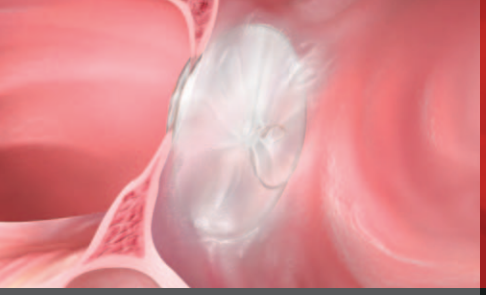
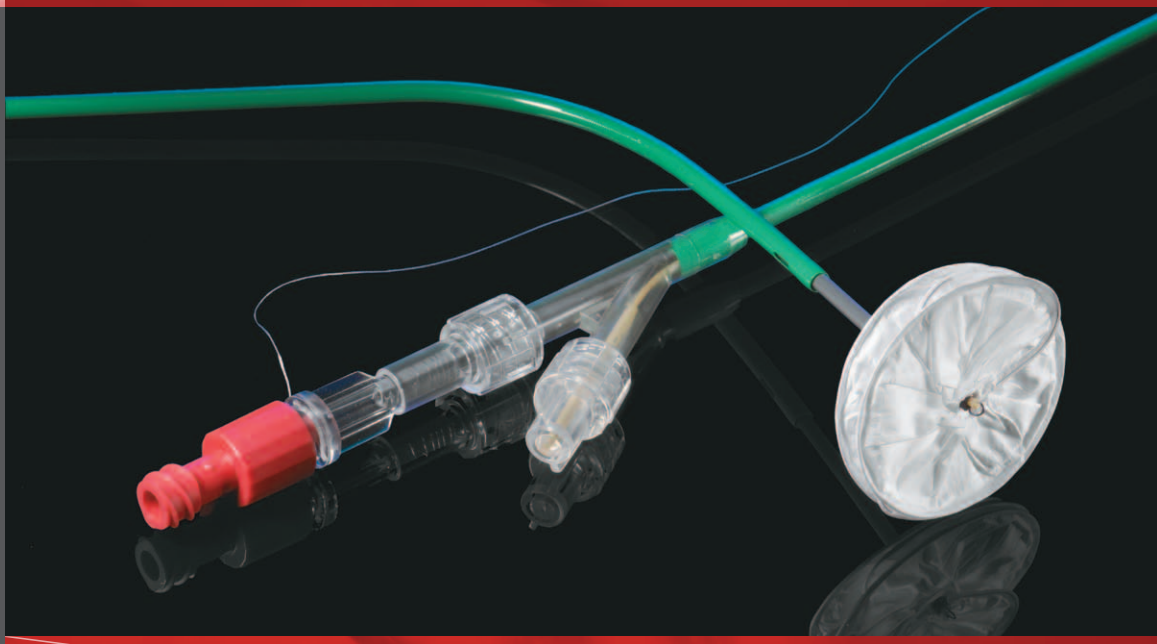


Closing Remarks



PERFORMANCE by design

In This Issue

goremedical.com/HELEX

Spring 2013 • Issue XXII

CASE STUDY

Placement of a Large GORE® HELEX® Septal Occluder in a Patient with Deficient Aortic Rim and Atrial Septal Aneurysm

Louai Razzouk, MD, MPH
Muhamed Saric, MD, PhD
James N Slater, MD
Leon H. Charney Division of Cardiology, Department of Medicine
New York University Langone Medical Center, New York, USA

A 55-year-old woman with a history of type II diabetes mellitus, hypertension, severe chronic obstructive pulmonary disease and atrial fibrillation on anticoagulation presented with worsening dyspnea on exertion. The patient reported a limited exercise tolerance to less than half a city block, and was

Continued on inside cover...

GORE HELEX® SEPTAL OCCLUDER

…Case Study continued from cover

Placement of a Large GORE® HELEX® Septal Occluder in a Patient with Deficient Aortic Rim and Atrial Septal Aneurysm

referred for a possible percutaneous closure of a newly diagnosed secundum atrial septal defect (ASD) with a mobile atrial septal aneurysm seen on echocardiography (*Figure 1, Video 1**). Her comorbidities precluded her from surgical repair of the ASD.

Hemodynamic evaluation of the defect revealed a left-to-right shunt with a Q_p:Q_s of 2.4:1.0, with severe right atrial and right ventricular (RV) dilatation and paradoxical interventricular septal motion due to to RV volume overload. The contractility of the RV and left ventricle (LV) was normal, and there was moderate elevation in the pulmonary artery systolic pressure to 47 mmHg.

Full evaluation of ASD morphology and size was subsequently performed on 2D and 3D transesophageal echocardiography (TEE). The ASD was ovoid in shape. Using multiplane reconstruction technique of 3D TEE, the defect was sized precisely; it measured 22 x 17 mm and had a minimal aortic rim (*Figure 2*). Attached to the superior and inferior rim of the defect, there was a mobile atrial septal aneurysm (*Figure 3, Videos 2 and 3**). Of note, the coronary sinus was dilated, likely due to a persistent left superior vena cava.

The ASD was crossed with a multi-purpose catheter over a J-wire, and a stiff AMPLATZ Wire was positioned in the left upper pulmonary vein. A 25 mm sizing balloon was used to measure the size of the ASD, and stop-flow analysis revealed defect size of approximately 18 mm in diameter (*Figure 4, Video 4**). Although the atrial septal aneurysm, attached to the rim of the ASD, was noted floating freely in the right atrium, the balloon passed without difficulty into the left atrium. Given the oblong shape of the ASD and the absence of aortic rim as shown on 3D TEE, the decision was made to perform ASD closure with a GORE® HELEX® Device in order to minimize the risk of erosion into the aortic wall.

The largest GORE® HELEX® Septal Occluder (35 mm nominal diameter) was therefore chosen, and positioned with fluoroscopic and TEE guidance. After initial placement, there was significant residual left-to-right flow on color Doppler around the aortic rim. The device was then retrieved and repositioned more anteriorly. After repositioning the device, the ASD was well covered with only minimal residual left-to-right flow around the posterior portion of the device (*Figure 5*). Given the near-optimal result, the device was released (*Figure 6*).

A transthoracic echocardiogram (TTE) performed the following day did not visualize any definitive evidence of residual right-to-left shunt after intravenous infusion of agitated saline at baseline or after Valsalva maneuver.

No residual left-to-right flow was visualized on TTE by color Doppler. Left and right ventricular functions were normal, and the right ventricle was still dilated. The patient was discharged on aspirin and clopidogrel daily for six months, with follow-up in our cardiology clinic.

At six weeks follow-up, the patient reported a marked decrease in dyspnea on exertion, and an improvement in her exercise tolerance from one-half a city block to five city blocks.

At eight weeks follow-up, TTE showed normal biventricular systolic function and normalization of the right ventricular size. 2D / 3D TEE demonstrated a well-seated GORE® HELEX® Device across the interatrial septum and along the aortic rim (*Figure 7, Video 5**). There was no evidence of right-to-left shunting following intravenous infusion of agitated saline, and no color Doppler evidence of left-to-right shunting.

Continued on next page...

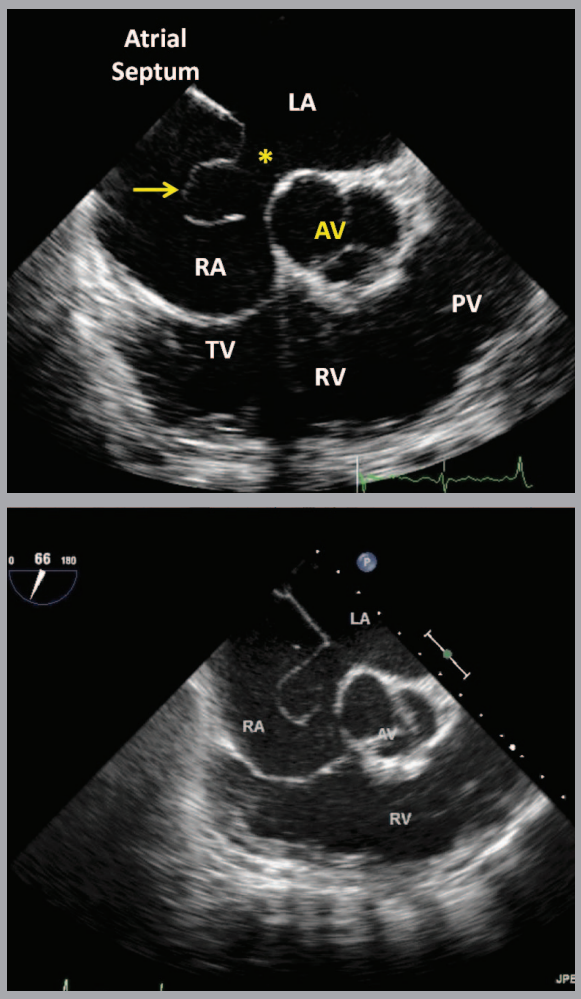


***Figure 1 / Video 1**.* Midesophageal 2D TEE image at the short axis of the aortic valve reveals a large secundum ASD (asterisk) and a mobile atrial septal aneurysm (arrow). Note that ASD lacks an aortic rim. AV, aortic valve; LA, left atrium; PV, pulmonic valve; RA, right atrium, RV, right ventricle; TV, tricuspid valve. Video 1 corresponds to Figure 1.

…Case Study continued from previous page

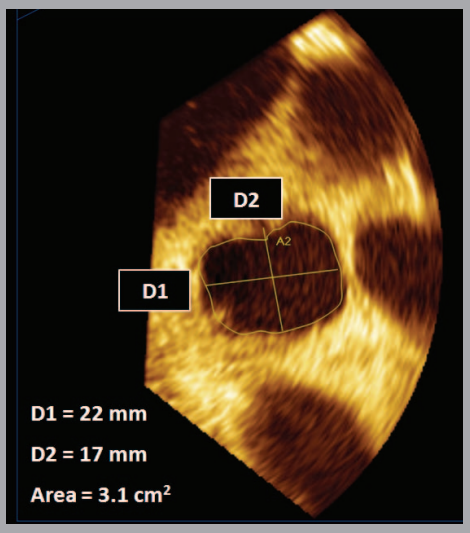
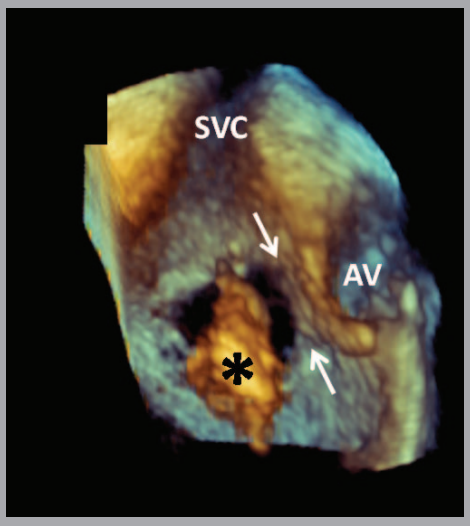
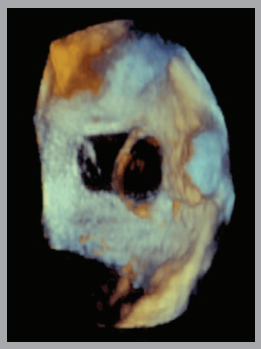


Figure 2. Multiplane reconstruction on 3D TEE demonstrates an ovoid ASD measuring 22 x 17 mm.





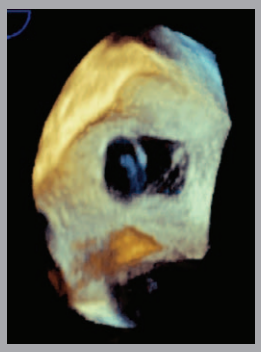


Figure 3 / Videos 2 and 3*. 3D TEE image demonstrates the right atrial aspect of the ASD with an atrial septal aneurysm (asterisk) and minimal aortic rim (arrows). AV, aortic valve; SVC, superior vena cava. Video 2 corresponds to Figure 3. Video 3 demonstrates the left atrial aspect of ASD.

Discussion

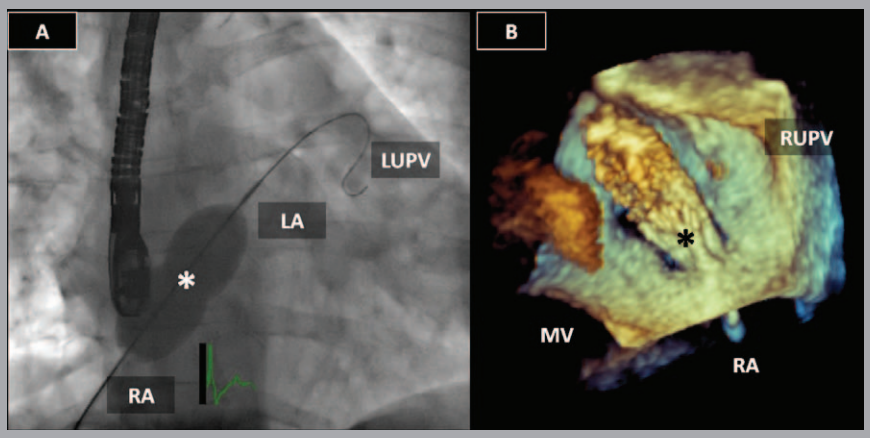
While a large AMPLATZER® Septal Occluder would have probably successfully closed the septal defect in this patient, the concern for distortion of the aortic root guided us towards a more compliant closure device.

Reports of erosion of the AMPLATZER® Septal Occluder into the aorta may have occurred in patients with a deficient aortic rim[1]. Furthermore, an oversized AMPLATZER® Septal Occluder may also increase the risk of erosion, as the device-to-unstretched ASD ratio has been noted to be significantly larger in patients with unfavorable outcomes. Even though the incidence of AMPLATZER® Septal Occluder erosion into the aortic root is low (approximately 1 in 1,000 cases), such a complication may often be avoided in patients with deficient rims with a use of a more compliant ASD closure device.

The large size of the defect in our patient was of concern to us, as it

approached the 2:1 sizing ratio limit of the GORE® HELEX® Device. The repositioning of the largest GORE® HELEX® Device available was required for successful closure of the defect.

The risk of device embolization can increase with large defects and minimal rims. Interventional cardiologists thus face a challenge of choosing the optimal device with the smallest occluding size in order to minimize the risk of erosion, but also large enough to ensure stable placement to prevent embolization. Given its pliability, the GORE® HELEX® Device may be well suited for closure of large ASDs with deficient aortic rims.



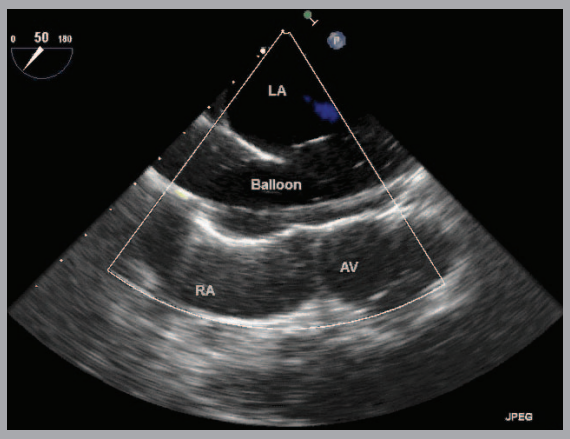


Figure 4 / Video 4*. Sizing balloon (asterisk) seen across the ASD on fluoroscopy (Panel A) and on 3D TEE (Panel B). LA, left atrium; LUPV, left upper pulmonary vein; MV, mitral valve; RA, right atrium; RUPV, right upper pulmonary vein. Video 4 corresponds to Figure 4 and demonstrates no flow around the balloon on color Doppler.

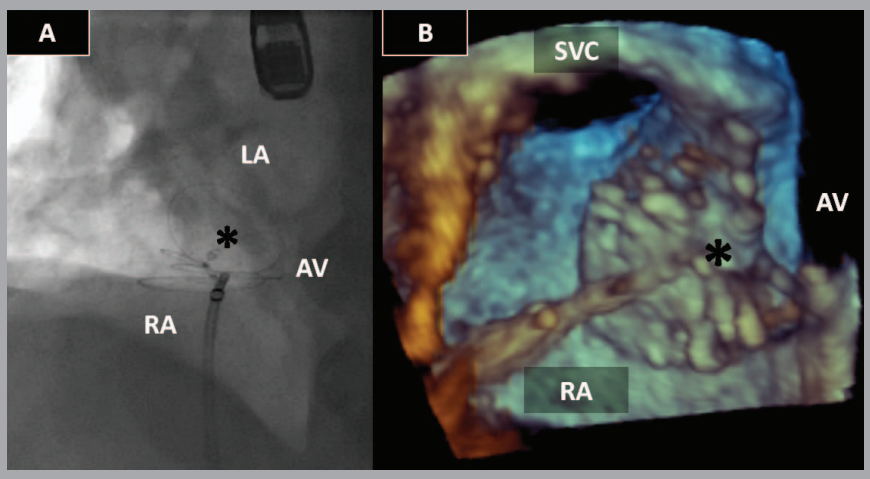


Figure 5. GORE® HELEX® Septal Occluder (asterisk) being positioned in the ASD on fluoroscopy (Panel A) and on 3D TEE (Panel B). AV, aortic valve; LA, left atrium; RA, right atrium; SVC, superior vena cava.

References

1. Amin Z, Hijazi ZM, Bass JL, Cheatham JP, Hellenbrand WE, Kleinman CS. Erosion of Amplatzer septal occluder device after closure of secundum atrial septal defects: review of registry of complications and recommendations to minimize future risk. *Catheterization & Cardiovascular Interventions* 2004;63(4):496-502.

Continued on next page...

…Case Study continued from previous page

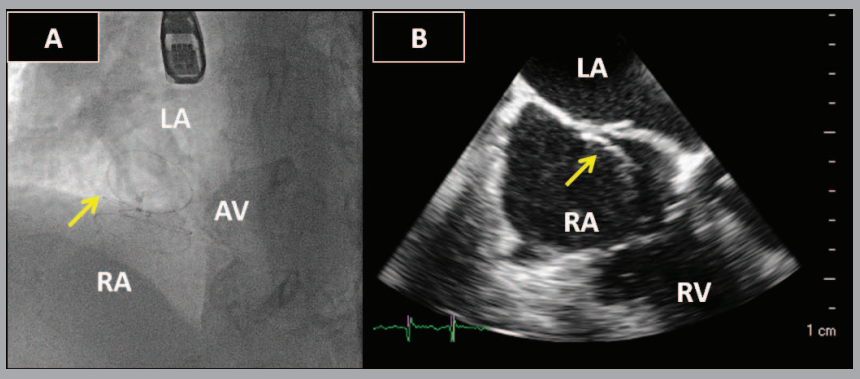
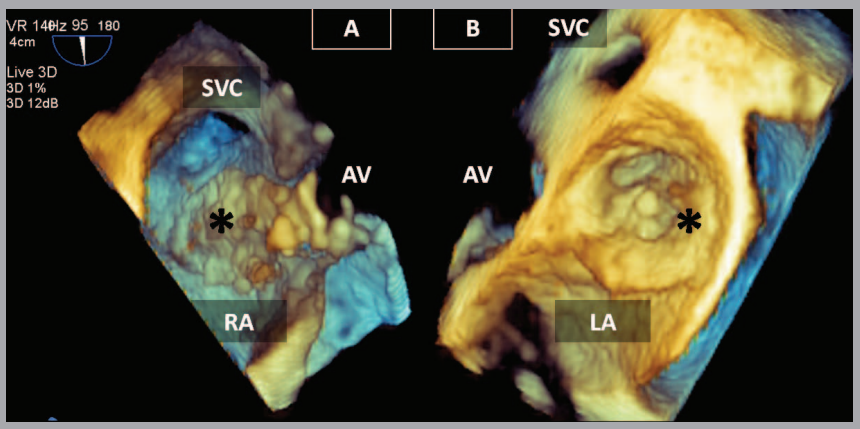


Figure 6. GORE® HELEX® Septal Occluder (arrow) fully deployed on fluoroscopy (Panel A) and on 2D TEE (Panel B). AV, aortic valve; LA, left atrium; RA, right atrium.



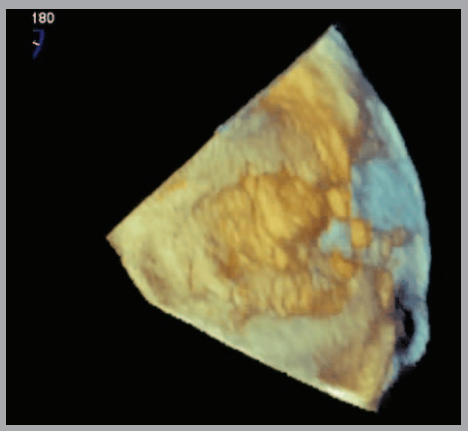


Figure 7 / Video 5*. 3D TEE appearance of GORE® HELEX® Septal Occluder (asterisk) from the right atrial (Panel A) and left atrial (Panel B) perspective. AV, aortic valve; LA, left atrium; RA, right atrium; SVC, superior vena cava. Video 5 corresponds to Figure 7; it first reveals the right atrial aspect of the GORE® HELEX® Device, then it shows the cusps of the aortic valve and finally the left atrial aspect of the device.

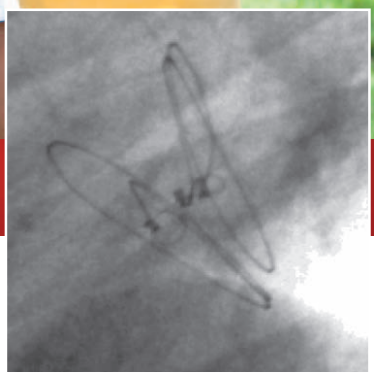
* The video files referenced in these articles are available in our online version of the *Closing Remarks* newsletter: www.goremedical.com/HELEX/library/newsletters

Please refer to GORE® HELEX® Septal Occluder *Instructions for Use* at goremedical.com for a complete description of all indications, contradindications, warnings, precautions, and adverse events.

This case study is not intended to express the views, opinions, or recommendations of the device manufacturer, W. L. Gore & Associates, rather the views, opinions, or recommendations expressed herein are exclusively the authors' own.

Outcomes You Can Count On.

Watch On-Demand! Webinar Review of
FDA Circulatory System Devices Advisory Panel Meeting
www.goremedical.com/HELEXWebinar



Rest assured knowing your patient is implanted with a GORE® HELEX® Septal Occluder.

High closure rates and low major adverse event rates demonstrated through clinical study data*

No reported erosions**

No reported late emergent surgical interventions**

* Results from the Feasibility, Pivotal, Continued Access, and Post-Approval Studies demonstrate 98.3% closure rate and a Major Adverse Event rate < 5% at one year. Major Adverse Events were defined as any event requiring reintervention, readmission to the hospital, or resulted in permanent damage or deficit.
** Data on file.

GORE® HELEX® SEPTAL OCCLUDER

PERFORMANCE by design

FEATURED TOPIC

Gore Fine Filtration Technology: Meeting the Demands of the Electronics Industry

It sounds counter intuitive: a filter that can capture extremely fine particles at a high rate while also processing liquids at a very fast rate, but Gore has achieved this with its fine filtration technology, currently used in the manufacture of semiconductor materials for the electronics industry.

Semiconductors are found in all modern electronic devices that use circuitry, for example, computers, cell phones, IPOD® Mobile Devices, BLACKBERRY® Devices and navigational systems. Because even extremely small particles can damage their performance, semiconductors require a clean manufacturing process, including the use of filtered, ultrapure water and high-purity chemicals. Gore's filters retain particles from these liquids without slowing the rate of liquid flow through the filter.

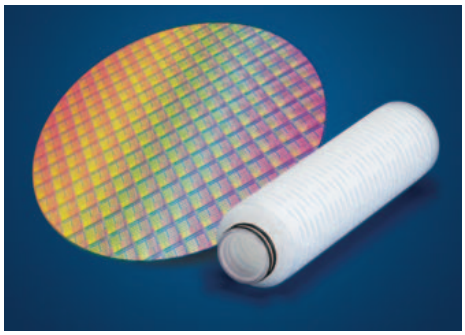
"Normally, filters cannot achieve both high particle retention rates and high flow rates; you have to sacrifice one for the other," explains marketing associate Virginia Gatch. "By delivering both, our filters offer a level of performance completely unmatched in the industry."

To understand the difficulty of achieving simultaneously high flow and high retention rates, imagine sifting flour before baking a cake. To successfully remove the smallest of impurities, you would need a sifter with extremely tiny grates. But this would also slow the sifting process, because it would take longer for flour to flow through small openings than large ones. Of course, in this case, if an impurity falls through the cracks or if efficiency is reduced, the impact is minimal.

But imagine removing microscopic particles from the liquids used in semiconductor manufacturing processes. If a particle gets through, it could greatly compromise the performance of the finished product. With one semiconductor wafer worth nearly half a million dollars, it is understandable why manufacturers want to retain the smallest particles possible and also maintain fast manufacturing rates. As business leader Kent Steeves, notes, "In the world of semiconductor manufacturing, yield is everything."

A Technology Breakthrough

In 2007, Gore achieved a breakthrough with its fine filtration technology. For decades, the liquid microfiltration media business had sold ePTFE filter media to outside companies for use in their filtration devices. But after creating a next generation material that offered both improved retention and flow rates, the business decided to begin manufacturing its own finished filters.



Gore's filter cartridges, like the one pictured above, retain particles from the ultrapure water and high-purity chemicals used in semiconductor manufacturing. Also pictured above is a silicon wafer—the building block for semiconductor chips.

Semiconductors are found in all modern electronic devices that use circuitry, such as computers and cell phones.

"We already had the best media in the world, and we had a very successful business as a media supplier," Kent says. "But our breakthrough in technology caused us to pause and investigate

whether we were truly understanding the value that we bring, and if we were adequately capturing the value."

Following the technology breakthrough and subsequent business model change, product specialist Dan Lash, worked with the team behind Gore's first filter device to drive a key win with one of the world's largest semiconductor chip manufacturers. Since then, the fine filtration business has continued to make inroads with other key customers based on its distinct technology.

The business also continues to supply media to other filter makers, but, since 2007, has only used new ePTFE materials in Gore filters. Dan explains, "We offer something truly unique. Our filters have greater porosity than competing options. This means we can fit more small pores in a given space, allowing us to achieve high flow rates without sacrificing retention."

Unparalleled Performance

Soaring Su, an Asia-Pacific sales leader, says this has helped the business overcome many of the challenges associated with entering an already established market. "We don't have as broad a product line or as much experience making finished filters as the competition, but we do have better performance. And this is what our target market really values."

Gore's filters can capture particles as small as 20 nanometers, or 20 billionths of a meter in diameter. And the business is developing technologies to meet the even tighter industry demands expected in the coming years. In addition to semiconductor manufacturing, Gore's filters are used in the manufacture of LCDs (liquid crystal displays), LEDs (light-emitting diodes), solar cells and hard disk drives.

"The requirements in these industries are getting tighter and tighter, and the demand for better performance is increasing. Our technology is able to meet these needs," Dan says. "We also have better access now to equipment makers and end users, which helps us develop technologies that meet their most pressing needs."

IN THE NEWS

In Pursuit of the PFO Closure Indication

Two doctors involved in the ongoing Gore REDUCE Clinical Study reflect on the meaning of the much-discussed results from St. Jude Medical's RESPECT Study

The cardiology community is still discussing the findings from St. Jude Medical's RESPECT Study, which were presented last fall at the 2012 Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium in Miami. The results — while not reaching statistical significance to demonstrate the superiority of device closure to medical therapy — offer support for further investigation of device closure's potential benefit for patients with cryptogenic stroke and PFO.

Seeking greater insight into the study's findings and what they mean on the clinical side, industry publication *Cardiac Interventions Today*[1] recently spoke with Robert Sommer, MD of Columbia University Medical Center in New York, investigator for the Gore REDUCE Clinical Study; and John Rhodes, MD of Duke University Medical Center in Durham, North Carolina, the US cardiologist principal investigator for the Gore REDUCE Clinical Study.

In this interview excerpt, the doctors explain how results from the St. Jude study could potentially influence treatment of PFO for the prevention of recurrent stroke; they also address some criticisms of the data.

What are the significant take-home points regarding the data from the RESPECT Study?

Dr. Rhodes: I would point out that this is a well-done study with a large patient population, but in an environment with off-label use and other insurance-related issues that potentially make it difficult to enroll and make the enrollment period longer. I think knowing that, and what the outcomes were, it is a good study that gives us a lot of information about which direction to move toward regarding therapy for patients with cryptogenic stroke.

What are the criticisms of the RESPECT data that need to be addressed?

Dr. Sommer: Well, the RESPECT Study data in general are excellent. It was a very well-run study. The major issue for somebody reading these results would be that the intent-to-treat analysis led to a result in which a third of the patients who had a stroke in the closure arm never underwent closure. This obviously confounds the results of the study. But, from a statistical point of view, if that aspect of the trial is invalid because of unequal dropout in the two groups, and if the intent-to-treat analysis and per-protocol analyses are not valid either because you affect the randomization and there is potential bias introduced into the study, then potentially none of the outcomes are statistically significant.

1. Cardiac Interventions Today. The RESPECT Trial. Robert Sommer, MD, and John Rhodes, MD, share their insights on the recently presented data and how this will influence clinical practice. *Cardiac Interventions Today* 2013;7(1):34-37.

> **Dr. Rhodes:** The other issue in the way that the RESPECT Study was designed is that it included patients in the medical arm who were on warfarin. I think if you're randomizing warfarin as a therapy versus device closure, the real risk / benefit balance is going to be long-term risk of bleeding complications from warfarin rather than recurrent stroke on warfarin. If 25% of your medical arm is on warfarin, that 25% in the follow-up time period that they had may not have had an adverse event of recurrent stroke but would have a significant and well-understood risk of bleeding adverse events in the years to come. So, 25% of your medical arm may be less likely to have the endpoint of recurrent stroke compared to the aspirin or clopidogrel arm.

To read more of the interview, access the complete article from *Cardiac Interventions Today*[1].

As Dr. Rhodes and Dr. Sommer pointed out in the article, results from the RESPECT Study showed significant promise for device therapy. Still, it is important to note that there is no device available in the US indicated for this therapy. These data continue to be digested by the physician community, investigators, as well as the FDA, and should be considered alongside the totality of evidence that has been generated to date.

Meanwhile, the Gore REDUCE Clinical Study — the only remaining PFO Stroke Study in the US — continues to enroll patients. The study seeks to determine which option is better at reducing the risk of having another stroke: closing a patient's PFO with the GORE® Septal Occluder plus taking some antiplatelet medication, or taking antiplatelet medication alone without closing the PFO.

As noted previously by the Gore REDUCE Clinical Study steering committee, Gore's study shares many similarities with St. Jude Medical's study in terms of enrollment criteria, such as exclusion of patients who had transient ischemic attacks or lacunar infarct syndrome.

Furthermore, the Gore REDUCE Clinical Study should also benefit from stringent patient selection, consistency in the prescribed medical therapy across treatment arms, and the required neuroimaging of every patient at two years post randomization.

Gore recently reported its best enrolling month in the history of the study, reaffirming the investigators' commitment to obtaining the answer to this important research question. Gore encourages physicians to continue to refer applicable patients to the Gore REDUCE Clinical Study sites for enrollment consideration.

Find more details about the Gore REDUCE Clinical Study at www.clinical.goremedical.com/REDUCE.

UPCOMING EVENTS

Please Join Us…

The Society for Cardiovascular Angiography and Interventions (SCAI 2013)

May 8 – 11, 2013 Orlando, Florida Booth #1101

Congenital and Structural Interventions (CSI 2013)

June 27 – 29, 2013 Frankfurt, Germany

If you have a topic that you would like us to consider in a future issue of Closing Remarks, please contact your local Gore Sales Associate or e-mail ClosingRemarks@wlgore.com

GORE
Creative Technologies Worldwide

W. L. Gore & Associates, Inc.
Flagstaff, AZ 86004

+65.67332882 (Asia Pacific) 800.437.8181 (United States)
00800.6334.4673 (Europe) 928.779.2771 (United States)

goremedical.com

INDICATIONS FOR USE IN THE US: The GORE® HELEX® Septal Occluder is a permanently implanted prosthesis indicated for the percutaneous, transcatheter closure of *ostium secundum* atrial septal defects (ASDs). **INDICATIONS FOR USE UNDER CE MARK:** The GORE® HELEX® Septal Occluder is a permanently implanted prosthesis indicated for the percutaneous, transcatheter closure of atrial septal defects (ASDs),such as *ostium secundum* and patent foramen ovale. Refer to *Instructions for Use* at goremedical.com for a complete description of all contraindications, warnings, precautions and adverse events. ℞ Only