Development of Bioresorbable Self Expanding Implantable Neurovascular Device for Intracranial Aneurysm

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Abstract

An intracranial aneurysm can be treated with an implantable self-expanding ultrathin bioresorbable neurovascular device. The self-expanding bioresorbable neurovascular implanted device obstructs the blood flow to enter inside an aneurysm. The biocompatible and bioresorbable structure with a specified arrangement and reduced pore size helps to redirect blood flow to limit blood flow inside the aneurysm sac. A neurovascular implant with an elastomeric compound coating provides helps to gain sufficient radial strength, axial flexibility, and excellent self-expanding capabilities to the implant. The self-expandable bioresorbable scaffold retains structural integrity for about a year before resorbing over a two- to three-year time frame.

Key Words: Self-expanding Bioresorbable • Neurovascular • Aneurysm

Introduction

Aneurysms can be caused by several factors, including high blood pressure and atherosclerosis, trauma, genetics, and irregular blood flow [1-3]. A gigantic aneurysm can be more than 2.5 centimeters wide and include more than one artery. High blood pressure (hypertension) causes damage and the weakening of blood vessels over time. The formation of fatty plaques (atherosclerosis) causes a weakening of the blood vessel wall [4-5]. Inherited illnesses that cause blood vessel walls are observed weaker than usual. A gigantic aneurysm can be more than 2.5 centimeters wide and include more than one artery [6-8]. The anterior (carotid) circulation accounts for approximately 86.5% of all cerebral aneurysms. An infected arterial wall causes a mycotic aneurysm an abnormal bulge on the inside of an artery.

For more than 40 years, surgical clipping has been performed to treat cerebral aneurysms [9-11]. Aneurysm clipping and endovascular procedures like coiling, stent-assisted coiling, and flow diversion stents are two of the most common treatment choices. A ruptured cerebral aneurysm prognosis is determined by the aneurysm size and location, as well as the patient's age, health, and neurological status [12,13]. An aneurysm is ballooning at a weak spot in an artery wall. An aneurysm's walls can be thin enough to rupture [14,15]. Early bleeding from a burst brain aneurysm can kill some people [16]. A bad outcome, death, or lifelong impairment affects around two-thirds of patients. It is an endovascular procedure that entails introducing a microcatheter into the femoral artery [17]. Instead of introducing a device inside the aneurysm sac, as with coiling, a device is placed in the main blood vessel to divert the flow of blood away from the aneurysm [18,19].

In the present treatment, the use of a self-expanding nondegradable flow diverter has drawbacks such as corrosion and toxicity in the implant location. Present work also pertains to a process for producing a bioresorbable flow diverter for neurovascular implants that has high strength, great flexibility, and small pore size [20]. This is especially connected to employing poly lactide-based polymer material to fabricate tubular devices. The construction with smaller pore sizes helps to divert the blood flow and prevent blood from penetrating the aneurysm sac [21,22]. The treatment of intracranial aneurysms with devices involves covering the aneurysm neck to redirect blood flow. Mechanisms of the delayed rupture are not completely elucidated [23]. Very late thrombosis of the flow diverter is possible and long-term follow-up of treated patients is certainly required [24]. Another potential mechanism involves Intra aneurysm thrombosis created by flow diversion which can be associated with an inflammatory reaction.

Materials and Methods

The microporous bioresorbable device provides high strength, flexibility, and small pore size. The groups of several shape memory polymers such as Poly L-Lactide-Co-Caprolactone (PLC), Poly Caprolactone (PCL), Poly-dl -Lactic Acid (PDLLA), Poly Glycerol Sebacate (PGS), Poly L-lactide (PLLA), Poly Glycolic Acid (PGA), Poly L- lactide co-glycolic acid (PLGA) or mixture therefore used in the braiding process.

The extruded monofilament is annealed for allowing it to endure high tension braiding. The implant is coated with a bioresorbable elastomer. Heat treatment was carried out under vacuum conditions. An anti-thrombogenic, anti-inflammatory or any specific hormonal drug is coated on an elastomer coated flow diverter device. The microporous braided bioresorbable implant was made with 20 to 50-micron monofilaments and used 32 to 96 carrier braiding machines. Each implant has a porosity of about 12 pores/30 mm^2 to 30 pores/30 mm^2. Many filaments are braided together over a mandrel with braiding angles ranging from 30° to 200°.

The flow-diverter braiding angle is inversely proportional to the pore size. The polymer braided tube is fixed on a mandrel at both ends and then annealed to stabilize the braided structures. Mandrels are held in a controlled vacuum and annealed at a temperature ranging from 90°C to 130°C, for a period ranging from 14 hours to 20 hours. Braided mandrels are kept under a vacuum in a controlled environment of 500 mm Hg-800 mm Hg pressure. The terminal annealing, on the other hand, is carried out from 1 hour to 5 hours with a temperature of 90°C to 110°C.

To check the implant after placement over the aneurysm neck, the implant contains some radiopaque markers in the form of monofilament or any other tubular markers over the device. The monofilament markers are 2 to 6 in number with 20 microns to 50-micron diameter of monofilaments, with an additional elastomer coating thickness ranging from 1 micrometer to 10 micrometers. The tubular markers on the device contain a diameter between 35 microns to 45 microns, while the wall thickness is 2 microns-5 microns. Each tubular marker is 0.1 mm-0.2 mm long or as specified by the braided construction. A flow diverter with elastomeric coating was packed in vacuum desiccators for 8 hours-20 hours at room temperature and then cured between 70°C to 140°C. The radial strength of non-elastomers coated braided tubes ranged from 5 N to 20 N, but it can be improved up to 20 N to 30 N with the help of elastomeric coating (Figures 1-6).

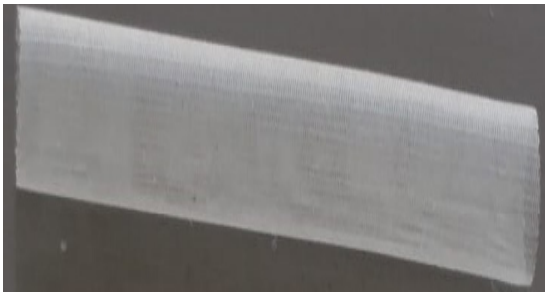


Figure 1. Bioresorbable braided tube.

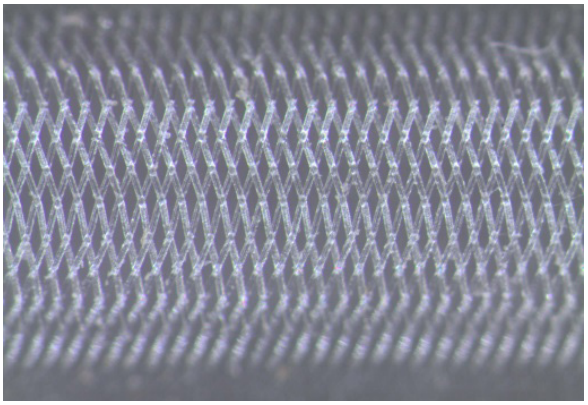


Figure 2. Braiding angle after braiding process.

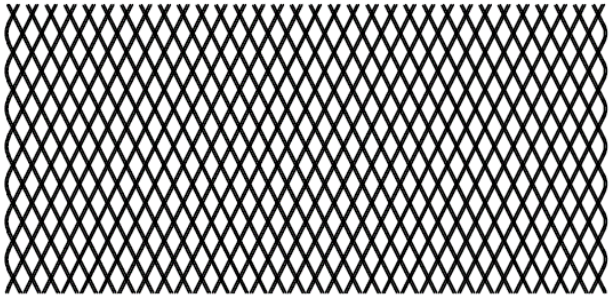


Figure 3. Open cell at both side of flow diverter.

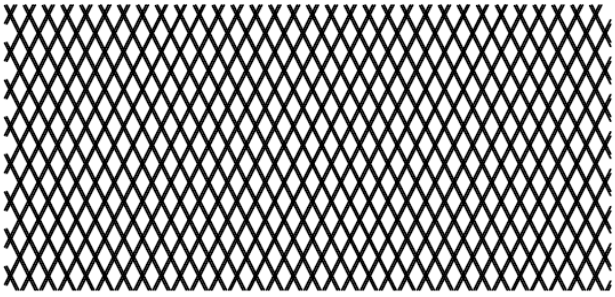


Figure 4. Closed cell at both side of flow diverter.

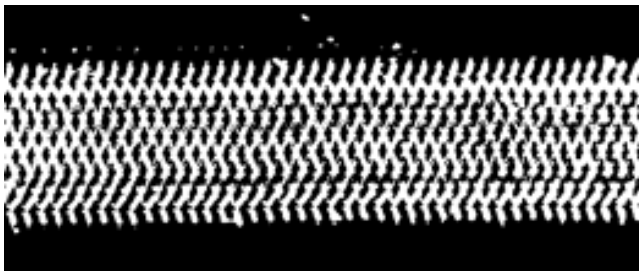


Figure 5. Braiding pattern after elastomer coating.

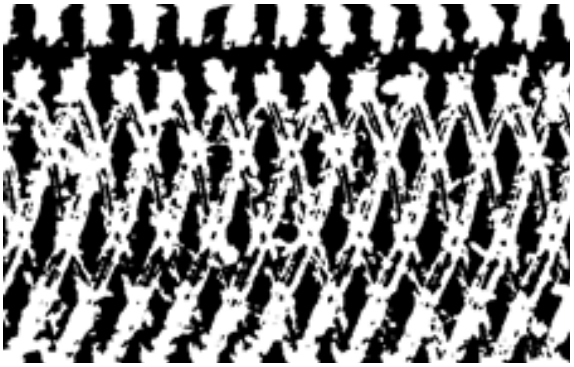


Figure 6. Coated flow diverter implant.

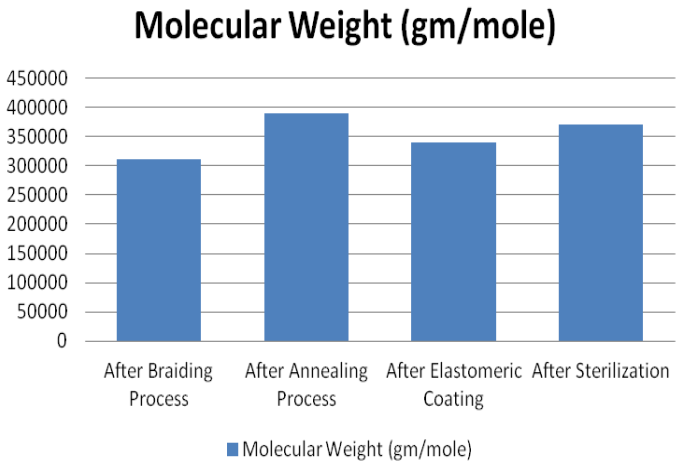
Result and Discussion

Intracranial aneurysm stenting is a procedure that involves redirecting and rerouting the arterial blood flow and creating a way to avoid rupture of the aneurysm to prevent blood from entering the brain. The microporous braided implant incorporates small pores of bioresorbable material with a particular braiding structure, resulting in sufficient radial strength, foreshortening, and other self-expanding stent properties [25-27]. The initial annealing procedure aids in the elimination of monomer and the relaxation of internal stress in braided monofilament. The flow-diverter braided mesh angle has a direct impact on its pore size and as a result, radial stiffness which is a critical characteristic determining the integrity and structure after being inserted into the body lumen. Annealing of the braid cross wire by lowering the melting point of the polymer increases the mechanical strength of the braided arrangement and allows for a comparable configuration following deployment in the artery lumen. The analytic evidence presented here clearly demonstrates that the microporous structure maintains its properties throughout the operation [28-29].

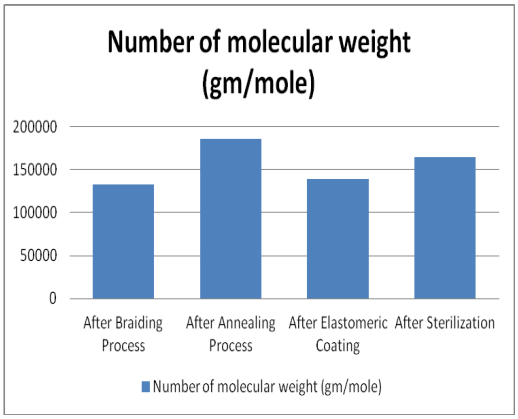
The following graphs show the properties of the polymer, such as molecular weight, number of molecular weights, Polydispersity Index (PDI), glass transition temperature, melting temperature, and percent crystallinity.

Graph 1 mentioned the Molecular weight of the material exposed after each process during the development of the implantable device. Molecular weight (gm/mole) is a measure of the sum of the atomic weight values of the atoms in a molecule. Molecular weight changes within the expected range as per requirement without affecting the final product when it is exposed to different process parameters - such as temperature and time according to the manufacturing process.

Graph 2 mentioned the number average molecular weight (Mn) of the material exposed after each process during the development of the implantable device. The number average molecular weight (Mn) measuring system requires counting the total number of molecules in a unit mass of polymer irrespective of their shape or size. The average molecular weight (Mn) changes within the expected range as per requirement



Graph 1. Molecular Weight (gm/mole).

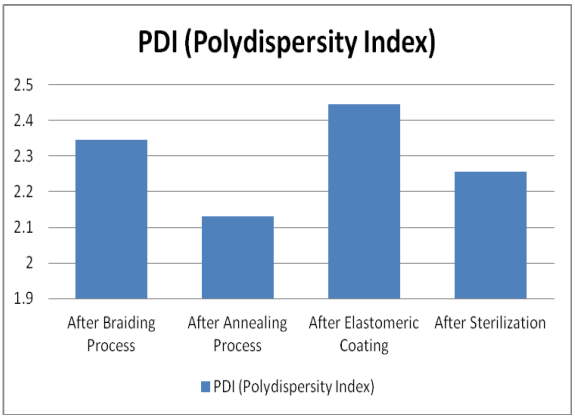


Graph 2. Num. of Molecular Weight (gm/mole).

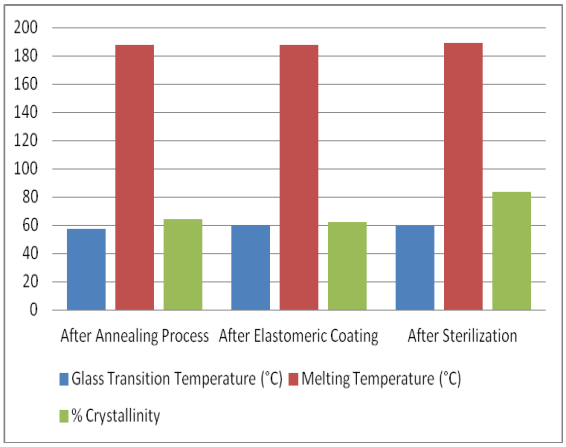
without affecting the final product when it is exposed to different process parameters, such as temperature and time according to the manufacturing process.

Graph 3 mentioned the PDI polydispersity index of the material exposed after each process during the development of the implantable device. PDI usually refers to the ratio of weight average molecular weight (Mw) to number average (Mn) sometimes also called molecular weight distribution. PDI is used to indicate the distribution of polymer chain molecular weights in a given polymer. PDI changes within the expected range as per requirement without affecting the final product when it is exposed to different process parameters - such as temperature and time according to the manufacturing process.

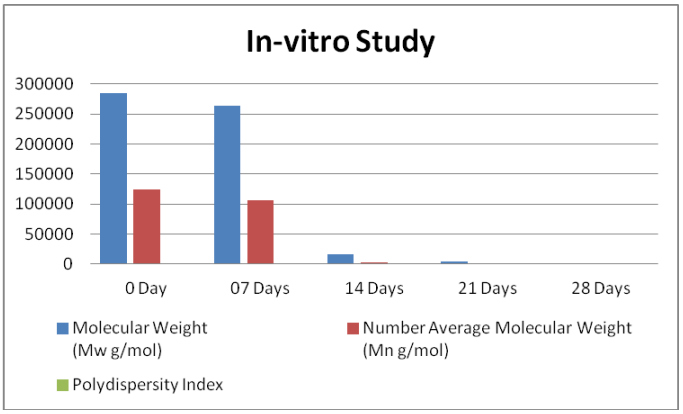
Graph 4 mentioned the glass transition temperature, melting temperature, and percentage of crystallinity of the material exposed after each process during the development of the implantable device. The glass transition temperature (Tg) is the temperature of amorphous polymers at which increased molecular mobility results in significant changes in the thermal properties. The melting temperature (Tm) is defined as the temperature at which the maximum absorbance change (dA/dt) occurs. Crystallinity can be defined as the degree of long-range structural order comprising a crystal lattice within a (solid) material. Any of the parameters changes within the expected range as per requirement without affecting the final product when it is exposed to different process parameters, such as temperature and time according to the manufacturing process.



Graph 3. Polydispersity Index (%).



Graph 4. Glass transition, melting temperature, and percentage crystallinity.



Graph 5. Accelerate *in-vitro* study.

The following Graph 5 shows, that when a flow diverter is subjected to accelerated degradation, the molecular weight and number of molecular weight was tested at different interval time which shows a decrease in the molecular weight and number of molecular weight when exposed at 70°C temperature under Phosphate buffer saline. Based on this degradation study, we can assume the polymer will degrade over a minimum 2 years.

Conclusion

The treatment of intracranial aneurysms with flow diverters seems to be highly efficacious. A bioresorbable ultrathin braided mesh structure with a smaller pore size redirects blood flow to prevent blood from flowing into an aneurysm. The safety of this treatment appears to be satisfactory, specifically in the context of treating a complex aneurysm. Flow diverters have been proposed for use in very small ruptured aneurysms that are untreatable using standard endovascular techniques. Bioresorbable materials are thought to be safer and more biocompatible. The biodegradable solution could meet the short-term needs of a sick patient while avoiding the long-term risks of dense metal mesh.

References

1. Arat, Anil., et al. "Bioresorbable vascular scaffolds in interventional neuroradiology." *Clin Neuroradiol*. 28.4 (2018): 585-592.
2. Grotenhuis, J. A., J. De Vries, and S. Tacl. "Angioscopy-guided placement of balloon-expandable stents in the treatment of experimental carotid aneurysms." *min-Minimally Invasive Neurosurg* 37.02 (1994): 56-60.
3. Henkes, H., and W. Weber. "The past, present and future of endovascular aneurysm treatment." *Clin neuroradiol* 25.2 (2015): 317-324.
4. Shapiro, M., et al. "Stent-supported aneurysm coiling: a literature survey of treatment and follow-up." *A J Neuroradiol.* 33.1 (2012): 159-163.
5. Sadasivan, Chander, et al. "Treatment of rabbit elastase-induced aneurysm models by flow diverters: development of quantifiable indexes of device performance using digital subtraction angiography." *IEEE Trans Med imaging* 28.7 (2009): 1117-1125.
6. Chen, Yanfei, et al. "Microstructured thin film nitinol for a neurovascular flow-diverter." *Sci Rep* 6.1 (2016): 1-10.
7. Howe, Connor, et al. "Stretchable, implantable, nanostructured flow-diverter system for quantification of intra-aneurysmal hemodynamics." *ACS nano* 12.8 (2018): 8706-8716.
8. Arrese, Ignacio, et al. "Flow-diverter devices for intracranial aneurysms: systematic review and meta-analysis." *Neurosurgery* 73.2 (2013): 193-200.
9. Merletti, Roberto, et al. "Advances in surface EMG: recent progress in detection and processing techniques." *Crit Rev Biomed Eng* 38.4 (2010).
10. Biondi, Alessandra, et al. "Neuroform stent-assisted coil embolization of wide-neck intracranial aneurysms: strategies in stent deployment and midterm follow-up." *Neurosurgery* 61.3 (2007): 460-469.
11. Indolfi, Ciro, Salvatore De Rosa, and Antonio Colombo. "Bioresorbable vascular scaffolds-basic concepts and clinical outcome." *Nat Rev Cardiol*. 13.12 (2016): 719-729.
12. Ferns, Sandra P., et al. "Coiling of intracranial aneurysms: a systematic review on initial occlusion and reopening and retreatment rates." *Stroke* 40.8 (2009): e523-e529.
13. Naggara, Olivier N., et al. "Endovascular treatment of intracranial unruptured aneurysms: systematic review and meta-analysis of the literature on safety and efficacy." *Radiol* 256.3 (2010): 887-897.
14. Sadasivan, Chander, et al. "An original flow diversion device for the

treatment of intracranial aneurysms: evaluation in the rabbit elastase-induced model." *Stroke* 40.3 (2009): 952-958.

15. Jamshidi, Mehdi, et al. "A novel self-expanding primarily bioabsorbable braided flow-diverting stent for aneurysms: initial safety results." *J. NeuroInterventional Surg.* 12.7 (2020): 700-705.
16. Lieber, Baruch B., Alfred P. Stancampiano, and Ajay K. Wakhloo. "Alteration of hemodynamics in aneurysm models by stenting: influence of stent porosity." *Ann Biomed Eng* 25.3 (1997): 460-469.
17. Pierot, Laurent. "Flow diverter stents in the treatment of intracranial aneurysms: Where are we?." *J of Neuroradiol* 38.1 (2011): 40-46.
18. Wakhloo, Ajay K., et al. "Self-expanding and balloon-expandable stents in the treatment of carotid aneurysms: an experimental study in a canine model." *Am J Neuroradiol.* 15.3 (1994): 493-502.
19. Wakhloo, A. K., et al. "Coated and non-coated stents for vessel reconstruction and treatment of aneurysms and AV-fistulas: an experimental study." *Neuroradiol* 34. (1992): 24.
20. Aenis, M., et al. "Modeling of flow in a straight stented and nonstented side wall aneurysm model." (1997): 206-212.
21. Giacomini, Leonardo, et al. "Neurovascular reconstruction with flow diverter stents for the treatment of 87 intracranial aneurysms: clinical results." *Interv Neuroradiol.* 21.3 (2015): 292-299.
22. Sadasivan, Chander, et al. "Angiographic assessment of the performance of flow divertors to treat cerebral aneurysms." *Conf Proc IEEE Eng Med Biol Soc. IEEE*, 2006.
23. Uurto, Ilkka, et al. "Drug-eluting biodegradable poly-D/L-lactic acid vascular stents: an experimental pilot study." *J Endovas Ther.* 12.3 (2005): 371-379.
24. Panchendrabose, Kapilan, Sandeep Muram, and Alim P. Mitha. "Promoting endothelialization of flow-diverting stents: a review." *J of NeuroInterventional Surg* 13.1 (2021): 86-90.
25. Kallmes, David F., et al. "A new endoluminal, flow-disrupting device for treatment of saccular aneurysms." *Stroke* 38.8 (2007): 2346-2352.
26. Pierot, Laurent, Laurent Spelle, and Fabien Vitry. "Immediate clinical outcome of patients harboring unruptured intracranial aneurysms treated by endovascular approach: results of the ATENA study." *Stroke* 39.9 (2008): 2497-2504.
27. Raymond, Jean, et al. "Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils." *Stroke* 34.6 (2003): 1398-1403.
28. De Vries, Joost, et al. "New generation of flow diverter (Surpass) for unruptured intracranial aneurysms: a prospective single-center study in 37 patients." *Stroke* 44.6 (2013): 1567-1577.
29. Seong, Jaehoon, Ajay K. Wakhloo, and Baruch B. Lieber. "*In vitro* evaluation of flow divertors in an elastase-induced saccular aneurysm model in rabbit." (2007): 863-872.

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