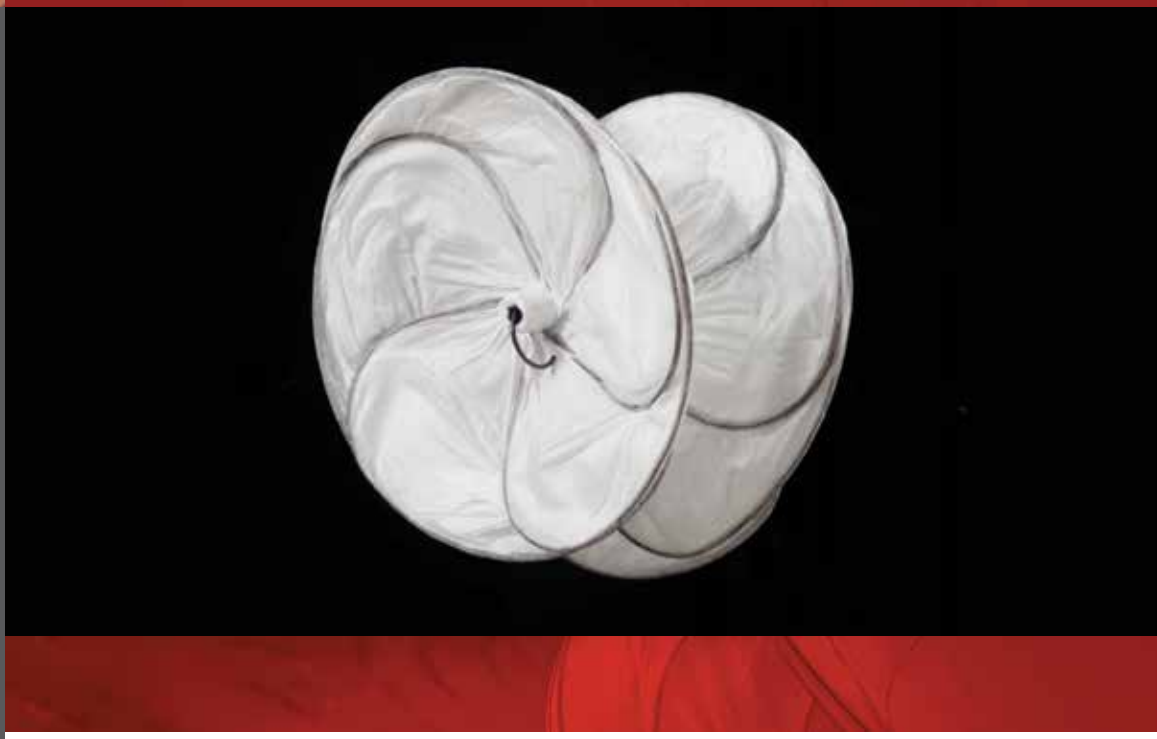
Closing Remarks
INTERNATIONAL



IN THIS ISSUE

GAIN NEW INSIGHT ON HOW GORE® CARDIOFORM SEPTAL OCCLUDER CAN SUPPORT POSITIVE OUTCOMES IN YOUR PATIENTS

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IN THE NEWS

Gore announces positive results from Gore REDUCE Clinical Study for PFO closure

Study met its primary endpoint with PFO closure in conjunction with antiplatelet therapy, reducing recurrent stroke by > 75 percent over antiplatelet therapy alone

W. L. Gore & Associates, Inc. (Gore) announces positive results from its REDUCE Study assessing closure of patent foramen ovale (PFO) for the reduction of recurrent ischemic stroke and new brain infarct. The data were shared May 16 at the European Stroke Organisation Conference (ESOC) in Prague, Czech Republic. Gore plans to submit the positive data to the U.S. Food and Drug Administration (FDA) to seek a PFO indication for the GORE® CARDIOFORM Septal Occluder by year-end 2017.

“The REDUCE data is groundbreaking for patients who have suffered a cryptogenic stroke attributed to a PFO,” said Scott Kasner, MD, Neurologist in the Perelman School of Medicine at the University of Pennsylvania, and U.S. Neurology National Principal Investigator for the REDUCE Study. “Until now, there has never been a study of a PFO closure device that showed statistically significant reduction in stroke recurrence in the primary intent-to-treat analysis. Other PFO closure device trials had

GORE CARDIOFORM SEPTAL OCCLUDER

IN THE NEWS

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to rely on secondary analysis, including following patients for up to a decade, before achieving statistical significance. Also of note is the level of safety the GORE® CARDIOFORM Septal Occluder demonstrated, with no significant difference shown in the rate of serious adverse events between patients implanted with the device and those in the control arm. This trial demonstrates noteworthy verification that PFO closure with the GORE® CARDIOFORM Septal Occluder is a valuable procedure to reduce recurrent stroke and brain infarct when utilized in an appropriate patient population."

The controlled, open-label REDUCE Study assessed the efficacy and safety of PFO closure using Gore Septal Occluder Devices in 664 randomized subjects, ages 18 to 59 with a history of cryptogenic stroke, across 63 investigational sites in seven countries. **The trial met its primary endpoint by showing a statistically significant, 76.6 percent (p = 0.001), reduction in recurrent ischemic stroke in patients that underwent PFO closure in conjunction with antiplatelet therapy versus those who underwent antiplatelet therapy alone after an average of 3.4 years follow-up.**

In addition to the primary endpoint of reduction of recurrent stroke, the study also met its co-primary endpoint of reduction of new brain infarct, inclusive of silent brain infarct (SBI), through PFO closure. An increased risk of clinical stroke, dementia, and cognitive dysfunction has been associated with SBI. This marks the first time a study assessed the relationship between PFO closure and reduction of new brain infarct. Patients underwent baseline and two-year follow-up MRI scans to determine if new brain infarct occurred. **New brain infarct was present in 5.7 percent of test arm subjects and 11.3 percent of control arm subjects, yielding a 49.6 percent (p = 0.024) relative risk reduction for PFO closure on new brain infarct.**

The data showed no difference in the subject-based rate of serious adverse events between test and control groups. Device- and procedure-related serious adverse events occurred in 1.4 and 2.5 percent, respectively, of test patients. Patients experienced low rates of bleeding, deep vein thrombosis, and pulmonary embolism, with no significant difference between test and control groups. There was a significantly higher rate of serious atrial fibrillation in the test group (2.3 percent versus 0.4 percent) but the majority of atrial fibrillation was peri-procedural (80 percent had onset within 30 days of the closure procedure) and had rapid resolution (70 percent with resolution within two days of onset).

In the U.S., stroke is the leading cause of long-term severe disability and the fourth leading cause of death. Roughly 25 percent of first-time strokes are cryptogenic, or due to unknown cause. Studies have shown that PFO can be found in up to 40 to 50 percent of patients who have had a cryptogenic stroke.

Most people with a PFO — a hole occurring in the upper wall between the left and right atria of the heart — do not experience any issues when blood flows from one atrium to the other; however, serious problems such as stroke can arise if a blood clot passes from the right to left atria through a PFO and then to the brain. The data from the REDUCE Study suggest the risk of recurrent stroke can be dramatically reduced when the PFO is closed using Gore Septal Occluder Devices.

"It is of the utmost importance to us to be transparent and share clinical data as quickly as possible," said Jake Goble, PhD, Gore Structural Heart Pipeline Leader. "We completed our two-year primary endpoint follow-up with patients in March and have worked diligently to release these important data to the public. Closure of PFO to reduce recurrent strokes and brain infarcts is not widely practiced today, mainly due to a lack of sufficient data. We're excited by the very positive results from our study. We are looking forward to our next steps of taking the GORE® CARDIOFORM Septal Occluder through the submission process to make this viable treatment option for recurrent cryptogenic stroke available to physicians and their patients."

The GORE® CARDIOFORM Septal Occluder is inserted through a catheter that is placed in a leg vein and advanced to the heart. In the U.S., the GORE® CARDIOFORM Septal Occluder is currently approved for closure of atrial septal defects (ASDs), and is under investigation for the closure of PFOs. It is designed with two independent conformable discs that span and cover the anatomy. The minimal wire frame of the device provides optimal apposition to the anatomy and is covered in Gore's proprietary, thromboresistant ePTFE material, allowing tissue ingrowth for short-and long-term performance.

CLINICAL SUMMARY

Closure of patent foramen ovale defects using GORE® CARDIOFORM Septal Occluder: Results from a prospective European multicenter study

Design

Study size: 150 subjects were included from 10 sites within Germany, Denmark, Italy, United Kingdom, and Sweden. Follow-up time was six months.

Study population: Subjects of at least 18 years of age with a PFO confirmed by TTE or TEE and an estimated defect size < 17 mm. The majority of the subjects had a history of stroke or TIA (86%). The remaining indications included patients with peripheral embolism, diver with a risk of decompression disease, patients with planned neurosurgery in supine position and risk of paradoxical air embolism during surgery or significant shunting of an ASD in the presence of an additional PFO.

Results

Age (years, median ± std dev): 46.4 ± 12.4

Weight (kg, mean ± std dev): 77.9 ± 16.4

Defect characteristics:

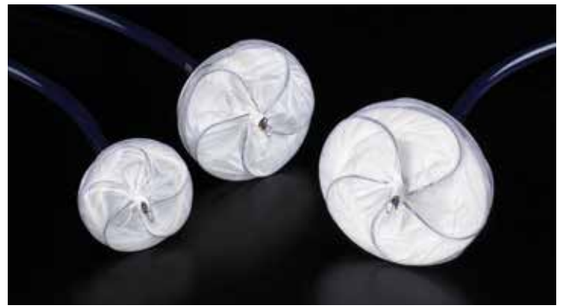
- Stop flow balloon size (mm, mean ± std dev): 9.3 ± 3.7
- PFO length by balloon sizing (mm, mean ± std dev): 10.7 ± 5.1
- PFO tunnel > 10 mm by balloon sizing: 41 / 67 (61.2%)
- Atrial septal aneurysm: 34 / 150 (22.7%)

Conclusions

- No post-procedure embolization or re-intervention
- Composite clinical success was high in this cohort of 150 PFO subject implants. This included:
  - Ability to successfully implant the device
  - Completely occluded or trivial residual shunt at six-month follow-up
  - Freedom from serious adverse events or device-related events

"The GORE® CARDIOFORM Septal Occluder is an easy-to-use and efficient device for patent foramen ovale closure. In particular, it has an excellent midterm safety profile with very high procedural and closure success in various anatomies."[1]

1. Hardt SE, Eicken A, Berger F, *et al.* Closure of patent foramen defects using GORE® CARDIOFORM septal occluder. *Catheterization & Cardiovascular Interventions.* In press.



GORE® CARDIOFORM Septal Occluder

Procedure outcomes	
Mean (std dev) total procedure time (minutes)	41.3 (24.8)
Mean (std dev) fluoroscopy time (minutes)	5.7 (4.6)
Technical success[1]	99.3%
Procedural success[2]	99.6%
Closure results	
Clinical closure success[3]	
Discharge	94.2%
6 months measured	96.9%
Composite clinical success	
6 months	96.0%
Safety	
Adverse events	4.0%
Paroxysmal atrial fibrillation	2.7%
Thrombus	0.6%
TIA	0.6%
Six-month device events[4]	0.0%

1. Successful deployment and retention of a GORE® CARDIOFORM Septal Occluder.
2. Successful implantation of a GORE® Septal Occluder and demonstration of successful PFO-closure during the intervention.
3. Clinical closure success discharge and at six-month follow-up (completely occluded or a trivial residual shunt).
4. Post-procedural device embolization, post-procedural device removal, or any reintervention to the septal defect.

CLINICAL EVIDENCE

Recently Published Clinical Experience with GORE® CARDIOFORM Septal Occluder

Increase in anatomical complexities

Tunnel PFO

MacDonald ST, Daniels MJ, Ormerod OJ. Initial use of the new GORE® Septal Occluder in patent foramen ovale closure: implantation and preliminary results. *Catheterization & Cardiovascular Interventions* 2013;81(4):660-665.

Atrial Septal Aneurysm

Butera G, Danna P, Musto C, *et al.* GORE® Septal Occluder: early clinical results. *Congenital Cardiology Today* 2012;10(6):1, 3-7.

Geis NA, Pleger ST, Katus HA, Hardt SE. Using the GORE® Septal Occluder (GSO) in challenging patent foramen ovale (PFO) anatomies. *Journal of Interventional Cardiology* 2015;28(2):190-197.

Thomson JD, Hildick-Smith D, Clift P, *et al.* Patent foramen ovale closure with the Gore septal occluder: initial UK experience. *Catheterization & Cardiovascular Interventions* 2014;83(3):467-473.

Knerr M, Bertog S, Vaskelyte L, Hofmann I, Sievert H. Results of percutaneous closure of patent foramen ovale with the GORE® septal occluder. *Catheterization & Cardiovascular Interventions* 2014;83(7):1144-1151.

Darsaklis K, Freixa X, Asgar A, *et al.* A novel system for transcatheter closure of patent foramen ovale: clinical and echocardiographic outcome comparison with other contemporary devices. *Canadian Journal of Cardiology* 2014;30(6):639-646.

Butera G, Saracino A, Danna P, Sganzerla P, Chessa M, Carminati M. Transcatheter PFO closure with GORE® septal occluder: early and mid-term clinical results. *Catheterization & Cardiovascular Interventions* 2013;82(6):944-949.

MacDonald ST, Daniels MJ, Ormerod OJ. Initial use of the new GORE® Septal Occluder in patent foramen ovale closure: implantation and preliminary results. *Catheterization & Cardiovascular Interventions* 2013;81(4):660-665.

Long-Tunnel PFO (≥ 10 mm overlap)

Butera G, Piazza L, Heles M. PFO "angioplasty": the preparation of a very stiff and long tunnel for device closure. *Catheterization & Cardiovascular Interventions* 2017;89(3):480-483.

Geis NA, Pleger ST, Katus HA, Hardt SE. Using the GORE® Septal Occluder (GSO) in challenging patent foramen ovale (PFO) anatomies. *Journal of Interventional Cardiology* 2015;28(2):190-197.

Thomson JD, Hildick-Smith D, Clift P, *et al.* Patent foramen ovale closure with the Gore septal occluder: initial UK experience. *Catheterization & Cardiovascular Interventions* 2014;83(3):467-473.

Freixa X, Ibrahim R, Chan J, *et al.* Initial clinical experience with the GORE septal occluder for the treatment of atrial septal defects and patent foramen ovale. *EuroIntervention* 2013;9(5):629-635.

Atrial Septal Aneurysm and Long-Tunnel PFO (≥ 10 mm overlap)

Geis NA, Pleger ST, Katus HA, Hardt SE. Using the GORE® Septal Occluder (GSO) in challenging patent foramen ovale (PFO) anatomies. *Journal of Interventional Cardiology* 2015;28(2):190-197.

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