhongshan Hospital between July 2021 and August 2021. The hospital has rich experience in transcatheter occlusion of ASD and performs ~400 cases per year. This study was approved by Ethic Committee of Zhongzhan Hospital, Fudan University (No. B2021-339R), and written informed consents were obtained. The ReAces device was used for transfemoral ASD closure under the guidance of TTE and fluoroscopy. TTE examination

FIGURE 3 Evaluation of the Atrial Septal Repuncture by Epicardial Echocardiography



(A) The central hole of occluder was thin on 60 days after ReAces implantation, and no atrial septal shunt was found. **(B)** Two-dimensional echocardiography showed that the 14F sheath was successfully inserted into the left atrium through central hole after the repuncture of atrial septum at central hole. **(C)** Three-dimensional echocardiography showed that the sheath successfully accessed the left atrium through central hole. **(D)** A shunt was seen after the atrial septum repuncture.

was performed within 24 hours, at 30 days, and at 90 days after the operation. The patients were treated by oral aspirin (100 mg once a day) for 6 months.

The adverse events included pericardial tamponade, death, malignant arrhythmia, device-related thrombosis, device migration, embolization, infection, and vascular complications of approach. Acute procedure success was defined as the successful implantation of device, and the defect was successfully closed within 24 hours after the operation, with no residual shunt noted. The primary efficacy endpoint was a composite endpoint including acute procedure success and sustained complete closure of the ASD at 90 days. The safety endpoint was no occurrence of adverse events during follow-up. In addition, the procedural time (from femoral vein puncture to the withdrawal of delivery system from the human body) and fluoroscopy time (time of x-ray irradiation during operation) were recorded, and the morphology of the occluder and thickness of central hole were assessed by TTE and computed tomography angiography (CTA).

Patients. Inclusion criteria were as follows: 1) 18 to 70 years of age; 2) with congenital secundum ASD; 3) a maximal ASD diameter ≤38 mm; 4) with atrial-level left-to-right shunt, with Qp-to-Qs shunt ratio ≥1.5:1, or TTE or clinical manifestations indicating the existence of defect that inducing overfilling of the right atrium; 5) a distance from the margin of defect to coronary sinus, atrioventricular valve, and right superior pulmonary vein ≥5 mm, according to the echocardiography measurements; and 6) volunteering to participate in this study and signing informed consents.

Procedure. The procedure was performed under local anesthesia, and intravenous injection of unfractionated heparin (100 IU/kg) was performed during the procedure to maintain the activated clotting time >250 seconds. TTE examination was performed during the procedure. Colored Doppler ultrasound was performed to display the ASD shunt flow and measure the maximal diameter of the shunt flow, which was defined as the defect diameter.

TABLE 1 Results of the Animal Experiments

Number of swine	14
Male	9 (64)
Weight, kg	47.9 ± 3.8 (41.0-52.0)
Established ASDs	
Single hole	14 (100)
Defect diameter, mm	12.2 ± 0.7 (11.0-13.0)
Device size	
Diameter, mm	18
Diameter larger than the defect, mm	5.8 ± 0.7 (5.0-7.0)
Procedures	
Success rate of ASD closure	14 (100)
Success rate of atrial septum repuncture	4 (100)
Repuncture time, min	2.7-4.2
Follow-up on 45th day	
Closure rate	14 (100)
Residue shunt	0 (0)
Adverse events	0 (0)

Values are n, n (%), mean ± SD (range), or range.
ASD = atrial septal defect.

Device with size 6 to 10 mm larger than the defect diameter was used for the closure. The device was implanted through the right femoral vein, and the process of the device releasing is similar to that of a traditional ASD occluder (see Figures 2C to 2F).

STATISTICAL ANALYSIS. Continuous data are shown as mean ± SD or range. Categorical data are shown as count with percentage. Normal distribution was assessed by the Kolmogorov-Smirnov test. Statistical analyses were performed using SPSS software version 22 (IBM Corporation).

RESULTS

RESULTS OF ANIMAL EXPERIMENTS. Outcomes of ASD closure. The puncturable occluder was successfully implanted in 14 adult swine with established ASD, in which the ASD were all at the oval fossa and the average defect diameter was 12.2 ± 0.7 mm (range 11-13 mm). The device success rate was 100% (n = 14 of 14), and all the animals were treated with the occluder with waist diameter of 18 mm. All the animals were alive at the end of experiment, no adverse event occurred during the perioperative phase or follow-up, and no behavioral abnormality of the swine was found. The food intake of all the animals was normal; 45 days after procedures, TTE indicated that the atrial septum closure rate was 100% (n = 14 of 14).

Outcomes of atrial septum repuncture. Puncturing the device and crossing it with a 14-F catheter were successfully performed for the 2 swine at 60 days after the implantation of occluder, and for the other 2 swine at 180 days postimplantation, and thus the success rate was 100%. The puncture sites in both the animals were at the central hole of occluder. After the withdrawal of the 14F sheath, colored Doppler ultrasound examination showed that the left-to-right shunt was at the central hole of occluder, and the maximal diameter of the shunt was 4 mm in all the swine (Figure 3, Videos 1 to 3). The repuncture time was 2.8 minutes and 3.5 minutes for the 2 swine punctured at 60 days postimplantation and 2.7 minutes and 4.2 minutes for the 2 swine punctured at 180 days. The data pertaining to the animal experiments are shown in Table 1.

Gross anatomy. Ten swine were explanted 45 days after the implantation of occluder. Gross anatomy showed that the occluders maintained stable position and morphology at the created ASD. The surface of occluders was completely covered by a translucent layer, indicating the complete endothelialization. The disc surface at bilateral sides of occluder was merged with the surrounding tissues, with no neoplasm or thrombus attached. Figures 4A and 4B show the gross observations 45 days after the implantation of puncturable occluder. The thickness of the center portion of the occluder was measured as 2.2 ± 0.2 mm. Figure 4C shows a paraffin-embedded occluder sample explanted on 45 days after implantation. It can be seen that the center portion of the occluder is very thin and transparent.

Four swine underwent atrial septal repuncture 60 or 180 days after the procedure and then were explanted. Gross anatomy also showed that the complete endothelialization on the surface of the occluder, without neoplasm or thrombus. A clear defect at the central hole was found, in which the maximal diameter was 4 mm. The position and morphology of the occluder were normal, no dislocation of the occluder because of the repuncture was found, and the architecture of the occluder was not distorted. There were no rips or tears in the membranes of the central hole. Figure 4D shows the gross observations after atrial septal repuncture.

SHORT-TERM RESULTS OF FIRST-IN-HUMAN STUDY. During the study period, 10 patients with secundum ASD were included, 3 (25%) were male, and the mean age of the patients was 33.3 ± 7.7 years (range 25.0-49.0 years). Only 1 defect was found in each of the included patients, and the mean defect diameter size was 14.5 ± 4.8 mm (range 8.0-20.0 mm). Four patients had deficiency of the aortic rim. No patient was accompanied with pulmonary atrial hypertension, and the mean shunt ratio of the patients was 2.3 ± 0.6 (range 1.5-3.2).

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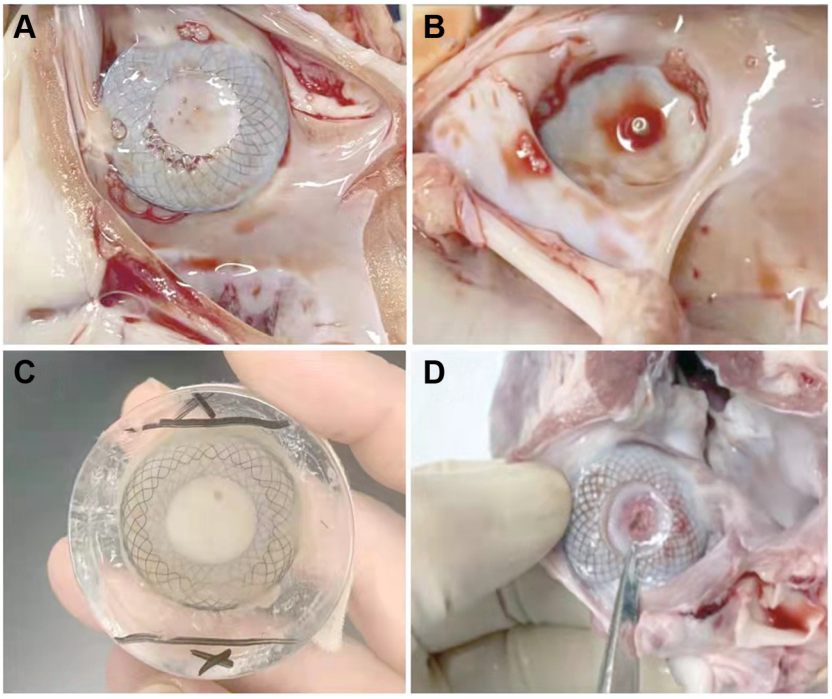
FIGURE 4 Gross Observations of the Occluder After Implantation



(A) Occluder disc in the right atrium. **(B)** Occluder disc in the left atrium. Complete endothelialization on the left and right discs of the occluder was found, and the central hole could be clearly visualized. **(C)** A paraffin-embedded occluder sample explanted on 45 days after the implantation. The center of the occluder is very thin and transparent. **(D)** Complete endothelialization on the occluder surface was still found, and the residual defect on the central hole at the site of repuncture by 14-F sheath could be clearly seen.

The device selection for all the patients was performed under the guidance of intraoperative TTE. Each of the patients was treated with only 1 occluder for ASD closure. The mean waist diameter of the occluders was 21.2 ± 5.4 mm (range 14.0-30.0 mm), which was larger than the defect diameter measured by TTE by 6.8 ± 1.3 mm (range 6.0-10.0 mm). The mean procedural time and mean fluoroscopy time were 22.8 ± 9.3 minutes and 4.8 ± 2.5 minutes, respectively.

The acute procedure success rate was 100% (n = 10 of 10). The mean follow-up time for the patients was 104.6 ± 9.5 days (range 80.0-112.0 days) and no adverse events were found during the follow-up. TTE examination was performed for all the patients within 24 hours and at 94.3 ± 5.8 days (range 80.0-101.0 days) on average after the procedure: this showed that the occluders were correctly positioned, with no residual shunt, and the closure rate was 100%. The procedure and follow-up findings of the patients are shown in Table 2. In addition, TTE showed that the occluders had excellent morphology and well apposed the atrial septum. No occluder-related thrombosis was found. The area of central hole was substantially thinner than the surrounding framework area. Five patients received enhanced CT scanning at 30 or 90 days after the implantation of puncturable occluder; this showed effective ASD closure and that the area of central hole was thin, considerably thinner than with a conventional occluder. Figure 5 shows the TTE and CTA images of the patient at 90 days after the procedure in 1 patient.

DISCUSSION

ASD is one of the most common congenital heart diseases throughout the world and also has the highest incidence in adults, of which secundum ASD accounts for the highest percentage.[1,7-11] Compared with surgical interventions, transcatheter device closure of secundum ASD is equally safe and effective, and more minimally invasive and economical, thus becoming the preferred treatment for patients with suitable anatomical conditions.[12,13] Unfortunately,

TABLE 2 Acute Results of Procedure and 90-Day Follow-Up in Human Study (N = 10)

Primary efficacy endpoint	
Acute procedure success	10 (100)
Closure rate in 90 d	10 (100)
Device size	
Mean diameter, mm	21.2 ± 5.4 (14.0-30.0)
Diameter larger than the defect, mm	6.8 ± 1.3 (6.0-10.0)
Procedural time	
Mean procedural time, min	22.8 ± 9.3
Fluoroscopy time, min	4.8 ± 2.5
Safety adverse events (90 d)	
Death	0
Pericardial tamponade	0
Malignant arrhythmia	0
Device-related thrombosis	0
Device migration	0
Embolization	0
Infection	0
Vascular complications of approach	0

Values are n (%) or mean ± SD (range).

most patients undergoing ASD closure are young patients, for whom the probability of accompanying atrial arrhythmia such as AF in the long term is higher than that of the general population. In addition, mitral regurgitation may be associated with ASD closure in such patients.[2,3,14,15] Currently, these diseases are increasingly treated by transcatheter interventions, which all require atrial septal puncture.[4-6] At present, the structures of all conventional ASD occluders with marketing availability are 2 disc and 1 waist self-expanding structures. The framework of occluders is metal meshes weaved by nickel-titanium wire, such as the AMPLATZER Septal Occluder (Abbott-St. Jude Medical). The mesh diameter of the Gore HELEX/CARDIOFORM Occluder (Gore Medical) is larger, but there are also a lot of overlapped metal meshes after self-inflation.[16] Moreover, the space between the left disc and the right disc is also thick and then filled with newborn tissue after implantation (**Figure 5D**), further making it difficult to puncture and cross the convention occluder. The transatrial septum treatment commonly requires the insertion of a sheath with the diameter of 3 to 9 mm through the multilayer metal mesh with small cells and the PET membrane, which is very difficult or even impossible. Some small case series have reported success in puncturing and crossing the conventional AMPLATZER ASD occluder, but this is done with experienced hands using special techniques, such as cutting balloon, electrocautery, and sequential balloon dilatation, and the procedure time is dramatically longer.[17-19] One study reported the feasibility for perforating the GORE CARDIOFORM septal occluder to gain access to the left atrium,[20] but it used a radiofrequency needle and cutting balloon, and if using the standard needle and Mullin's sheath and cutting balloon, the success rate is just 50%.

Several bioabsorbable ASD occluders, such as BioSTAR and Double BioDisk, have been previously developed and studied,[21-23] although none are commercially available. In addition, findings of some animal experiments have shown that the implantation of bioabsorbable ASD occluders could stimulate the hyperplasia of atrial septal fibrous tissues, with a resultant thick atrial septum, which could make the puncture of the device zone difficult.[24] Therefore, patients undergoing ASD device closure, particularly with larger devices, may not easily undergo transatrial septal interventional therapies, including radiofrequency ablation for AF, percutaneous left atrial appendage occlusion, and transeptally directed transcatheter mitral valve repair and replacement. Owing to the difficulty of puncturing the ASD occluder device, the European Heart Rhythm Association/European Association of Percutaneous Cardiovascular Interventions expert consensus statement suggests to close the left atrial appendage simultaneously even if the patients do not have AF when performing the transcatheter occlusion for some ASD patients, which is called as "primary" prevention.[25]

The ReAces occluder used in this study preserved the 2 disc and 1 waist structure of conventional occluders. The difference is that there is a central hole close to the waist diameter of the occluder, which has very few metal structures and is covered with a thin PET membrane. This device enables safe and effective ASD closure but also provides a channel for future atrial septal puncture. The availability of a guaranteed reaccess to the left atrial with the ReAces device might make it the device of choice for ASD closure after transcatheter mitral valve intervention, which till now seems to be a common issue with transseptal transcatheter mitral valve intervention systems (eg, EVOQUE valve [Edwards Lifesciences]).[26] Moreover, the puncturable occluder may be a better choice for the patients with secundum ASD and pulmonary hypertension who have borderline pulmonary artery resistance because this device will provide an opportunity to reopen the atrial septal shunt if the pulmonary hypertension progress after ASD closure.

The procedure success rate and long-term ASD closure rate are both >96% for conventional ASD occluders.[27,28] In our studies, the acute procedure success rate and short-term ASD closure rate of the puncturable occluder in both swine models and patients were 100%, which confirmed the

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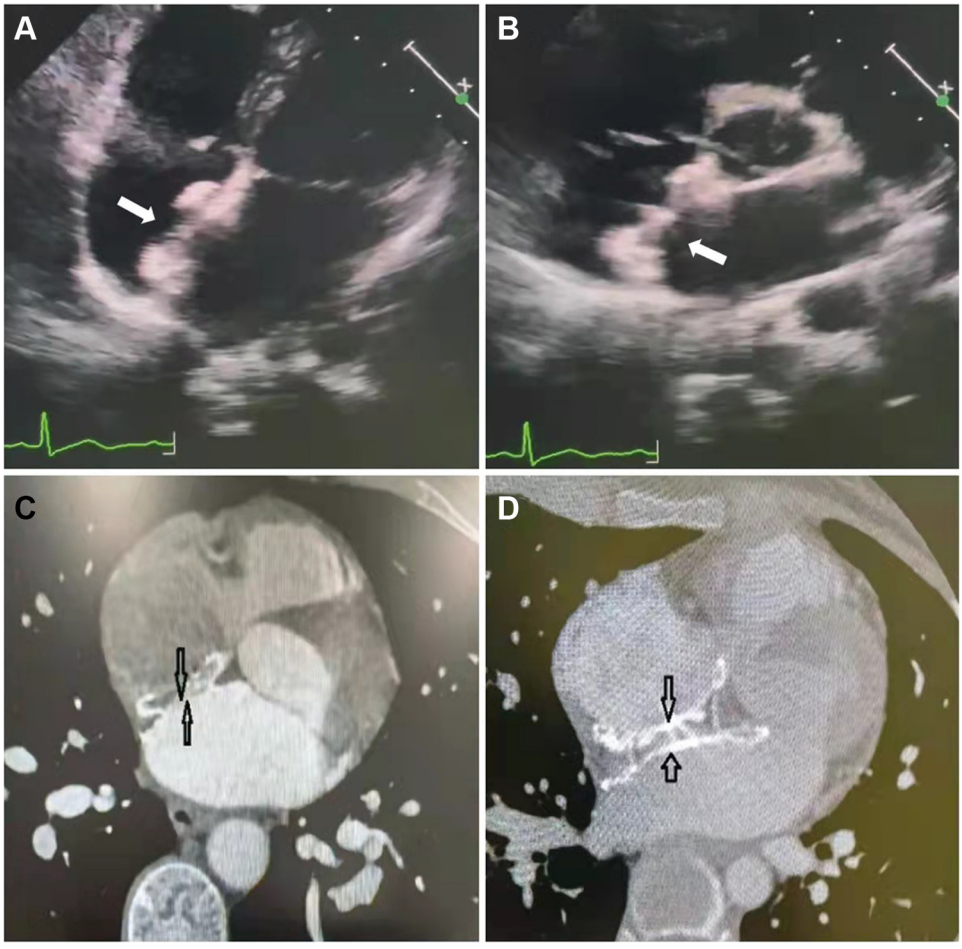
FIGURE 5 TTE and CT Angiography Images of the Occluder After Implantation



(A to C) The transthoracic echocardiography (TTE) and computed tomography (CT) images of a patient at 90 days after implantation of puncturable occluder. **(A)** The apical 4-chamber view by TTE. **(B)** Aortic short-axis view by TTE. **(C)** CT angiography image. All the images showed that the occluder had excellent morphology and fit the atrial septum well. The area of the central hole was substantially thinner than surrounding framework area **(arrow)**. **(D)** CT image at 6 months after the implantation of a conventional occluder; as compared with the puncturable occluder, the atrial septum was substantially thicker for the conventional occluder (distance between the **2 arrows**).

effectiveness of the device. In addition, no adverse events such as occluder migration, pericardial tamponade, thrombosis, or embolism occurred in the animal experiment or first-in-human study, which further confirmed the safety of the device. In the first-in-human study, TTE and fluoroscopy both demonstrated that the occluder had excellent morphology and well apposed the atrial septum.

In the preclinical animal experiments of this study, repuncture at the center portion of the device was performed for 4 swine at 60 or 180 days after occluder implantation. A 14-F sheath could be easily inserted through the puncture site, and the time of puncturing and crossing the device was only about 3 to 4 minutes. Both intraoperative imaging and postoperative gross anatomy confirmed that the site of puncture was at the central hole of occluder, which met the design expectation of the puncturable occluder, and further proved the feasibility of puncturing and crossing. The TTE and CTA images, and paraffin-embedded occluder sample post-implantation, also clearly displayed that the area of central hole was thin, indicating that the puncture at this area was feasible and simple. No clinically significant difference was found during the deployment of puncturable versus conventional occluders. In the first-in-human study, the procedural time and fluoroscopy time were very close to the time of the

implantation of conventional occluders, indicating ease of implantation for operators qualified for transcatheter ASD closure by conventional occluders. **STUDY LIMITATIONS.** First, only short-term findings were reported in both the animal experiments and first-in-human study. Longer follow-up is needed to evaluate the hyperplasia of tissue surrounding occluder, as well as the moderate- and long-term effectiveness and safety. The short-term findings and puncture feasibility in animal experiments might not mirror the ReAces device in humans after many years of device implant. Second, the patients included in the first-in-human study all had relatively small secundum ASDs. However, the main structure and working mechanism of the ReAces device is similar to that of a conventional occluder, and we think that it is not a problem for the ReAces device to close a large defect. A large-scale premarketing multicenter clinical trial including patients with large or multiple defects in China will be launched very soon. Third, the ASD closure was performed under local anesthesia with the guidance of TTE and x-ray fluoroscopy in this study. Although this is rather uncommon in Europe and the United States (which mostly rely on transesophageal echocardiography), it is usually always applied in China and has been tested by many Chinese studies. Fourth, all swine underwent device puncture and were sacrificed immediately after the puncture, so we had no follow-up data after puncturing the device. However, autopsy results showed a tiny crack in the membrane (**Figure 4D**) that would most likely not have a significant impact on hemodynamics and self-close in the future. For a larger puncture hole, closing the hole with a normal occluder or the ReAces device is feasible. We will test these hypotheses in future animal experiments. Finally, the feasibility of puncture of the occluder was tested only in the animal study because of ethical issues involved with testing in the human study. This should be future tested in human studies when necessary.

CONCLUSIONS

The ReAces device is a novel puncturable ASD occluder and appears safe and effective for the transcatheter closure of secundum ASD. The findings in swine models demonstrate that puncturing and crossing the central portion of occluder are feasible and simple. This device may offer an advantage over conventional ASD occluders in the lifetime management of structural heart disease, enabling the atrial septal puncture after implantation. A large-scale clinical trial (NCT05371366) has just been launched to further confirm the safety and efficacy of this device.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The ReAces device is a novel puncturable transcatheter ASD occluder designed for easy puncturing and crossing of the atrial septum. The animal experiment and first-in-human study show that it is safe and effective to use the ReAces device for closure of ASD, and puncturing and crossing the device with large catheter is feasible and simple.

TRANSLATIONAL OUTLOOK: The ReAces device may become a promising device to solve the clinically important issue caused by the difficulty in puncturing the atrial septum after transcatheter ASD occlusion, which is an important step for left-sided interventional procedures.

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KEY WORDS atrial septal defect, atrial septal puncture, occluder, transcatheter closure

APPENDIX For supplemental videos, please see the online version of this paper.