ALTERING THE TREATMENT OF ABNORMAL BLEEDING WITH SHAPE MEMORY POLYMER EMBOLIZATION PLUGS

Andrew Browne abb91@pitt.edu, Julia Mascho jem332@pitt.edu, Caitlin Sexton cns67@pitt.edu

Abstract*—Embolization, or the formation of an artificial blockage or blood clot, is a medical technique used to treat specific vascular conditions typically caused by abnormal bleeding. Common cases include aneurysms and extreme trauma, but embolization surgeries are increasingly used to block blood supply to tumors as well. Modern embolization techniques, while integral to many procedures, have deficiencies that reduce their effectiveness. To address this, engineers at Texas A&M created an embolization plug utilizing memory material technology. The device is based on a polyurethane memory polymer, which grows to a predetermined size and shape after its insertion into the body by a catheter. Its expanded scaffold-plug and anchor coil structure is designed to obstruct the rate of blood flow inside a target blood vessel.*

This technology was then adopted by Shape Memory Medical (SMM), a medical device company, as the IMPEDE Embolization Plug. The difference between IMPEDE and other embolization devices is its long-term effectiveness, faster deployment time, and minimally invasive procedure. The memory material design of IMPEDE shows a reduced need for further treatment, due to increased biocompatibility and shortened healing period. Embolization plugs utilizing shape memory materials, like IMPEDE, show great promise in improving the lives of those affected by abnormal vasculature and bleeding.

Key Words—Aneurysm, Cancer, Embolization, IMPEDE embolization plug, Polyurethane shape memory polymer, Shape Memory Medical

THE NEED FOR IMPROVED EMBOLIZATION TECHNIQUES

What is the Purpose of Embolization?

Endovascular embolization is a simple procedure that is often vital to saving lives. In general, endovascular embolization procedures involve taking a certain material, called an embolic agent, and injecting it into a blood vessel through a catheter with the goal of blocking blood flow to that specific region [1]. The surgery has many specific purposes, most notably for treating excess bleeding due to trauma and tumors. Internal excess bleeding is the most common condition treated with this procedure. Typically, the procedure is used on trauma patients who have dangerous excess bleeding in the stomach or pelvic region to quickly block the source of the bleeding.

Another common application of embolization procedures is for treating aneurysms, which are parts of an artery wall that have become weak and begin to bulge. An aneurysm can become very dangerous if it ruptures and can lead to internal bleeding [2]. Aneurysms were previously treated with more invasive surgeries that completely removed them from the body. However, there were limitations with this procedure as some aneurysms were considered inoperable due to their sensitive location in the body. With the implementation of endovascular embolization procedures, aneurysms that were previously inoperable, are now accessible through the catheter-based procedure [3].

A more recent application of this procedure is in relation to tumors. Endovascular embolizations are often used in treating benign uterine fibroid tumors, which can often cause many issues in a woman’s menstrual cycle [1]. This procedure is also used as a preoperative measure to cut off the blood supply to kidney and spinal tumors in order to decrease blood loss during operation [4]. Overall, embolization procedures have become a necessary component in the treatment of many serious medical conditions over the last few decades, making their advancement crucial to the medical field.

The Issue with Current Embolization Procedures

With the vast importance of endovascular embolization procedures in the treatment of a multitude of medical conditions, it is vital to assess and improve the procedure as technology advances. Currently, embolization procedures are largely effective in terms of treating the desired medical condition, but the procedure itself is not always efficient.

There are various embolic agents on the market today, such as gel foams, coils, and plugs. Each one has its own purpose: plugs can usually only be used in larger arteries, while coils and gel foams can be inserted into smaller blood vessels for occlusion [5]. Like many surgeries, there are risk factors associated with this procedure that cause it to be an ineffective and inefficient treatment. The most notable risk is device migration, where the inserted coil or plug does not fit the blood vessel correctly, leading to movement from the desired location. This movement, while rare, often has permanent and dangerous consequences, including death [6]. Another risk factor includes regaining blood flow in that vessel from lack of full occlusion. While this can be treated with the insertion of additional embolic materials, it is often inconvenient and costly for the patient. For these reasons, multiple occlusion devices are often inserted at once to ensure full occlusion, but this also adds to cost and procedure length [5].

To improve upon the efficiency of this vital procedure, research has developed a new embolization plug now called IMPEDE. The design of this product is largely focused around the use of polyurethane shape memory polymers, which were researched and developed for over twenty years at Texas A&M and Lawrence Livermore National Laboratory [7]. The Landsman Dissertation describes the prototype of the IMPEDE embolization plug in detail, including advantages of this new device over current embolization devices on the market [8]. Since its invention, the IMPEDE embolization plug has been adopted by Shape Memory Medical, Inc. to make the product marketable in the medical industry [9]. The innovative design of this embolization aims to fix the current risks associated with embolization procedures, particularly in smaller blood vessels, for increased application and success of embolization procedures. This includes combining coil and plug technology to speed up occlusion time, as well as utilizing the polyurethane shape memory polymers to reduce the likelihood of regaining blood flow to the targeted blood vessel [8]. The overall goal of the device is to provide ease for both doctors and patients in the treatment of a multitude of diseases and medical complications.

DESIGN OF THE IMPEDE EMBOLIZATION PLUG

Polyurethane SMPs

Shape memory polymers (SMPs) are materials with the ability to return to a preset default shape when exposed to a specific external stimulus [10]. In general, SMPs have two phases: a “hard” phase and a “soft” phase [11]. The “hard” phase is responsible for the stability and retention of the activated shape while the “soft” phase reacts to an external trigger [10]. The overall shape is maintained by the unique physical or chemical cross-links of the polymer itself [8]. The external stimulus acting as the trigger to return to the permanent shape depends on the type of SMP, but most respond to a temperature, frequency of light, or exposure to an electric or magnetic field. Additionally, polyurethane SMPs can be deactivated, meaning going from hard phase back to soft, a rare trait in shape memory polymers [11].

Polyurethane is a plastic material that is commonly used in applications that include insulation, cushioning, car parts, adhesives, and shoe soles. As a result, the infrastructure for polyurethane mass production is already present and the material is incredibly cheap and easy to obtain compared to chemicals used for similar biomedical applications. Like other plastics, polyurethane is made of a long chain of complex, repeating molecules known as monomers. Polyurethanes are an incredibly diverse group of plastics; however, all of them are made from di-isocyanates and polyols [12]. Polyurethane does not appear in nature and must be synthetically produced; however, it is a recyclable material and its production is projected to become a closed-loop supply chain industry, in which all polyurethane is made entirely from recycled material [13]. Due to its ubiquity in virtually every single modern building, mattress, phone, shoes, and other products, it is incredibly easy to access and cheap to use.

Polyurethane memory polymers are notable for their unique properties. First, polyurethane memory polymers demonstrate impressive biocompatibility, supporting rapid clot formation and immune response [14]. Rapid clot formation is important in the context of embolization plugs, as the clotting of blood will serve to bolster the device’s blood flow stoppage. Biocompatibility is determined by several factors, and these include implant size, geometry, surface chemistry, sterility, and chemical composition. Polyurethane SMPs tested over the span of a year have demonstrated better biocompatibility than the current silk and polypropylene devices as measured by the patient’s inflammation response, and therefore show great promise for use [8]. Polyurethane SMPs also possess much lower densities than shape memory alloys (SMAs) and cost 90% less than the average price of a comparable SMA [8]. Additionally, polyurethane SMPs have easily adjustable transition temperatures (the temperature at which the polymer switches from soft to hard phase), along with finely tunable mechanical properties [8].

There are numerous ways to manufacture polyurethane SMPs. Every process creates a final product known as a scaffold, which is a porous structure. The pores of the structures used for embolization are miniscule and can only be seen with electron microscopes; however, embolization plugs also have larger pores in order to maximize their deployment volume. Each technique has its own distinct advantages; however, gas-blowing and electrospinning are the most common methods of manufacturing, which can be seen, along with other methods, in Figure 1 below [8].

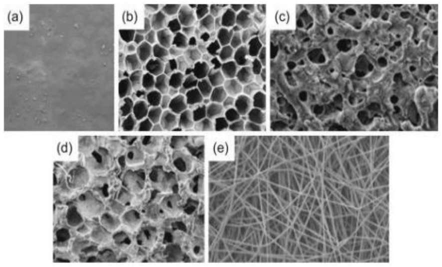

FIGURE 1 [8]
The figure above shows scanning electron microscope images of SMP scaffolds: a) solvent casting, b) gas blowing, c) emulsion templating, d) particle leaching, and e) electrospinning.

In the case of IMPEDE, the goal is to create a fine mesh that is effective for use in the impedance of blood flow. The polyurethane mesh creates conditions that are ideal for clotting in the blood vessels, and these include low blood shear rates (the change in velocity of the blood) and the creation of recirculation zones, in which the blood flows around in loops [8].

Another distinct advantage of polyurethane SMPs is their ability to expand considerably from an initial crimped size, which is necessary for catheter insertion. Polyurethane SMPs can grow to one hundred times their insertion size, which is substantially larger than competing materials. These devices can also be crimped to a radius of less than half a millimeter, allowing their insertion to be minimally invasive [8]. In other words, polyurethane enables less hinderance for the patient upon insertion via a catheter and more effective stoppage due to their higher volume change ratio compared to other materials in embolization applications.

In conclusion, polyurethane memory polymers are made from readily available plastic that has numerous mechanical and thermodynamic properties that allow for dynamic use in embolization and other applications. Additionally, polyurethane SMPs demonstrate incredibly high biocompatibility, higher than popular embolization materials. Polyurethane production, despite it being a plastic, is also sustainable and is projected to soon only use recycled polyurethane. Using this material will also allow superior embolization procedures due to its less invasive deployment, larger volume after activation, and its ability to encourage blood clotting.

Design of the Platinum-Iridium Coil

The other crucial component to the design of the IMPEDE embolization plug is the coil that is attached to the SMP plug. The primary components of the larger coil are a 90-10% platinum-iridium coil threaded around a super-elastic nitinol wire [8]. Platinum-iridium alloys, like the one used in this device, are known for their biocompatibility and resistance to corrosion. These features make the alloy ideal for medical devices, particularly in the case of permanent medical devices like embolization plugs. This high biocompatibility is a result of platinum metal properties, which mainly lie in the metal's low corrosion. Platinum is also a radiopaque material, meaning that it appears on x-ray [15]. This feature is particularly desirable for embolization plugs that rely on x-rays to ensure proper location of the device within the body during surgery and goes hand in hand with the biocompatibility of polyurethane shape memory polymers.

The other component of the coil, super-elastic nitinol wire, is also a crucial material in the manufacturing of this device. Nitinol is a shape memory material comprised of nickel and titanium. In a similar fashion to polyurethane SMPs, the polymer reverses back to its initial shape when exposed to heat. This heat activation can be altered depending on the ratio of metals in the alloy and the amount of heat applied when the material is "locked" into its shape. The heat activation is also accurate within a few degrees Celsius of the desired temperature [16]. This accuracy is ideal to account for the slight variations in body temperature that naturally occur in humans, which is vital for medical applications.

The setting of the permanent shape in the IMPEDE embolization coil follows a similar process to many shape memory polymers. The threaded platinum-titanium wire and nitinol wire are wound around a mandrel, which allows for the device to be shaped into its permanent coil shape, as depicted in Figure 2 below.

FIGURE 2 [9]
The figure above shows the IMPEDE embolization plug in its crimped form. The coil can be seen wound at the top all the way through the length of the device.

The coil and mandrel are then heated to 550 °C. After 15 minutes, the coil and mandrel are removed from the heat source and are immediately transferred to a water bath, which sets the final shape of the coil [8]. This special process allows the shape of the coil to easily activate and secure itself when inserted into the patient.

Analysis of Embolization Plug Assembly and Insertion

The main difference between the IMPEDE embolization plug and other embolization devices currently on the market is design. Typically, embolization plugs are used in larger arteries, while coils are used in smaller blood vessels [5]. These allocations are simply due to the size restrictions of the products, since coils are often available in sizes as small as two millimeters in diameter, while embolization plugs are not available in sizes smaller than four millimeters in diameter. IMPEDE combines the coil and plug embolization devices into one, as displayed in Figure 3 below. The coil helps anchor the device in the blood vessel immediately after insertion, while the polyurethane shape memory polymer plug is attached along the length of the device [8].

FIGURE 3 [9]
The IMPEDE embolization plug in its expanded form.

Like most embolization devices, a catheter is necessary for the insertion of the IMPEDE embolization plug. The catheter is first inserted into the patient and moved to the targeted blood vessel for occlusion. Then, the IMPEDE plug is pushed through the catheter coil-first. The coil exits the catheter, where exposure to internal body temperature of the patient restores the permanent shape. Once the coil is in place, the catheter is retracted to allow the SMP foam to expand over the course of a few minutes [9]. The entire surgery is monitored using x-ray scanning, and the IMPEDE device uses a radiopaque marker that can be seen via x-ray to ensure proper placement. Overall, the surgery is minimally invasive, and most patients leave the hospital within one to two days, depending on the placement and condition being treated with the IMPEDE device [1].

While the overall procedure is standard for embolization devices, the IMPEDE embolization plug provides greater ease for doctors performing the surgery with its advanced materials and structure. One advantage is the ability of these SMPs to react to the environment around the insertion point, which allows for complete occlusion in about four to five minutes, according to the Landsman Dissertation from Texas A&M University [8]. These times are as fast or faster than other embolization devices currently available. On top of the efficient speed of occlusion, Landsman also concludes that the chance of device complication, such as device migration, is significantly reduced due to the efficient occlusion with the polyurethane SMP in comparison to a popular embolization coil on the market [8]. This data is significant because it demonstrates that just one IMPEDE embolization plug will complete the occlusion, whereas it is currently common to have multiple coils or plugs inserted for complete occlusion. By reducing the number of plugs necessary to obtain complete occlusion, the surgery time is reduced, and likely the cost of the procedure for the patient.

POSSIBLE APPLICATIONS OF THE IMPEDE EMBOLIZTION PLUG IN CATHETER EMBOLIZATIONS

IMPEDE as a Treatment for Aneurysms

Aneurysms treated with embolization devices are usually treated with coils. The issue with inserting these coils is that they may migrate back into a large parent blood vessel, causing unintentional blockage, and serious medical complications for the patient. Another possibility is device compaction, which can also cause the same medical complications [8]. With the development of IMPEDE, which shows reduced tendency for device migration, the patient is less likely to experience these dangerous complications. However, more research on the IMPEDE embolization plug is necessary to understand the full application of its design to specific aneurysms. Based on the research within this paper, certain aneurysms, such as wide neck aneurysms that are ballooned out from the normal blood vessel, may not be treatable with the two-part plug and coil design of the IMPEDE embolization device. These wide neck aneurysms are depicted in Figure 4 below, which shows that the aneurysm usually needs to be filled completely, not just plugged off. Therefore, while the IMPEDE embolization plug may aid in occluding aneurysms of smaller diameters, there may be very little application of this specific device to large, ballooned aneurysms.

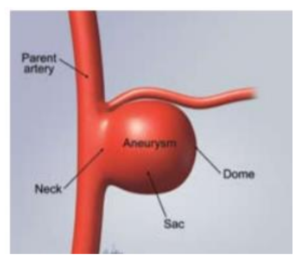

FIGURE 4 [17]
Ballooned, wide neck aneurysm in a blood vessel.

IMPEDE in Managing Abdominal and Pelvic Trauma

Trauma is defined as any sudden-onset and severe physical injury requiring immediate medical care. Patients suffering from traumatic injuries must be treated quickly and effectively at an appropriate trauma center for the best chance of survival. Trauma is the leading cause of childhood mortality and a major cause of mortality in adults under 45 [18] [19]. This is due in no small part to uncontrollable bleeding, which causes 30% to 40% of trauma-related mortality [19]. In addition, most preventable trauma deaths result from untreated hemorrhaging [19]. Thus, effective management of bleeding in trauma cases is vital to the survival of the patient.

When surgical intervention is not possible or preferable, radiological intervention plays a key role in the treatment of blunt organ trauma. Blunt trauma accounts for more injuries than penetrating trauma, with the spleen and liver being the most common organs to be affected [20]. Most liver injuries are managed with nonoperative measures. In cases of blunt liver trauma, the use of embolization for urgent hemostasis improves treatment success rates [19]. Spleen injuries were traditionally treated via the removal of the spleen, although modern treatments frequently involve splenic artery embolization [20]. Embolization is generally implemented with patients that are hemodynamically stable, although a study by Lin et al., researchers from the department of radiology of the China Medical University Hospital, suggests that transcatheter embolization in patients with blunt splenic injury is safe and effective even in hemodynamically unstable patients [21].

Abdominal trauma is the most frequent cause of unrecognized fatal injury in pediatric patients [22]. The most common form of pediatric abdominal trauma is blunt trauma and is managed without operation [22]. In 2016, Sweed et al., doctors and researchers of interventional radiology and pediatric surgery, studied the use and safety of embolization regarding blunt and penetrating abdominal trauma in children [18]. After examining case studies, they proposed emergency arterial embolization as a further treatment in children with ongoing bleeding following blunt abdominal trauma [18]. With this information, it can be concluded that the management of pediatric abdominal trauma would change with the introduction of improved embolization techniques into common practice.

In conclusion, the use of embolization in abdominal trauma is varied and frequent. Preferred methods of embolization change depending on the case and severity of the injury in question, and SMP embolization plugs will not be a perfect treatment for all trauma injuries. However, it is important to recognize the potential benefits of further implementation of SMP embolization plugs such as the IMPEDE embolization plug. In trauma situations, time is vital to the survival of the patient, and the quicker that bleeding can be stopped, the better. With a faster time to occlusion, the IMPEDE embolization plug would help minimize blood loss and help keep patients hemodynamically stable. In addition, with its increased biocompatibility, a stronger and more stable occlusion will form, decreasing the risk of delayed bleeding.

IMPEDE as a Preoperative Measure in the Treatment of Spinal Tumors

Cancers are a very broad group of diseases; however, all cancers are characterized by sudden and abnormal growth of tissue. Without intervention, tumors can grow large enough to spread to different parts of the body, a process known as metastasizing. A common place for tumors to metastasize is the spine due to the high volume of blood that passes through it. These tumors on the spine can very rapidly become life threatening, and nearly always require some form of surgery. Due to the large volume of blood in and around the spinal cord, surgeries that are in or near the spinal cord are limited in scope and operation time by blood loss in a patient. As a result, embolization is currently used to improve the process of spinal tumor removal by controlling the flow of blood in the spine. When spinal metastasis is treated with surgery, doctors will prepare for a surgery with processes known as decompression and stabilization. Spinal decompression therapy is a process by which a spine is stretched, taking the pressure off the spinal disks. Stabilization is a process by which the spine is immobilized [23]. Embolization allows these processes and the surgery itself to occur in a much smaller time frame, as embolization lessens the amount of blood circulating in a given operating zone.

Current devices used such as balloon coils are effective; however, the IMPEDE embolization plug has the potential to improve the capability of embolization therapies in the context of spinal tumor surgeries. Spinal operations must be performed in very small timeframes and IMPEDE would allow doctors to extend this timeframe as well as reducing blood loss in a patient, both of which can make a very significant difference. The IMPEDE embolization plug would have a far lower chance of migration, which is an even larger concern in the spinal region, and would also be more effective than current embolization technologies at blood stoppage [24].

IMPLICATIONS OF SHAPE MEMORY POLYMER EMBOLIZATION PLUGS IN WIDESPREAD PRACTICE

To ensure the success of the IMPEDE embolization plug on the market, it must satisfy the needs of society now and in the future. To meet this requirement, the product must be able to improve overall quality of life for medical patients, as well as be physically safe in terms of the production and use. Quality of life includes cost benefit to the consumer, who is seeking a permanent solution to their medical ailment. Safety is also crucial, both in terms of environmental factors during production of the device, as well as in clinical application. Without taking these factors into consideration, the IMPEDE embolization plug is unlikely to see long term success.

IMPEDE Plugs in Practical Clinical Application

To ensure the safety of the patient, medical devices must fulfill certain requirements. In the following subsection, two aspects of medical devices, their sterility and legality, are examined with respect to the IMPEDE embolization plug. While these are not the only practical qualities a medical device must have to be successful, if a device cannot be sterilized, or is not FDA approved, it cannot be commercially sold or used, and as such, would be an unsustainable product.

Before any instruments can be used in operation, they must first undergo disinfection and sterilization to kill any microbes and prevent spread of infection. Common methods of sterilization involve techniques such as exposure to dry heat, treatment with chemical antiseptics, and use of an autoclave [25]. In a hospital environment, autoclaving (applying steam and pressure over a period of time) is the primary form of sterilization [25]. As mentioned previously, SMPs are tailored to a specific transition temperature; as such, exposure to high heat and humidity can reduce the effectiveness of the SMP. In 2017, Muschalek et al., researchers at Texas A&M University's biomedical engineering department, studied the effects of alternate methods of sterilization on SMP embolic foam devices [26]. In comparing the effect of nontraditional ethylene oxide gas sterilization and electron beam irradiation on SMPs, they concluded that electron beam irradiation showed the most promise for application with SMP medical devices [26]. While further research needs to be done to determine the best method of sterilization, the work done by Muschalek et al. is important in order to recognize that SMP devices can be integrated into a sterile operating environment.

Additionally, medical devices in the U.S. must be FDA approved before being sold commercially. As according to section 510(k) of the Food, Drug and Cosmetic Act, companies who intend to distribute a device for sale must submit a 510(k) for approval [27]. The purpose of this submission is to ensure that the device to be marketed is at least as safe and effective as a current comparable device [27]. In June 2018, Shape Memory Medical received clearance for their 501(k) for the 5mm, 7mm, and 10mm maximum-diameter IMPEDE embolization plugs [28]. As such, it is now legal for IMPEDE embolization plugs to be sold commercially and are deemed as safe to use in a clinical environment.

Cost Benefit to the Consumer

In most cases, embolization is considered a last-resort procedure to be used in the case of no other options being applicable. Often, at the time of implementation, the patient has already spent thousands of dollars on procedures. As such, cutting down on the expenses of embolization procedures would be beneficial to the general public. SMP plugs like IMPEDE have potential advantages in this regard over embolic devices currently in use. In modern practice, multiple embolization devices, such as coils, are commonly used in conjunction to ensure complete occlusion [29]. This results in more time spent in operation and the potential to require multiple operations, which creates greater procedural costs. Because of its SMP material and scaffold structure, the IMPEDE embolization plug minimizes the time to occlusion and promotes mature tissue growth [8]. Faster occlusion results in shorter operation time and quicker stabilization of formed clots, which has been shown to create superior clinical outcomes [8]. In addition, the coil and plug shape of IMPEDE embolization plug may result in fewer devices needed for complete occlusion. All these features are appealing to the consumer, in this case the medical patient, who is seeking a financially minimal, yet effective, solution to their medical concern after possibly having many prior procedures. A procedure, like embolization, would likely have a significant increase in quality of life for the patient, especially if it provides permanent healing for the patient. In conclusion, greater implementation of the IMPEDE embolization plug and similar SMP embolization plugs over other forms of embolization could lead to a reduction in procedural costs for the patient and overall improvement to quality of life.

Long-Term Feasibility of IMPEDE's Design

IMPEDE's design is centered around the polyurethane shape memory polymer that provide complete occlusion of the blood vessel rapidly. One major concern in relation to the mass production of this medical device is the production of polyurethane. Traditionally, polyurethane is derived from crude oil, which is neither a renewable source, nor carbon-emission friendly. Due to the recent concerns over oil prices and climate change, research into creating these synthetic polymers from renewable resources has become crucial. Scientists are currently working on using plant oils to produce polyurethane polymers; however, it is currently unclear how well this process would work on a large scale. Polyols, which are the main building block of polyurethane, are typically produced form glycerin in plants. The most promising source of glycerin is currently plant oils, notably castor oil due to its low cost. Seeds are primarily used because plant oils are unsaturated fats, and the higher freezing points of saturated fats are disadvantageous, as it can occasionally solidify in solution [30].

Castor oil is a very valuable and highly renewable resource, making it the most promising renewable source of polyurethane raw materials. Castor beans are one of the world's oldest cultivated crops, and already have an extensive agricultural and industrial infrastructure in place [31]. Most people know castor beans by a toxic protein present in them, known as ricin. This toxic protein is a deadly poison that has been used in executions of prominent individuals and has no known antidote. There is a considerable amount of research going into increasing the oil yield of castor beans, which is currently on the order of 30-50% [31]. Castor-derived polyurethane has recently entered the market, and some large-scale producers are switching to its use, for example Foamex, Recticel, Carpenter, and Sanko Espuma [30]. However, the current processes used to develop these renewable polyurethanes may lead to a compromise in product performance, which threatens it success in replacing petroleum-based polyurethane currently on the market. Despite this, the high oil yield, existing infrastructure, and the viability of castor oil, currently make it the most promising renewable source for polyurethane production.

Another viable, although significantly less developed, option for renewable polyurethane are triglycerides from algae. Researchers are examining this possibility to avoid using food-stock for the development of polyurethane. The issue with using algae over other options like castor oil is the amount of saturated fat in the triglyceride. Saturated fat leads to solidification at higher temperatures, which makes the process of synthesizing polyurethane difficult. Also, little research has been done on how a polyurethane produced from algae triglycerides would perform, but since other plant-based oils tend to hinder performance in comparison to petroleum-based polyurethane, it is possible that synthesis of algae-based polyurethanes would encounter the same problem [30]. However, if these issues can be resolved as new syntheses are researched, algae-based polyurethanes offer an environmentally sound solution to the issues surrounding current polyurethane production.

SUMMARY OF TECHNOLOGY

Embolization devices have become a staple part of the medical field for many different conditions. The IMPEDE embolization plug attempts to maximize the efficiency and effectiveness of this crucial procedure. These advancements can be seen directly with the use of polyurethane SMPs, which improve the chances of complete occlusion with a singular plug. Another significant advancement is the combination of plug and coil technology. This design component aids in reducing the chances of device migration, a complication that can be deadly. Additionally, the design allows for reduced procedure times, since multiple embolization devices are not necessary and the time to complete occlusion of the blood vessel is significantly less than similar products on the market.

By improving embolization procedures, this device improves the treatment of a multitude of medical conditions. Many of these conditions are potentially deadly, such as aneurysms, blunt trauma, and tumors. For aneurysms, the IMPEDE embolization plug makes treating otherwise inoperable aneurysms much more efficient and lowers the risk of regaining blood flow to that region, which could result in rupturing of the aneurysm. In patients with uncontrolled bleeding due to blunt trauma, this embolization plug helps quickly resolve an emergency situation. As for spinal cancer patients, this device may become more common in relieving their pain.

Overall, the IMPEDE embolization plug shows significant promise in becoming a successful product on the market. Since the entire concept and design is focused, and largely proven, to ease the complications that come along with common embolization procedures, it would not be a surprise to find it in high demand over the next few years as more studies are conducted about the device's benefits and mass manufacturing begins with the new FDA approval. For many current and future medical patients, the IMPEDE embolization plug may be the key to efficient and effective relief.

SOURCES

[1] "Catheter Embolization." RadiologyInfo. https://www.radiologyinfo.org/en/info.cfm?pg=cathembol#common-uses
[2] "Aneurysms." MedlinePlus. 12.18.2018. Accessed 03.08.2019. https://medlineplus.gov/aneurysms.html
[3] "Embolization." Jefferson Health. Accessed 02.07.2019. https://www.ariahealth.org/programs-and-services/radiology/interventional-radiology/embolization
[4] A. Awad et al. "The Efficacy and Risks of Preoperative Embolization of Spinal Tumors." US National Library of Medicine. 08.14.2015. Accessed 02.07.2019. https://www.ncbi.nlm.nih.gov/pubmed/26276077
[5] S. Ramakrishnan. "Vascular Plugs – A Key Companion to Interventionists – 'Just Plug it'." Indian Heart Journal. 07.26.2015. Accessed 02.19.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4561770/#
[6] K. Lee et al. "Rescue Therapy of Inadvertent Coil Migration for Endovascular Treatment of Type II Endoleak." Vascular Specialist International. 03.31.2016. Accessed 03.07.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4816022/
[7] J. Reiley. "Novel Polymer Foam Device Receives FDA Clearance for Cardiovascular Treatments." Texas A&M University. 07.27.2018. Accessed 02.07.2019. https://engineering.tamu.edu/news/2018/07/novel-polymer-foam-device-receives-fda-clearance-for-cardiovascular-treatments.html
[8] T. Landsman. "Design and Verification of Shape Memory Polymer Embolization Devices for Peripheral Indications." Texas A&M University Libraries. 08.03.2016. Accessed 02.07.2019. https://oaktrust.library.tamu.edu/handle/1969.1/174257
[9] "IMPEDE." Shape Memory Medical, Inc. Accessed 02.19.2019. https://www.shapemem.com/impede
[10] M. Hager et al. "Shape Memory Polymers: Past, Present, and Future Developments." Progress in Polymer Science. 2015. Accessed 03.06.2019. https://www.sciencedirect.com/science/article/pii/S0079670015000489
[11] S. Thunkar and J. Hu. "Polyurethane: A Shape Memory Polymer (SMP)." IntechOpen. 07.27.2017. Accessed 03.06.2019. https://www.intechopen.com/books/aspects-of-polyurethanes/polyurethane-a-shape-memory-polymer-smp-
[12] "Composition and Production of Polyurethanes." ISOPA. Accessed 03.08.2019.
[13] "Closing the Loop: Polyurethane Recycling for a Sustainable Future." American Chemistry Council. Accessed 03.08.2019. https://incrediblepolyurethane.com/closing-the-loop-polyurethane-recycling-for-a-sustainable-future/

[14] A. Weems et al. "Shape Memory Polymers with Visible and Near-Infrared Imaging Modalities: Synthesis, Characterization and In Vitro Analysis" RSC Advances. 04.04.2017. Accessed 02.19.2019. https://pubs.rsc.org/en/Content/ArticleLanding/2017/RA/c6ra28165f#!divAbstract
[15] B. Woodward and A. Cowley. "The Sustainable Importance of Platinum in Biomedical Applications." UBM. 05.20.2011. Accessed 03.08.2019. https://www.mddionline.com/sustainable-importance-platinum-biomedical-applications
[16] "Nitinol - Shape Memory." Johnson Matthey Medical Components. Accessed 03.08.2019. http://jmmedical.com/nitinol/27072/Shape-Memory.html
[17] "Understanding Your Cerebral Aneurysm, Diagnosis and Treatment Options." Cordis. 10.2017. Accessed 03.08.2019. http://www.sw.org/misc/physicianresources/pdf/PtEd/PtEd_NeuroInterventionalSurgery_CordisAneurysmStentPatientBrochure.pdf
[18] Y. Sweed et al. "Angiographic Embolization in Pediatric Abdominal Trauma." Israel Medical Association. 11.2016. Accessed 03.08.2019. https://www.ncbi.nlm.nih.gov/pubmed/28466615
[19] J. Martin et al. "Evaluation and Management of Blunt Solid Organ Trauma." Techniques in Vascular and Interventional Radiology. 12.2017. Accessed 03.08.2019. https://www.ncbi.nlm.nih.gov/pubmed/29224654
[20] S. Gamanagatti et al. "Blunt Abdominal Trauma: Imaging and Intervention." Current Problems in Diagnostic Radiology. 2015. Accessed 03/08/2019. https://www.ncbi.nlm.nih.gov/pubmed/25801463
[21] W. Lin et al. "Emergent Transcatheter Arterial Embolization in Hemodynamically Unstable Patients with Blunt Splenic Injury." Academic Radiology. 02.2008. Accessed 03.08.2019. https://www.ncbi.nlm.nih.gov/pubmed/18206619
[22] T. Lynch et al. "Pediatric Abdominal Trauma." Current Pediatric Reviews. 2018. Accessed 03.08.2019. https://www.ncbi.nlm.nih.gov/pubmed/28814248
[23]"Spinal Stabilization." The Spine Health Institute. Accessed 03.04.2019. http://www.thespinehealthinstitute.com/services-and-specialties/treatments/spine-surgery/spinal-stabilization
[24] Mohammad H. Eslami. Professor of Surgery, MD, FACS, FACC. University of Pittsburgh Medical Center, Department of Surgery. Interview regarding embolization technologies. 02.28.2019.
[25] "The Surgical Domain: Creating the Environment." World Health Organization. Accessed 03.08.2019. https://www.who.int/surgery/Chapter2.pdf
[26] R. Muschalek et al. "Effects of Sterilization on Shape Memory Polymer Embolic Foam Devices." Journal of Medical Devices. 09.2017. Accessed 03.06.2019. https://www.ncbi.nlm.nih.gov/pubmed/29034056
[FDA] "Premarket Notification 510(k)." U.S. Food and Drug Administration. Accessed 03.27.2019. https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm
[28] "June 2018 510(k) Clearances." U.S. Food and Drug Administration. Accessed 03.27.2019. https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/ucm613084.htm
[29] M. Lubarsky et al. "Embolization Agents—Which One Should Be Used When? Part 1: Large-Vessel Embolization." Seminars in Interventional Radiology. 12.2009. Accessed 03.08.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3036462/
[30] D. Babb et al. "Polyurethanes from Renewable Resources." Advances in Polymer Science. 07.28.2011. Accessed 03.26.2019. https://link.springer.com/chapter/10.1007/12_2011_130
[31] V Patel et al. "Castor Oil: Properties, Uses, and Optimization of Processing Parameters in Commerical Production." Lipid Insights. 09.07.2016. Accessed 03.27.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5015816/

SOURCES CONSULTED

"Amplatzer Vascular Plug." Abbott. 01.02.2019. Accessed 03.08.2019. https://www.cardiovascular.abbott/us/en/hcp/resources/product/catalog/amplatzer-vascular-plug.html
"Autoclave Use." Princeton University. Accessed 03.08.2019. https://ehs.princeton.edu/book/export/html/380
"Memory Foam for Vascular Treatment Receives FDA Clearance." National Institute of Biomedical Imaging and Bioengineering. 07.19.2018. Accessed 02.19.2019. https://www.nibib.nih.gov/news-events/newsroom/memory-foam-vascular-treatment-receives-fda-clearance
A. Nathan et al. "Particulate Release from Nanoparticle-Loaded Shape Memory Polymer Foams." US National Library of Medicine. 01.16.2017. Accessed 02.07.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5253671/
"Nester Embolization Coil." Cook Medical. Accessed 03.08.2019. https://www.cookmedical.com/products/di_mwcen_webds/
M. Park et al. "Pipeline Embolization Device with or without Adjunctive Coil Embolization: Analysis of Complications from the IntrePED Registry." American Journal of Neuroradiology. 06.13.2016. Accessed 02.07.2019. http://www.ajnr.org/content/37/6/1127/tab-article-info
"Pulmonary Angiography and Embolization." UCLA. Accessed 02.19.2019. http://radiology.ucla.edu/pulmonary-angiographyand-embolization
"Traumatic Injury." University of Florida Health. Accessed 03.08.2019. https://ufhealth.org/traumatic-injury
P. Singhal et al. "Low Density Biodegradable Shape Memory Polyurethane Foams for Embolic Biomedical Applications."

Acta Biomaterialia. 10.01.2013. Accessed 02.19.2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4075478/
Y. Wong et al. "Biomedical Applications of Shape-Memory Polymers: How Practically Useful are They?"
Science China Chemistry. 04.2014. Accessed 02.07.2019. https://www.researchgate.net/publication/271951648_Biomedical_applications_of_shape-memory_polymers_How_practically_useful_are_they

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