4D printed bioinspired biodegradable occlusion devices with tailored mechanical properties

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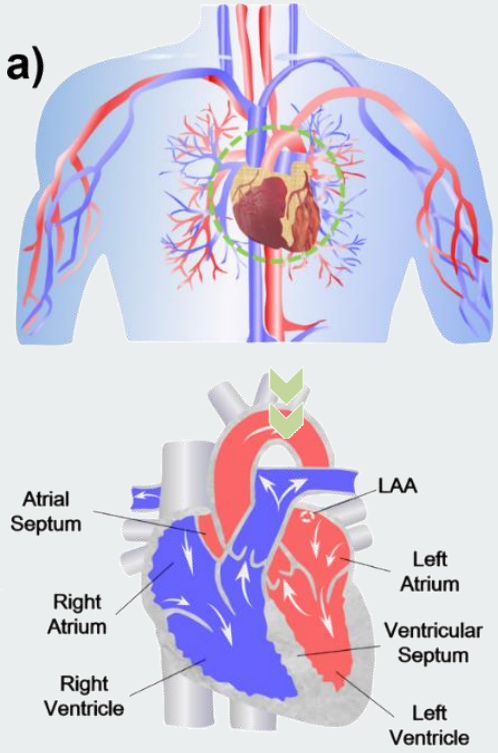
Part: 1

Research Background

1. Research Background - Congenital Heart Defects

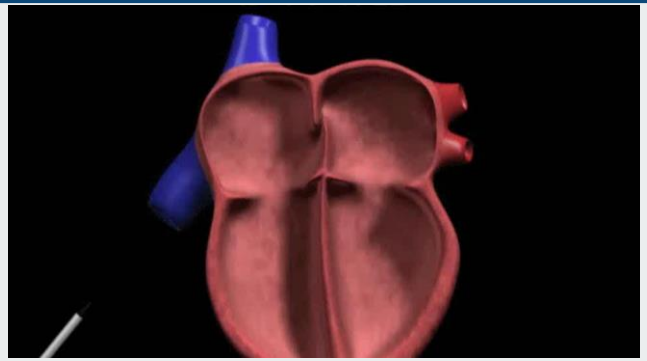


Nornal heart **Heart with defects**

- **Left atrial appendage (LAA) is a small pouch protruding from the left atrium with a complex internal structure. This leads to the tendency of thrombus to accumulate in LAA for specific patients.**
- **Atrial septal defect (ASD): a small hole between two atria**
- **Ventricular septal defect (VSD): an opening between two ventricles.**

Cheng Lin, Liwu Liu*, Yanju Liu, Jinsong Leng*, ***Acta Biomaterialia***. 2021, 128, 100-119.

1. Research Background - Traditional Metal Occluders



Occluding defect with occluder

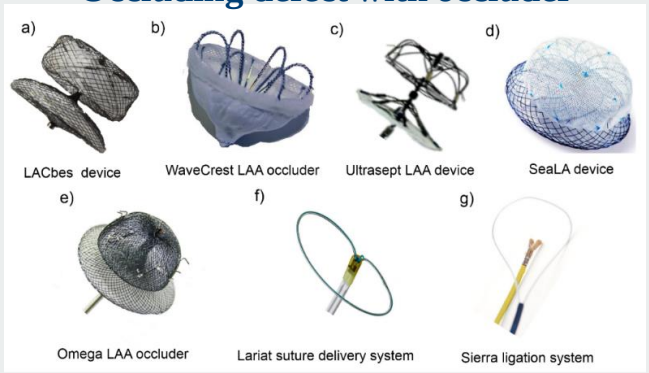
Bridge

Tissue ingrowth into occluder

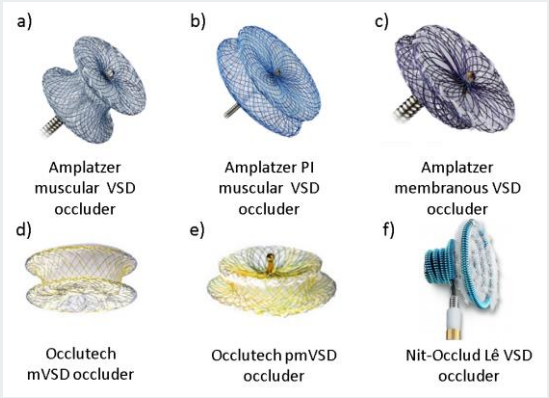
Endothelialization completed

3~6 months

Occluder
Mission accomplished



Left atrial appendage (LAA) occluder



Ventricular septal defect (VSD) occluder

Cheng Lin, Liwu Liu*, Yanju Liu, Jinsong Leng*, ***Acta Biomaterialia***. 2021, 128, 100-119.

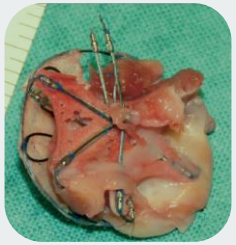
1. Research Background - Traditional Metal Occluders

➢ **Limitations of metal occluders**

- **Limited biocompatibility and non-degradability of metal occluders lead to serious complication, e.g., allergies, erosion, etc.**
- **The mismatch of mechanical properties between the implanted device and biological tissue cause wear and even perforation.**
- **Only a few X-ray markers on the device may cause inaccurate positioning**

Problems and complications of metal occluders

Thrombus



Frame fracture

Malformation

Incomplete expansion

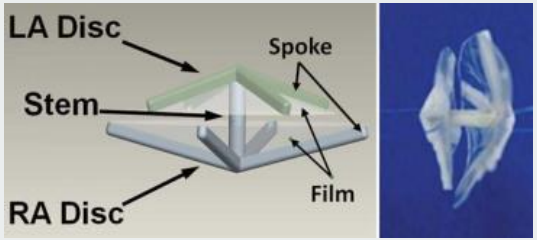
Expected performance improvements

Biocompatible, controllable and degradable occluder

Occluder with customizable mechanical properties and configuration

Overall radiopaque occluder

1. Research Background - 4D printing

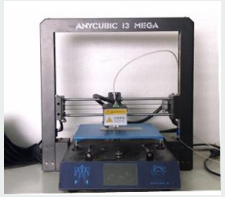


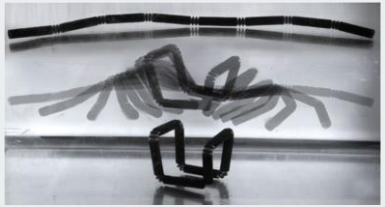
Biodegradable occluder

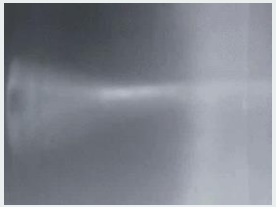
Shape-memory polymers (SMPs), a class of intelligent materials, are able to respond to external stimului, such as temperature, magnetic field, light and so on.

3D printing

SMP
Shape memory polymer (SMPs)







4D printing

- ✓ **Biocompatible**
- ✓ **Biodegradable**
- ✓ **Customized**
- ✓ **Deployment controllable**

MIT Self-Assembly Lab and Stratasys, 4D Printing, 2013
CY. Li, F.H Zhang. et.al, SCIENTIA SINICA Technological , 10.1360/N092018-00153.

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Part: 2

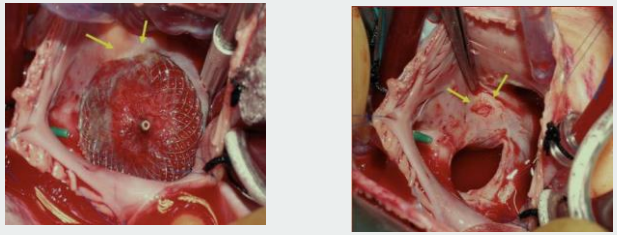
Bioinspired Left Atrial Appendage (LAA) Occluder with Tailored Mechanical Properties

Lin C, Liu LW, Liu YJ, Leng JS. ACS Applied Materials & Interfaces, 2021, 13, 12668-12678

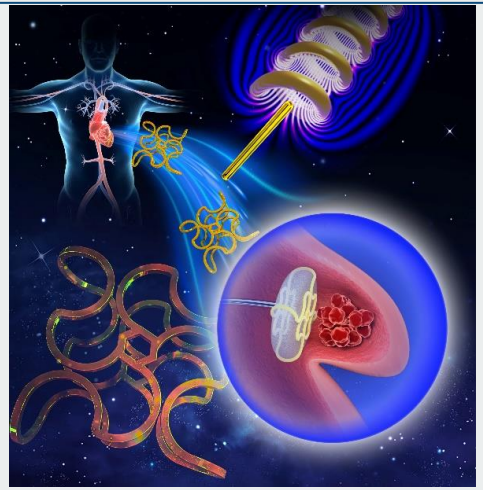
2. Bioinspired LAA Occluder with Tailored Mechanical Properties

- The risk of stroke in patients with atrial fibrillation (AF) is five times that in the general population; For nonvalvular AF patients, over 90% of atrial thrombi originate from the LAA; **LAA occlusion can reduce the risk of stroke by 80% in AF patients**
- **The significant mismatch of mechanical properties between the implanted medical device and biological tissue is prone to cause wear and even perforation**
- 4D printed bioinspired LAA occluders with customized mechanical properties and configurations were developed.

The complicated structure of LAA

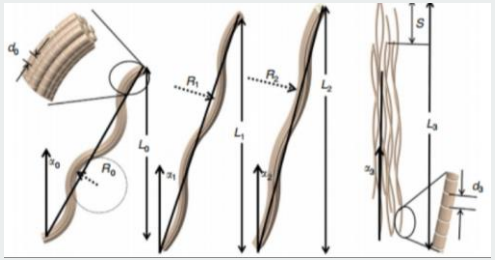


Perforation caused by alloy occluder (Amplatzer)

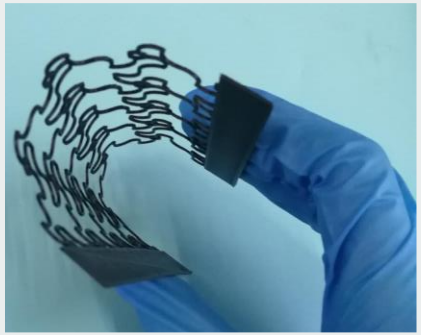


Schematic diagram of occluding the LAA with thrombus

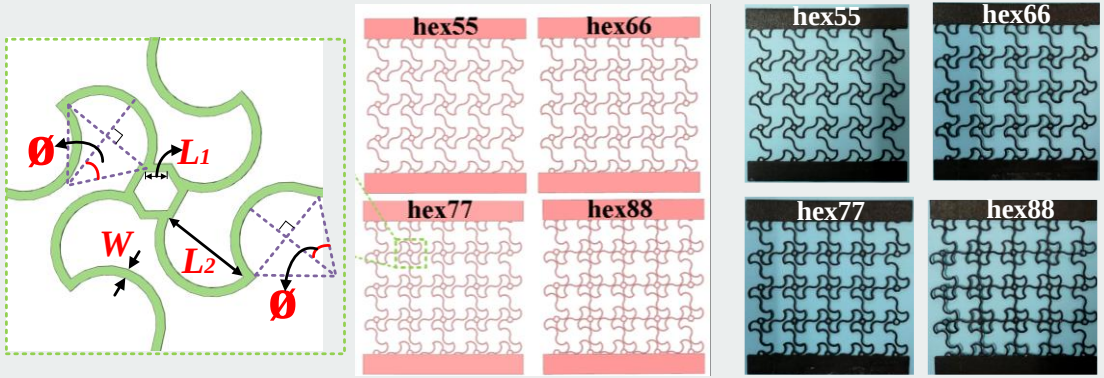
2. Bioinspired LAA Occluder with Tailored Mechanical Properties



Structure of collagen fibers

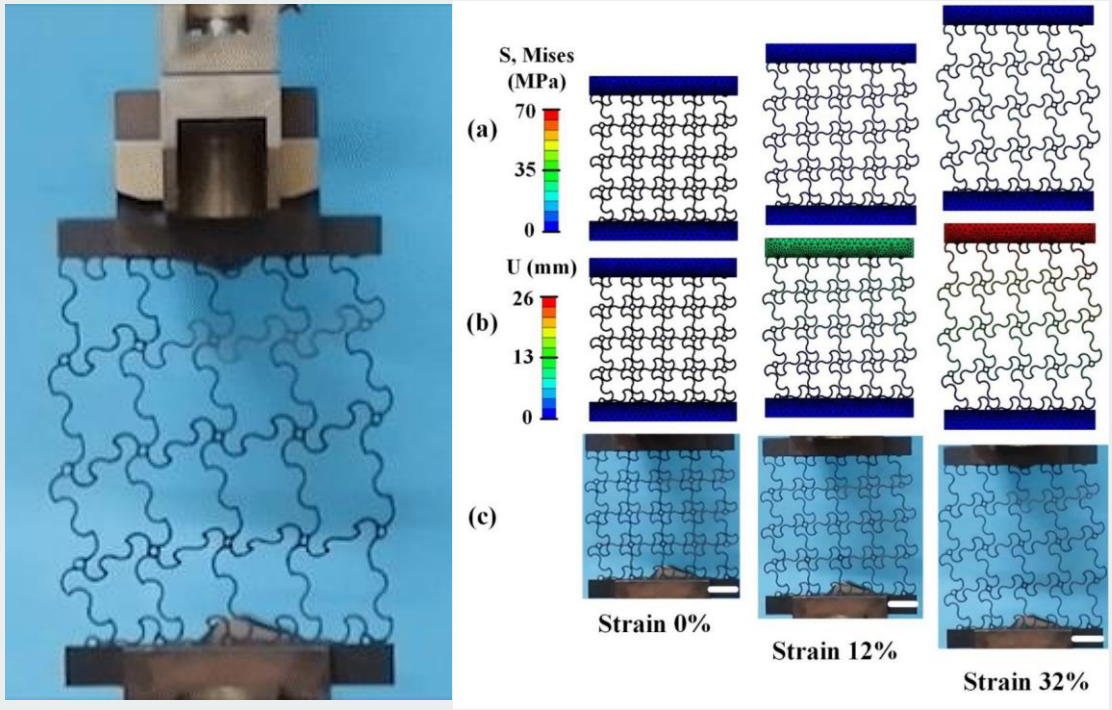


- Inspired by collagen fibrils, network materials with wavy microstructure were developed.
- The materials were able to mimic nonlinear “J-shaped” stress- strain curves of biological tissues and exhibited synergistic deformation with tissues.
- A bioinspired 2D network model library was built based on various design parameters. Under the guidance of searching a bioinspired 2D network similar to the deformation behavior of LAA (to deform cooperatively with LAA) but with higher stiffness (to provide sufficient support for LAA), the scope of the bioinspired 2D network model library was gradually reduced.

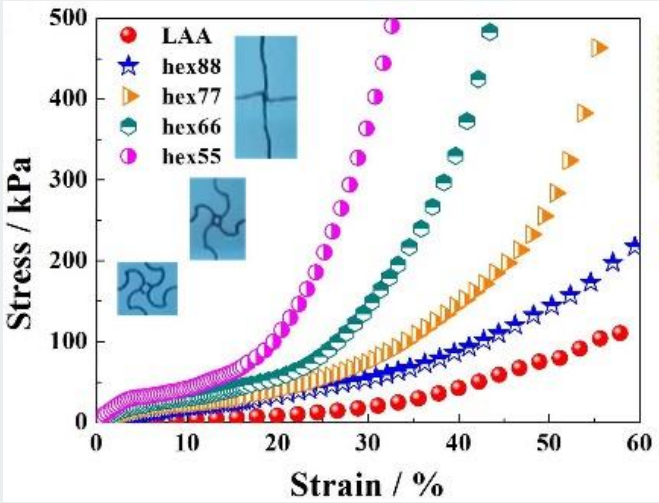


Bioinspired networks

2. Bioinspired LAA Occluder with Tailored Mechanical Properties



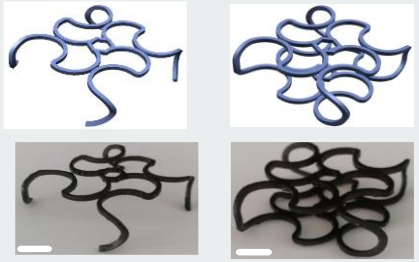
Experiments and Finite element analysis of bioinspired networks



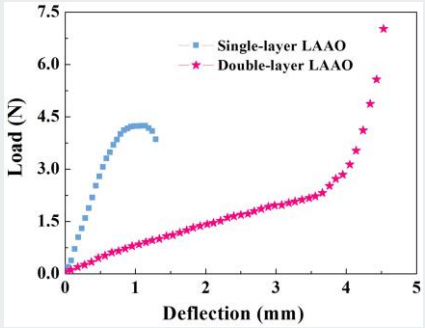
"J"shaped stress-strain curves

The stress-strain response of the hex88 network was the closest to LAA, with a modulus slightly higher than that of the LAA tissue, satisfying the requirements of providing sufficient mechanical support for LAA while matching LAA deformation.

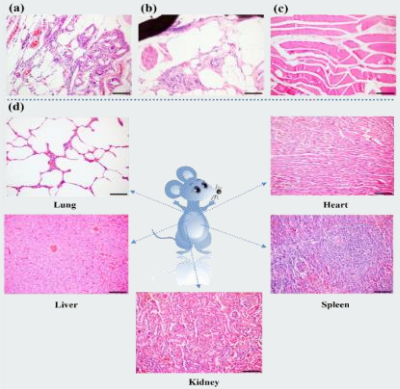
2. Bioinspired LAA Occluder with Tailored Mechanical Properties



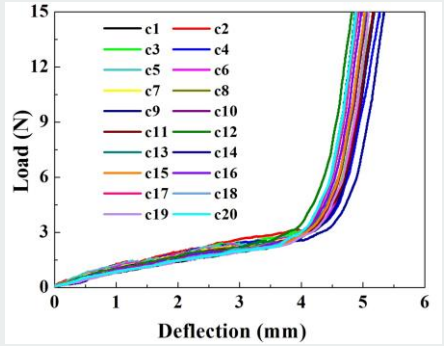
4D printed single-layer and double-layer ccluders



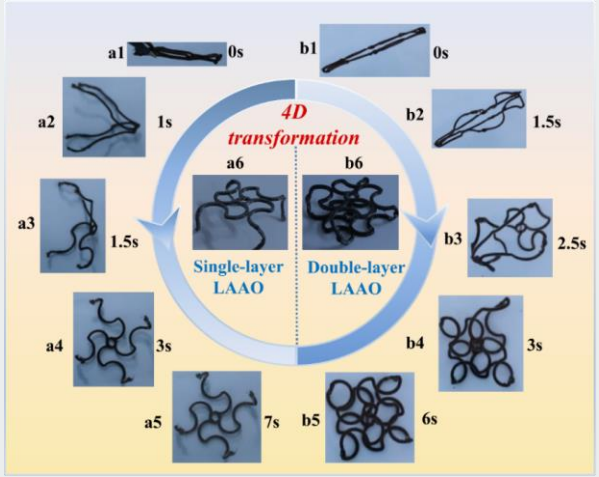
Compression tests



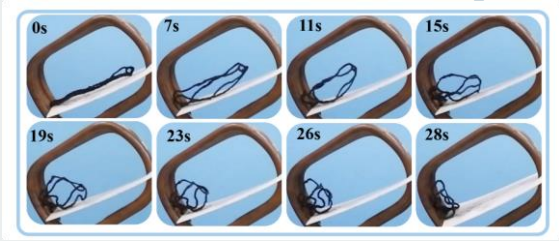
Histocompatibility (48 weeks)



20-cycle compression test



Heat-induced 4D transformation processes



Magnetic field-induced 4D transformation process

Lin C, Liu LW, Liu YJ, Leng JS. ACS Applied Materials & Interfaces, 2021, 13, 12668-12678

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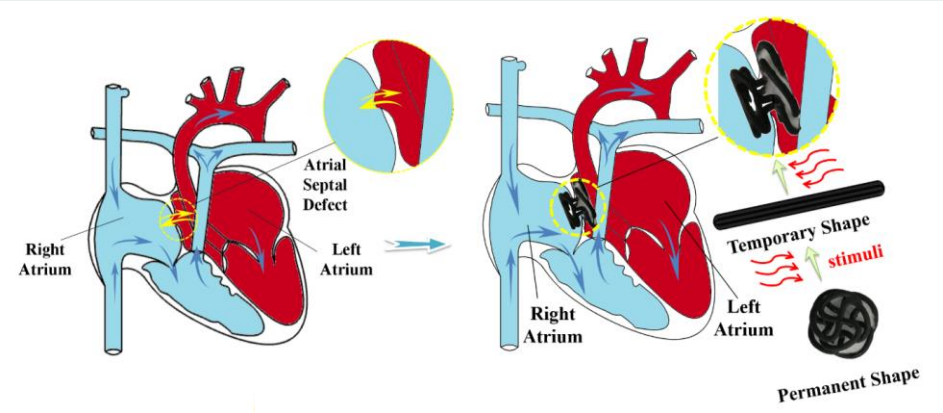
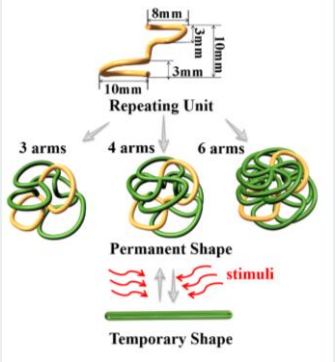
Part: 3

Remotely Controllable Atrial Septal Defect (ASD) Occluder

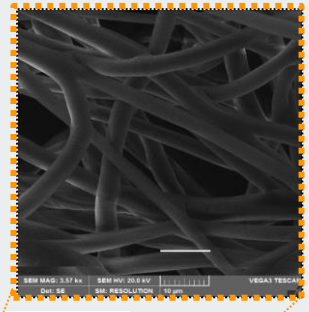
3. Remotely Controllable Atrial Septal Defect (ASD) Occluder

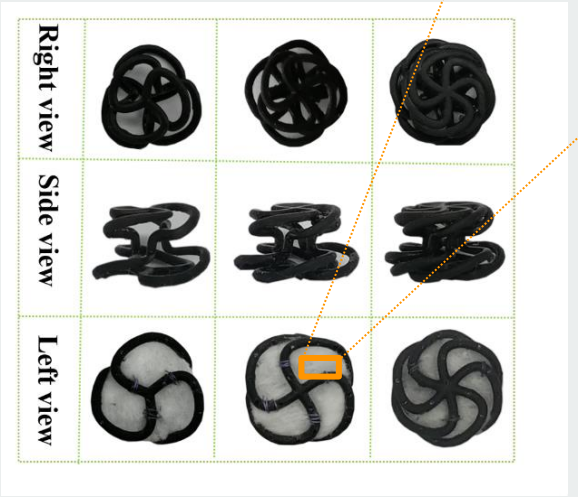


Occluder framework design schematic diagram



Occluding membrane



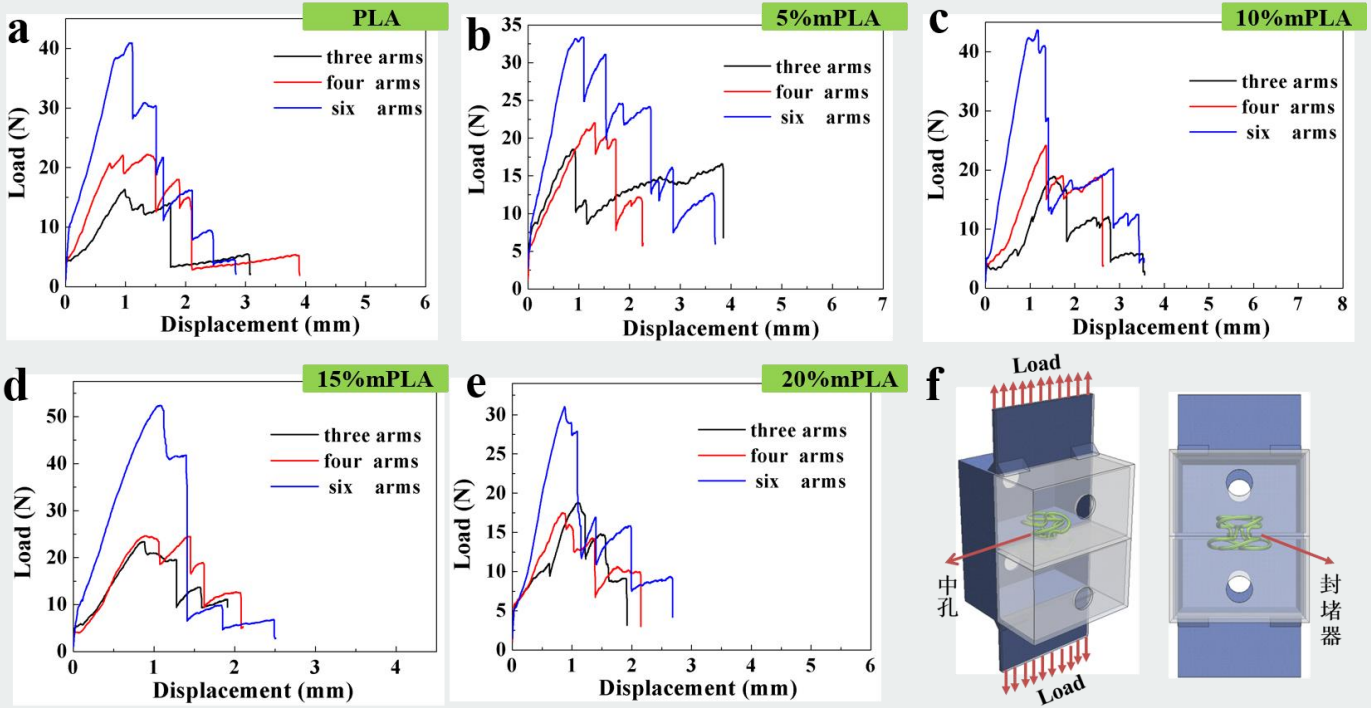


4D printing Remote controllable degradable atrial septal defect (ASD) occluder

3. Remotely Controllable Atrial Septal Defect (ASD) Occluder

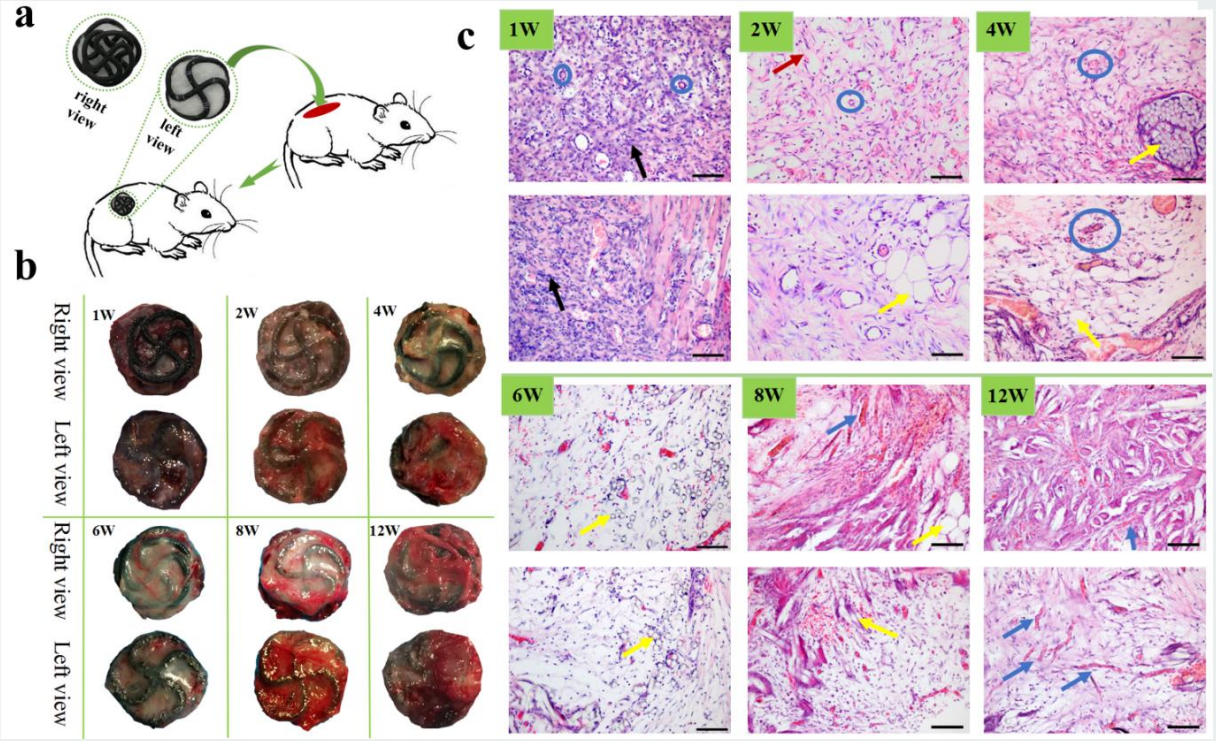
➢The stepped curve was related to the structure of the occluder.

When the tensile force reached the limit of the occluder, several repeating units break in turn.



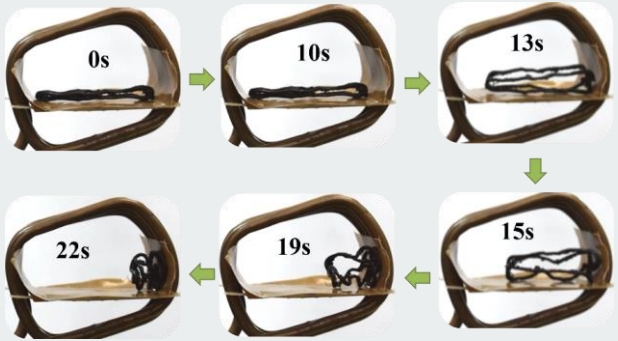
Waist loading capacity of occluder

3. Remotely Controllable Atrial Septal Defect (ASD) Occluder

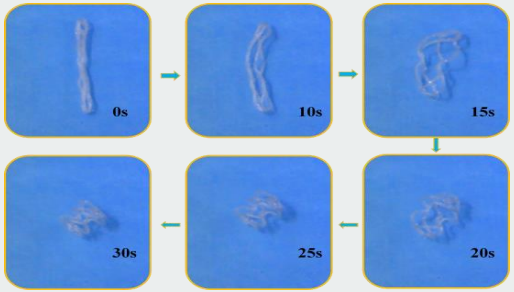


- Newly formed vessels can be seen within 1 week of implantation the material had good **biocompatibility**
- Degraded particles can be seen in 2 weeks, proving **degradability**

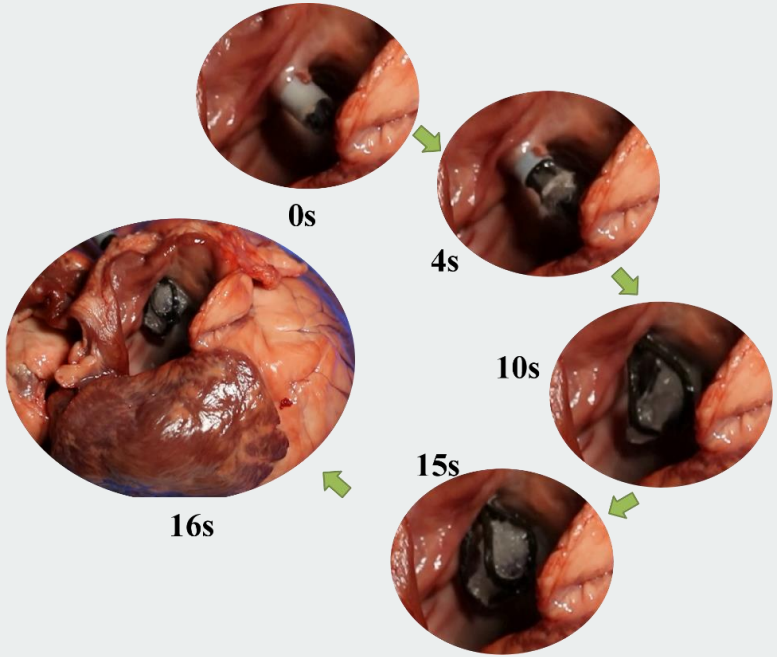
3. Remotely Controllable Atrial Septal Defect (ASD) Occluder



Magnetic field driven shape memory occluder recovery process



Recovery process of heat-driven shape memory occluder



Fast and complete closure of defects

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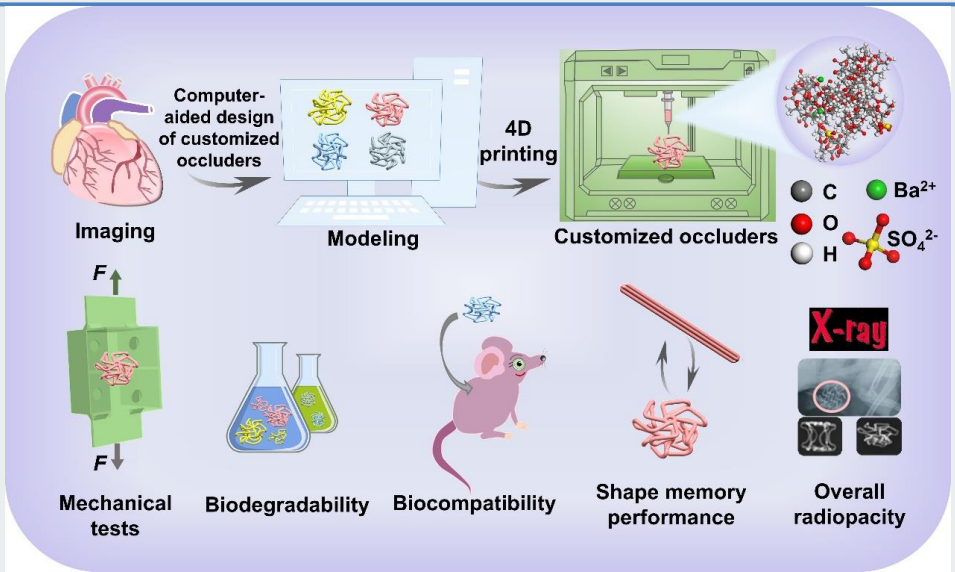
Part: 4

Overall Radiopaque Ventricular Septal Defect (VSD) Occluder

Lin C, Liu LW, Liu YJ, Leng JS et al. Advanced Healthcare Materials, 2022, 202201999

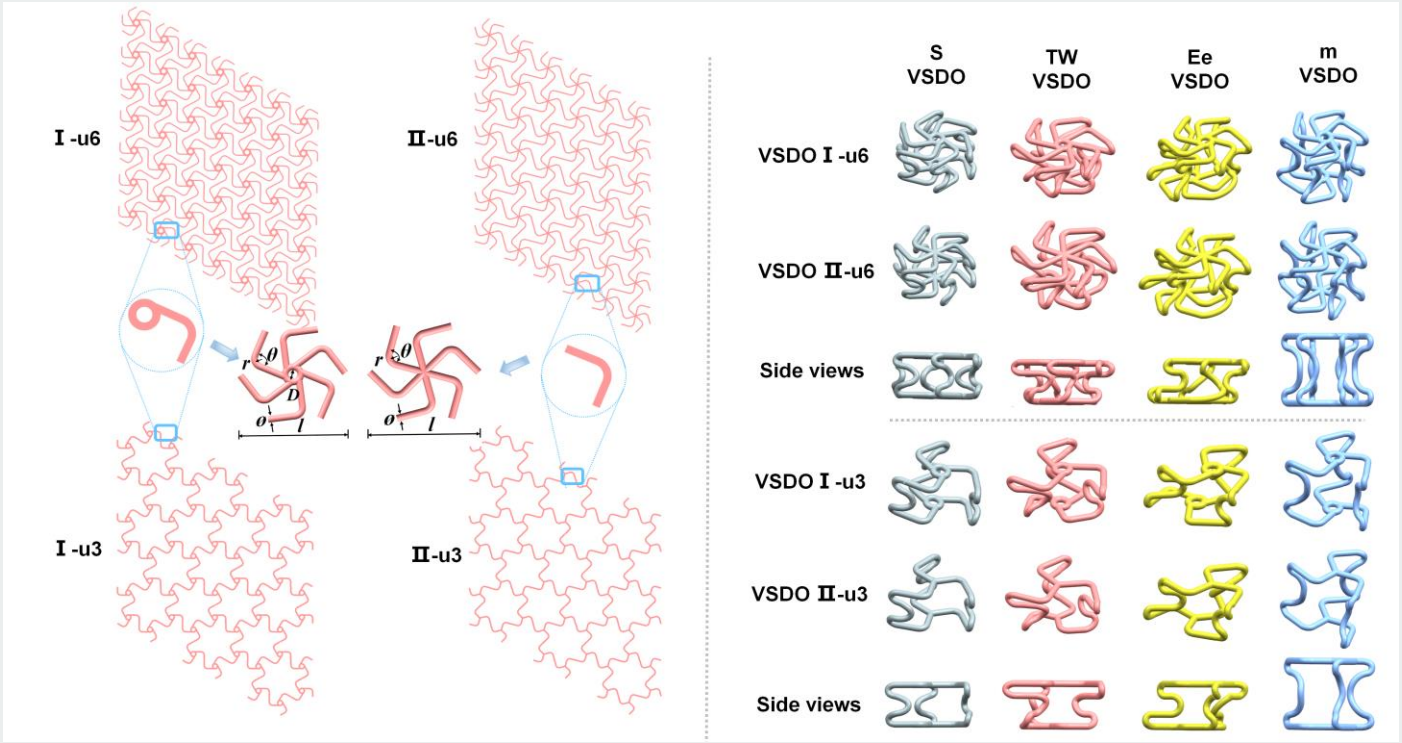
4. Overall Radiopaque Ventricular Septal Defect (VSD) Occluder

- Radiopaque barium sulfate was introduced into the SMP matrix, 4D printed customized, biodegradable, overall radiopaque occluders were developed, avoiding inaccurate positioning of conventional occluders with only a few radiopaque markers



Schematic workflow for fabricating and characterizing biodegradable, customized, and overall radiopaque 4D printed bionic occluders.

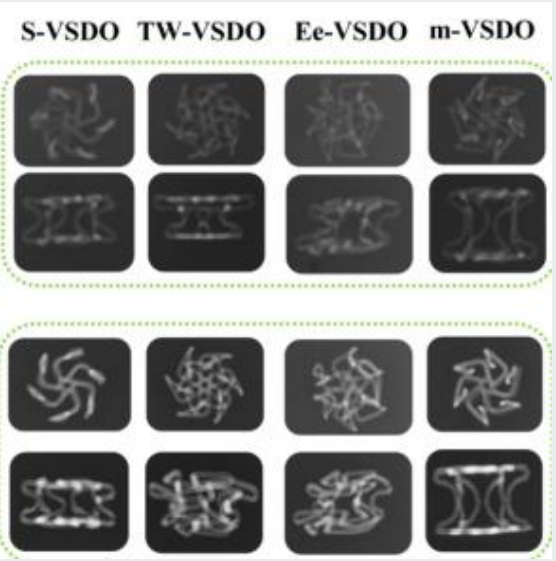
4. Overall Radiopaque Ventricular Septal Defect (VSD) Occluder

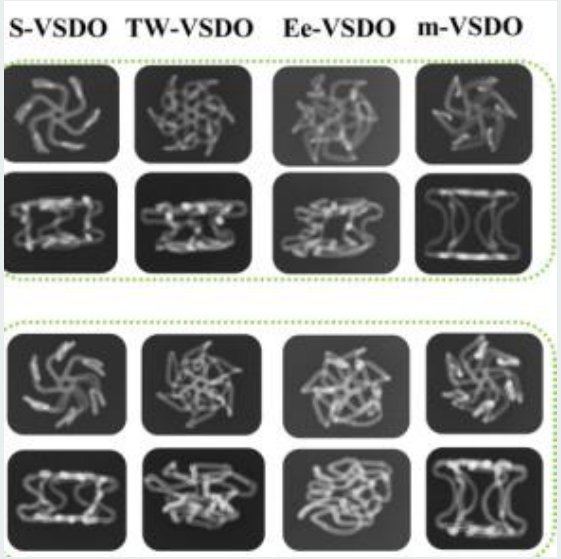


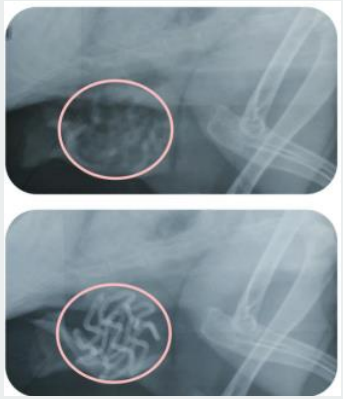
- VSD is characterized by higher incidence and diverse defect sites.
- Based on wavy bionic structures, various VSD occluders were designed to adapt to the position diversity of VSD.

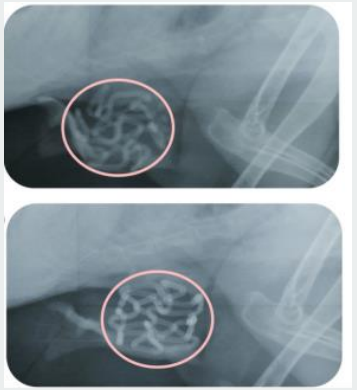
Symmetrical VSDO (S-VSDO), slender-waist VSDO (TW-VSDO), eccentric VSDO (Ee-VSDO) and muscle VSDO (m-VSDO)

4. Overall Radiopaque Ventricular Septal Defect (VSD) Occluder









- **The overall radiopacity of 4D printed VSD occluders was achieved ex vivo and in vivo**
- **Accurate positioning can be assured.**

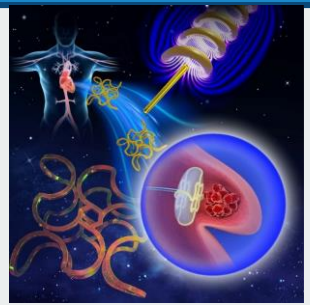
Lin C, Liu LW, Liu YJ, Leng JS et al. Advanced Healthcare Materials, 2022, 202201999

Part: 5

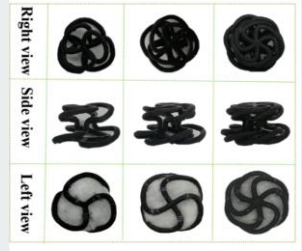
Conclusion

5. Conclusions

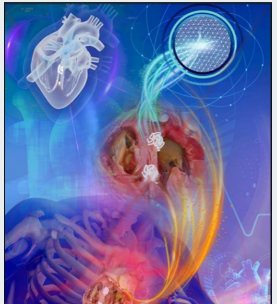
- 4D printed LAA occluders with customized mechanical properties were developed by optimize ligament configuration, which can match the deformation of LAA.



- Biodegradable, remotely controllable and personalized ASD occluder was developed, which has excellent shape recovery performance for rapid and perfect sealing



- 4D printed overall radiopaque occluders were developed, avoiding inaccurate positioning of conventional occluders with only a few radiopaque markers



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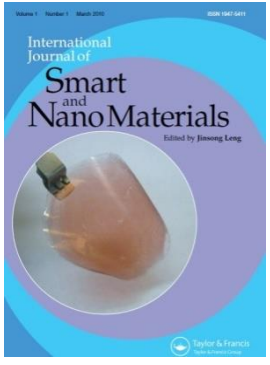

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29 days avg. from submission to first post-review decision
11 days avg. from acceptance to online publication

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Thank you !

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