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IMPEDE[®] Embolization Plug



Prepared for:

2019 R&D 100
Award Entry



LLNL-MI-774803

Prepared by LLNL under Contract DE-AC52-07NA27344.

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IMPEDE® Embolization Plug

1. **PRODUCT/SERVICES CATEGORIES**

A. Title

IMPEDE® Embolization Plug

B. Product Category

Life Sciences (biopharmaceuticals, DNA/RNA systems, food & beverage, genomics, proteomics, GMO, medical devices, medicine, medical implants, etc.)

2. **R&D 100 PRODUCT/SERVICE DETAILS**

A. Primary submitting organization

Shape Memory Medical Inc.

B. Co-developing organizations

Lawrence Livermore National Laboratory

Texas A&M University

C. Product brand name

IMPEDE® Embolization Plug



D. Product Introduction

This product was introduced to the market between January 1, 2018, and March 31, 2019.

IMPEDE's FDA Clearance was received on June 22, 2018.

E. Price in U.S. Dollars

\$875-\$1000

F. Short description

The IMPEDE® Embolization Plug is a permanently implanted vascular occlusion medical device featuring fast, easy deployment with low radial force and high vessel conformability. It combines a novel biodegradable shape memory polymer (SMP) foam with a radiopaque markerband and anchor coil for positioning, rapid clotting, and integrated healing response..

G. Type of institution represented

Company/Corporation

H. Submitter's relationship to product

Product developer

I. Photos

Attached inline

J. Video

<https://www.shapemem.com/impede>



3. PRODUCT/SERVICE DESCRIPTION

A. What does the product or technology do?

In cases of abdominal aortic aneurysm endoleaks, gastric and esophageal varices, blunt trauma, and arteriovenous malformations (AVM), blood flow through diseased or damaged vessels puts patients at increased risk of stroke, pain, uncontrolled bleeding, and even death in extreme cases. The IMPEDE Embolization Plug is intended to obstruct or reduce the rate of blood flow in the peripheral vasculature to reduce or eliminate these risks. The device is delivered to a diseased vessel through a catheter that is navigated to the target region in the vasculature through a small incision in the groin. Upon contact with circulating blood, the SMP foam expands up to ten times in diameter to fill the entire vessel and create a stable blood clot that effectively diverts blood flow away from the diseased vessel. The initial blood clot is then remodeled into connective tissue that results in a completely healed vessel.

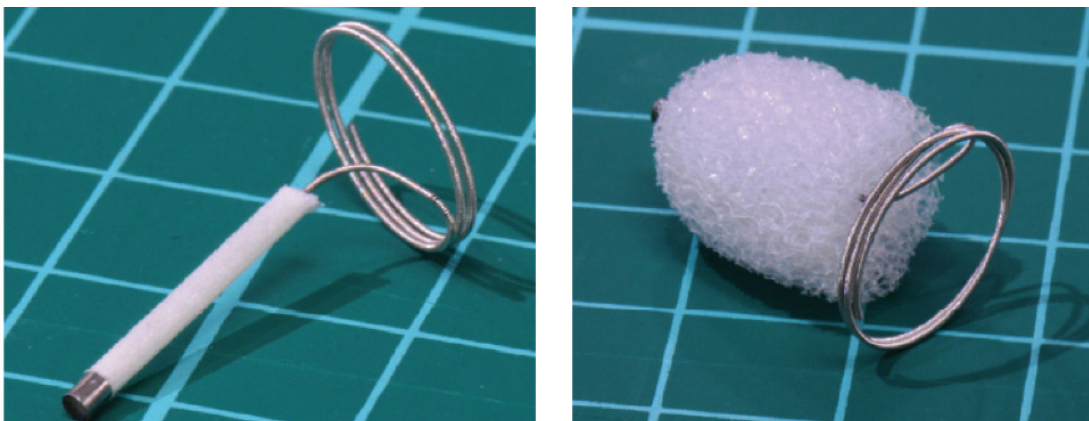


Figure 1. Crimped IMPEDE Embolization Plug (left) and expanded IMPEDE device (right)



B. How does the product operate?

Various diseases in both the arterial and venous circulations require embolization treatment. Vascular disease examples that require clinical intervention include abdominal aortic aneurysm endoleaks, gastric and esophageal varices, blunt trauma, varicoceles, and AVMs. Regardless of the anatomical location of these diseases, the goal of embolization is always to divert blood flow away from the diseased vessel to alleviate pain, prevent excessive bleeding, and/or minimize the risk of death in the most extreme circumstances. Current embolization treatments rely primarily on two minimally invasive methods to divert blood flow away from the treatment site. The first method is to provide a physical barrier to blood flow that allows sufficient thrombus (blood clot) to form on the barrier until it causes sufficient pressure drop across the device to cause blood diversion. The second method is to inject a detergent that chemically burns the inner lining of the target vessel in an attempt to cause scar formation that diverts blood flow. The IMPEDE device uses the first treatment methodology as it provides greater user control over where the vessel is treated and doesn't put adjacent vessels away from the treatment site at risk of damage.

Prior to embolization treatment, a small incision is made in the patient's groin to allow a standard guide catheter to be inserted into the femoral artery or vein, depending on the location of the disease. A guide catheter is a small, flexible conduit that is a fraction of the size of the diseased vessels that allows easy navigation to virtually all regions of the peripheral vasculature. A small, flexible wire known as a guidewire is then inserted through the lumen of the guide catheter to aid an interventional radiologist or vascular surgeon in navigating the catheter to the diseased vessel where embolization is required. When the diseased vessel is reached, a small contrast injection is made through the catheter to visualize and measure the target vessel using X-ray imaging to identify the optimal device size for implantation.

The IMPEDE Embolization Plug is comprised of a radiopaque markerband and anchor coil with a crimped polyurethane SMP foam between the two. There are three different sizes of the IMPEDE Embolization Plugs as shown below: IMP-05, IMP-07, and IMP-10. These three device sizes allow treatment of vessels 2–10 mm in diameter.



REF	Recommended Vessel Ø Range	Minimum Catheter ID Ø	Minimum Guidewire OD Ø
IMP-05	2–5 mm	0.038"	0.032"
IMP-07	4–7 mm	0.055"	0.035"
IMP-10	6–10 mm	0.070"	0.035"

Table 1. IMPEDE Embolization Plug device sizing.

The radiopacity of the markerband and anchor coil allows the device to be precisely delivered to the target vessel under X-ray imaging guidance. The foam is initially crimped to allow the device to be easily delivered to the treatment region with very little force using the same guidewire that was used to help navigate the catheter. The distal anchor coil is deployed from the catheter first and immediately forms a helical coil inside the vessel. Once the entire anchor coil is deployed from the catheter, the remainder of the device is then unsheathed by maintaining the position of the guidewire while retracting the catheter backwards. Once the entire IMPEDE device is delivered to the vessel, the distal anchor coil holds the device in place while the foam expands so that it does not migrate downstream and cause further complications. Subsequently, within 10 minutes, the SMP foam undergoes up to a 100-fold volume expansion to completely fill the target vessel. The porous morphology of the expanded foam creates thousands of microscopic zones where the blood recirculates and stagnates, which then initiates clot formation. Simultaneously, exposure of the large foam surface area to circulating blood, and contact of the foam with the vessel lumen, initiates a foreign body response that also causes rapid blood clot formation. As blood clot forms throughout the device volume, it creates an effective seal that diverts systemic blood flow away from the diseased vessel and towards healthy vessels. As the blood is diverted away from the diseased vessel, patient complications and symptoms subside. Over time, the initial blood clot is then replaced with connective tissue and collagen that eventually forms a stable scar at the implant site indicating a completely healed vessel. Typically, embolization procedures allow the patient to leave the hospital the day after treatment as the small incision in the groin to gain catheter access is the only surgical cut made in the patient for the entire procedure.

Over the course of a couple years, the polyurethane SMP foam undergoes slow oxidative degradation and is replaced with connective tissue and collagen without eliciting any untoward inflammation or toxicity effects. The SMP foam was specifically designed using polymers that



degrade over long periods of time into benign compounds to allow connective tissue deposition and subsequent scar tissue formation without distorting the native vessel. As the scar tissue forms within the vessel cross-section and creates a healed vessel, the foam is slowly degraded, the scar tissue contracts, and the treated vessel may resume its natural size.

C. Product Comparison

The IMPEDE device works with current clinical skillsets and techniques. For the placement of embolization devices, the current clinical practice is to use minimally invasive techniques whenever possible. Interventional radiologists and vascular surgeons use guidewires, catheters, fluoroscopy/CT imaging, injected radiopaque contrast agent, and other tools to achieve clinical embolization goals. Among many other skills, these clinicians have excellent tactile and tool manipulation skills, the ability to read two dimensional (2D) images and map the 2D image onto memorized and interpreted three dimensional anatomies, and the acumen to predict the vascular impact of implanting devices. IMPEDE works with the same tools and techniques, which is critical for both clinical adoption and patient outcomes.

Embolic coils, modified embolic coils, and vascular plugs are current embolization devices available to interventional radiologists for treating morbidities addressed by the IMPEDE device. For each type of device the design goals are as follows:

- Be easily delivered through tortuous vascular pathways
- Allow easy and reliable device placement without causing damage to the disease site
- Remain stationary (no migration) after deployment
- Rapidly embolize with the minimum number of devices and time
- Ensure long-term embolization over time (no recanalization), to prevent the need for retreatment

No embolization device currently on the market meets all of these criteria, as shown in Table 2. The biggest drawback of any embolic coil is the need to typically implant several coils to effectively fill the



diseased vessel and create occlusion. For instance, gonadal veins that have an average diameter of approximately 8 mm often require an average of 16 coils to completely treat each vein. On top of the large number of coils required for successful treatment, recanalization, or the recurrence of blood flow through the diseased vessel, is also seen in approximately 12–15% of cases where embolic coils are the primary form of treatment. In the majority of these cases, the patient has to undergo a second, or even a third, treatment to permanently occlude the diseased vessel. Embolic coil migration is also a risk in high flow vessels where device movement away from the treatment region can result in catastrophic consequences, such as a stroke. Vascular plugs offer a solution to the number of devices required to effectively fill a vessel by advertising a “one-shot” solution for embolization, however, oftentimes a combination of plugs and coils are required to completely embolize the target vessel. Additionally, plugs are often too stiff to navigate through tortuous anatomy and apply too much radial force to be used in diseased vessels that are at high risk of rupturing. Vascular plugs also cost between \$1500–2000, or three to four times the cost of an embolic coil.

In order to achieve the initial embolization, all devices attempt to create tortuous blood flow by first introducing as much foreign body surface area as possible, and then secondly by filling or packing the target vessel volume with as much material as possible. The surface area triggers clot formation, which is dominated by fluid mechanics and the foreign body contact area, while the volume filling creates a scaffold for stabilizing the clot to create effective embolization. Further, the materials used in these devices are focused on minimizing the foreign body response so as to keep the inflammation and immune response to a minimum. Numerous animal studies demonstrated that IMPEDE improves all of these factors to produce superior short-term occlusion and long-term healing compared to commercial embolization devices.

At implantation, the crimped IMPEDE foam expands to create a high surface area, highly tortuous scaffold that also gently fills the entire target volume with a safe outward radial force. **The surface area of the expanded IMPEDE foam is 100–1000 times greater than current devices.** The pores of the SMP foam create small, interconnected channels that rapidly and completely clot. After implantation, the IMPEDE device also offers a first-of-its-kind porous morphology that acts as a scaffold for encouraging **rapid long-term vessel healing**. No other embolization technologies on the market offer this same scaffolding to support connective tissue infiltration to prevent recanalization and enhance healing. Competitive technologies focus on the ability to permanently exclude space at the treatment site, whereas the IMPEDE device is the first device to incorporate the body’s natural healing mechanisms to support long-term healing and device stabilization. This

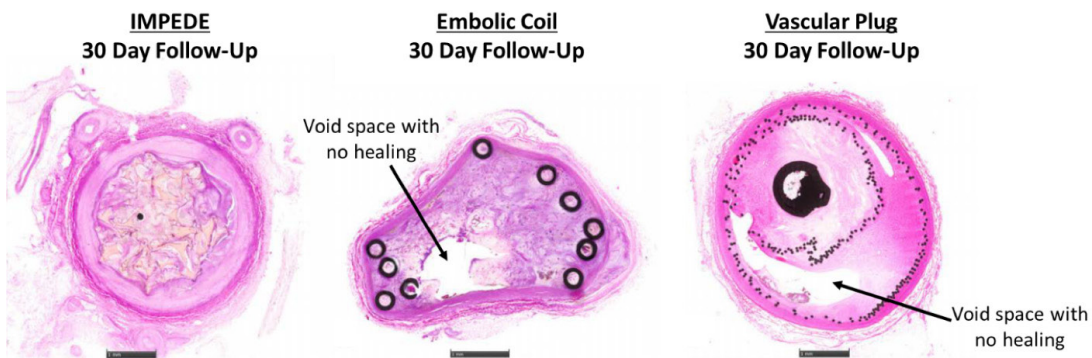


Figure 2. Cross-sectional view of porcine arteries treated with the IMPEDE device and the two market leading embolization devices (embolic coils and vascular plugs). Cross-sectional views clearly show large void spaces in the market leading devices which put the patient at an increased risk of recanalization, or reflow of blood, at the treatment site requiring the patient to undergo additional treatments. These same void spaces are not present in the IMPEDE-treated vessel, indicating a more advanced stage of healing and more complete occlusion of the target vessel.

is demonstrated in the histology images shown in Figure 2 captured at 30 days after implantation in an in vivo porcine study, which show large voids in the vessels treated with embolic coils and vascular plugs and no large voids in the IMPEDE-treated vessel.

Importantly, the IMPEDE Embolization Plug offers complete occlusion with a single device like a vascular plug, but retains the ability to navigate tortuous pathways and exert low radial forces due to the shape memory behavior and properties of the foam. As the SMP foam expands to fill the surrounding geometry, the low radial force of the foam allows it to conform to the surrounding anatomy while still providing a physical structure to support thrombus formation. This allows IMPEDE to be used in high risk regions where conventional vascular plugs are not suitable due to the risk of rupture while also offering greater volume filling than embolic coils.

Finally, IMPEDE has been used to treat over 80 patients worldwide. While this is early in the clinical adoption of IMPEDE, these cases include some of the most difficult morbidities to treat with embolization devices, such as pulmonary AVMs, blunt trauma to the spleen, abdominal aortic aneurysm (AAA) endoleaks, and gastric varices. In some of these patients, IMPEDE was used to salvage vessel occlusion cases where competitive devices failed to create acute occlusion or showed recanalization during follow-



up imaging. One case of blunt trauma caused excessive bleeding from the spleen, which was initially treated with an Amplatzer Vascular Plug (AVP) that failed to embolize the target vessel. An IMPEDE device was then deployed immediately behind the initial AVP and caused complete vessel occlusion in a matter of minutes- preventing excessive blood loss in the patient. Most impressively, the IMPEDE technology has been used in cases that cannot be treated with current devices on the market. These cases include stable occlusion of an aortic vessel dissection and rapid and complete occlusion of AAA endoleaks. In the case of the aortic dissection, one-month follow-up imaging showed approximately 50% shrinkage in the dissected vessel diameter- demonstrating effective stabilization of the vessel and eliminating the risk of rupture. While this is only one case and continued monitoring is needed, this is the first evidence that the healing in humans mirrors the anatomical shrinkage and healing observed in the preclinical studies (see Figure 2). This healing response is new to clinical treatment and will change the techniques and motivation to treat vascular diseases that may have been previously untreatable.

The low radial force, ability to fill the entire vessel lumen with a single device, and the unique morphology of the IMPEDE device offers a more effective embolization treatment across a broad range of indications at a decreased cost for both patients and healthcare facilities.

D. Comparison summary









	Device Migration	Risk of Recanalization	Number of Devices Required	Vessel Compliance	Cost
<u>Sclerotherapy</u>  <small>(polidocanol injectable foam) 1%</small>	✗	✗	✓	✓	✗
<u>Fibered/Hydrogel Coils</u>  	✗	✗	✗	✓	✓
<u>Bare Platinum Coils</u>  	✗	✗	✗	✓	✓
<u>Vascular Plugs</u>  	✓	✓	✓	✗	✗
	✓	✓	✓	✓	✓

Table 2. Comparison of IMPEDE Embolization Plug to other commercially-available embolization devices.



E. Limitations

The primary limitation of the IMPEDE Embolization Plug is the working time, which is the time permitted for the physician to completely deploy the device to the treatment site before the foam undergoes excessive expansion and creates friction inside the delivery catheter that prevents delivery. This would then force the physician to remove the entire catheter with the device and replace it with a new one. Inherent to the use of an embolization device is the desire for the user to experience minimal friction during device delivery, and rapid device expansion upon deployment to create effective occlusion. Over fifteen years of materials research went into understanding the dynamics and how to control the foam expansion rates within the SMP foams used in the IMPEDE device. As such, a foam formulation was chosen for the IMPEDE device that provides one minute of working time while also allowing the foam to passively expand in five to ten minutes after deployment to cause occlusion. If the working time was longer, the foam would then take longer to expand in the vessel and the physician would be forced to wait further to verify successful occlusion. If the expansion rate is shorter, then the time to occlusion may be faster, but the working time is insufficient to allow the physician adequate time for safe delivery of the device. However, the current foam formulation has proven to provide adequate working time as well as expansion rates, and **no adverse events have been reported in over 100 patients who have been treated worldwide.**



4. SUMMARY

Continued blood flow to diseased vessels can have serious consequences, such as severe pain, excessive blood loss, and death in the most dire circumstances. The IMPEDE Embolization Plug is a novel self-expanding polymer scaffold used for preventing blood flow to these vulnerable vessels. The IMPEDE device combines the advantages of existing embolization technologies while addressing each of their shortcomings.

IMPEDE offers 100-1000 times greater surface area than current technologies to more effectively initiate clotting in the target vessel and divert blood flow away from the at-risk region. The expansile polymer scaffold effectively fills the implant volume with a supportive tissue matrix- decreasing the number of devices required and the cost of successful treatment. Preclinical studies indicate increased filling with IMPEDE also leads to **improved long-term healing** compared to competitive devices, decreasing the risk of retreatment. IMPEDE provides **easy delivery and minimal risk of migration** while utilizing current treatment methodologies. **Over 100 patients have been successfully treated worldwide** for conditions such as pulmonary AVMs, tumor resection, and pelvic congestion syndrome with **no reported adverse effects**.



5. CONTACT INFORMATION

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7. REFERENCES

There are no references for this entry.

8. ATTACHMENTS

Appendix A – Principal Investigators Information

Appendix B – Development Team Details

Appendix C – IMPEDE Embolization Plug Video

