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Development of bioresorbable braided self expanding implantable neurovascular flow diverter for intracranial aneurysm

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SUMMARY

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

Keywords: Self expanding bioresorbable; Neurovascular; Aneurysm.

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INTRODUCTION

Aneurysms can be caused by a number of factors, including high blood pressure and atherosclerosis, trauma, genetics, and irregular blood flow. A gigantic aneurysm can be more than 2.5 centimetres wide and include more than one artery. High blood pressure (hypertension) causes damage and weakening of blood vessels over time [1]. The formation of fatty plaques (atherosclerosis) causes a weakening of the blood vessel wall. Inherited illnesses that cause blood vessel walls to be weaker than usual. A gigantic aneurysm can be more than 2.5 centimetres wide and include more than one artery [2]. The anterior (carotid) circulation accounts for approximately 86.5 percent of all cerebral Aneurysms. An infected arterial wall causes a mycotic aneurysism - an abnormal bulge on the inside of an artery. For more than 40 years, surgical clipping has been performed to treat cerebral aneurysms. Aneurysm clipping and endovascular procedures like as 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 age, health, and neurological status [3,4]. An aneurysm is a ballooning at a weak spot in an artery wall. An aneurysm walls can be thin enough to rupture. Early bleeding from a burst brain aneurysm can kill some people. A bad outcome, death or lifelong impairment affects around two third of patients. It is an endovascular procedure that entails introducing a micro catheter into the femoral artery. Instead of introducing a device inside the aneurysm sac, as with coiling, a device is placed in the main blood vessel to divert flow of blood away from the aneurysm. In present treatment, the use of a self-expanding non degradable 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 a small pore size [5]. This is more especially connected to employing PLLA or PLGA material to fabricate tubular braid devices. The braided construction with smaller pore sizes helps to divert the blood flow and prevent blood from penetrating the aneurysm sac. The treatment of intracranial aneurysms with devices by covering the aneurysm neck. Mechanisms of the delayed rupture are actually not completely elucidated. Very late thrombosis of the flow diverter is possible and long term follow up of treated patients is certainly required. Combinations of the bioresorbable filaments can also be used to make braided tubes. Another potential mechanism involves intra aneurysm thrombosis created by flow diversion which can be associated with an inflammatory reaction.

MATERIALS AND METHODS

The micro porous bioresorbable braided tube with open and closed angle provides high strength, flexibility and a 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 bioresorbable elastomer [6]. Heat treatment was carried out under vacuum conditions. An anti-thrombogenic, anti-inflammatory, or any specific hormonal drug is coated on an elastomers coated flow diverter device. The microporous braided bioresorbable implant was made with 20-50 micron monofilaments and a 32-96 carrier braiding machine. Each implant has a porosity of about 24 to 120. Many filaments are braided together over a mandrel with braiding angles ranging from 30°C to 200°C. The pores formed by the braiding pattern span from 12 to 30 pores per millimeter [7-9]. The flow diverter braiding angle is inversely proportional to the pore size. PET mandrels are held in a controlled vacuum and annealed at a temperature ranging from 90°C to 130°C, for a period of time ranging from 14 to 20 hours. The polymer braided tube is fixed on a mandrel at both ends and then annealed to stabilize the braided structures. Braided mandrels are kept under vacuum in a controlled environment of 500-800 mm Hg pressure. Annealing is a process in which the body is held at a temperature between 90°C to 130°C for 12 to 20 hours. The terminal annealing, on the other hand, is carried out from 1 to 5 hours with a temperature of 90°C to 110°C. The other forty six monofilaments are employed with the two 20-50 micron platinum tungsten monofilaments are used for each marker, with an elastomer coating thickness ranging from 1 to 10 m. The internal diameter of the marker is 35-45 microns, while the wall thickness is 2-5 microns [10]. Each marker is 0.1-0.2 mm long or as specified by the braided construction. A flow diverter with elastomeric coating was packed in vacuum desiccators for 8-20 hours at room temperature and then cured between 70°C to 140°C. The radial strength of non-elastomers coated braided tube ranged from 5 to 20 N, but increased from 20 to 30 N, when it was braided with the coating. The distance between the braided flow diverter and the spray gun should be kept between 2 to 4 cm and rotation should be between 20 to 30 rpm, which is important in achieving a smooth and uniform coating **(Fig. 1-6).**

RESULTS AND DISCUSSION

Intracranial aneurysm stenting is a procedure that involves redirecting and rerouting the arterial blood flow and

Fig. 1. Bioresorbable braided tube.

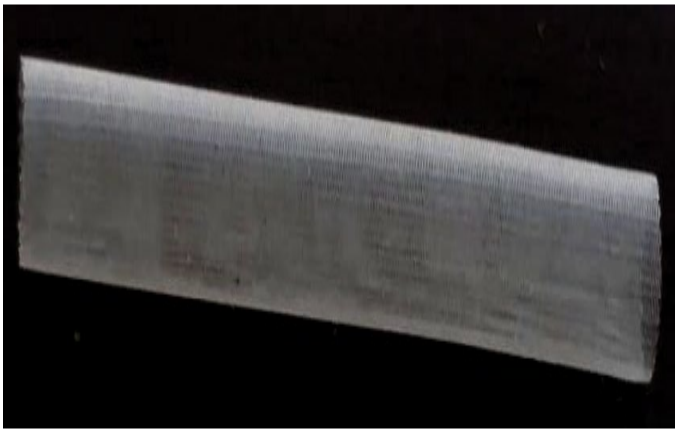


Fig. 2. Braiding angle after braiding process.

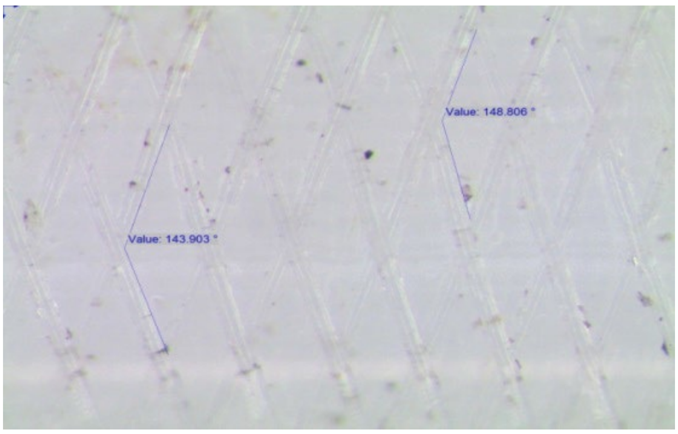


Fig. 3. Open cell at both side of flow diverter.

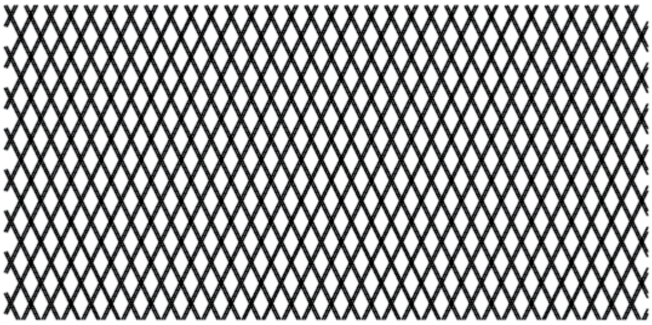


Fig. 4. Closed cell at both side of flow diverter.

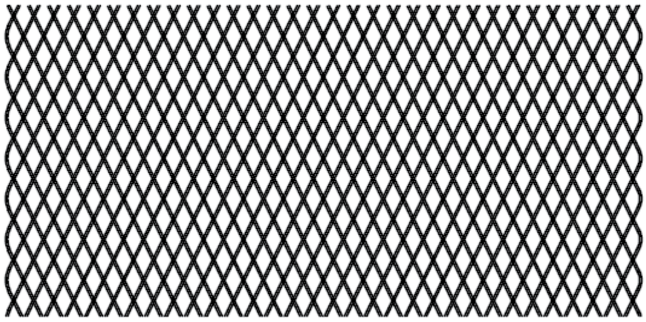


Fig. 5. Braiding pattern after elastomer coating.

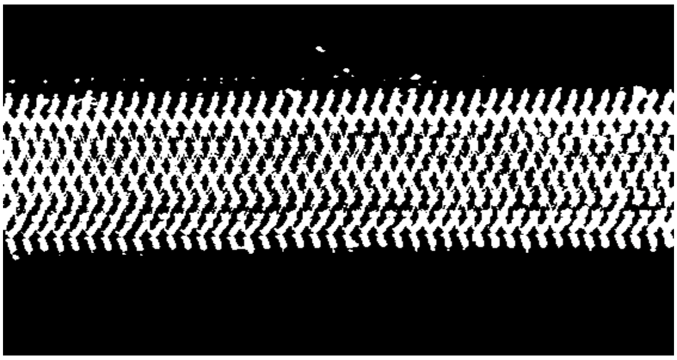
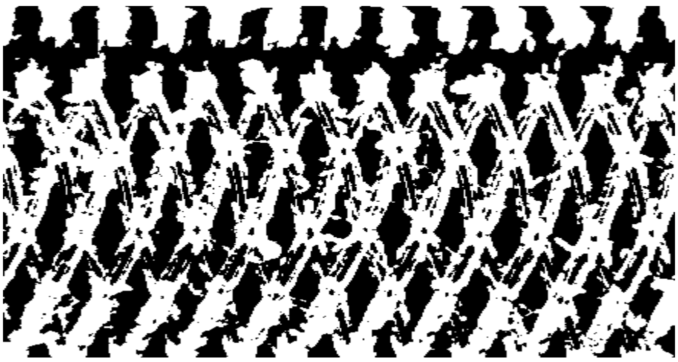


Fig. 6. Coated flow diverter implant.



creating a way to avoid rupture of aneurysm to prevent blood from entering the brain [11,12]. The microporous braided implant incorporates small pores of bioresorbable material with particular braiding structure, resulting in sufficient radial strength, foreshortening, and other self-expanding stent properties. The initial annealing procedure aids in the elimination of monomer and the relaxation of internal stress in braided monofilament [13]. 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 micro porous structure maintains its properties throughout the operation [14].

Sample results

Material characteristics of samples before and after monofilament annealing are given in following **Chart. 1-4**.

The material properties of BRS flow diverter without coating shown in below **Tab. 1**.

The material properties of BRS flow diverter was coated with elastomeric coating, which given the following results **(Tab. 2).**

Chart. 1. Molecular weight (gm/mole) and Num. of molecular weight (gm/mole).

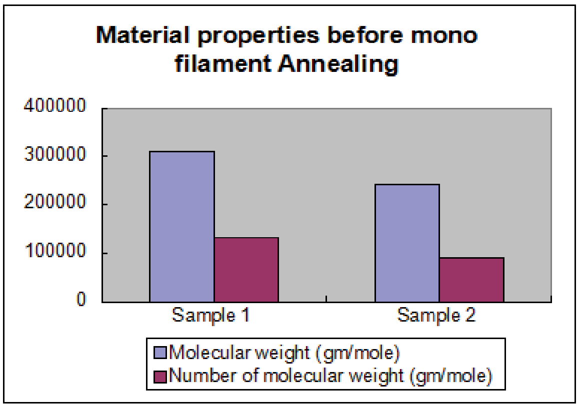


Chart. 2. Poly diversity Index (%) (Material properties before mono-filament annealing).

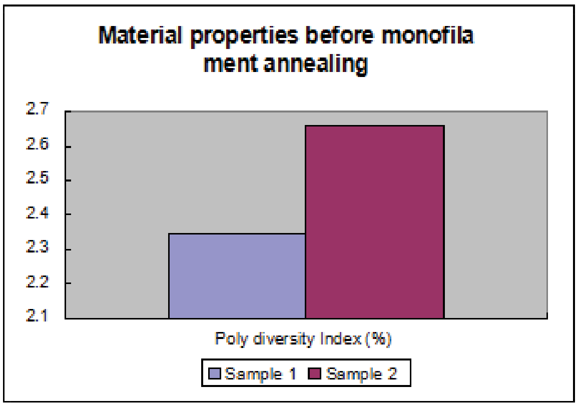


Chart. 3. Molecular weight (gm/mole) and Num. of molecular weight (gm/mole).

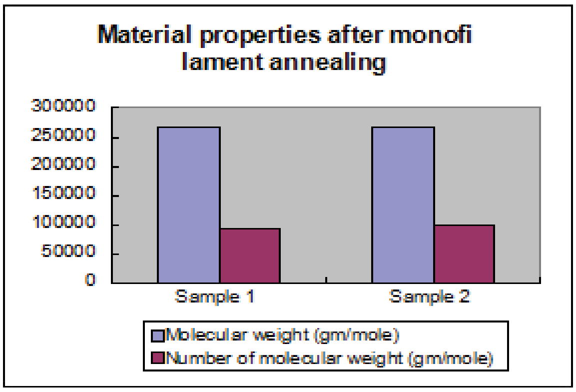
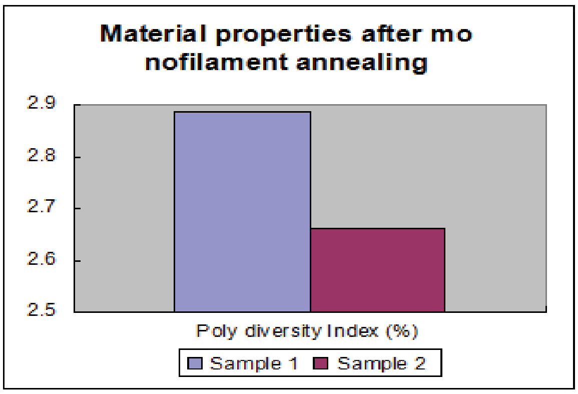


Chart. 4. Poly diversity index (%) (Material properties after mono-filament annealing).



Process sample results

The properties of polymer, such as molecular weight, number of molecular weights, polydispersity index (PDI), glass transition temperature, melting temperature, and percent crystallinity, do not change when the polymer is exposed to different process parameters - such as temperature and time shows in the **Chart. 5-8**.

Degradation process result

The following **Charts. 9-11** shows, when a flow diverter is subjected to accelerated degradation, the parameters of the polymer, such as glass transition temperature, melting temperature, and % crystallinity, steadily decrease with time.

Tab. 1. Material properties after annealing of BRS flow diverter (without coating).

Material Properties after Annealing of BRS Flow Diverter (without coating)		
Sample Details	Sample-1	Sample-2
Molecular weight (gm/mole)	377678	402250
Number of molecular weight (gm/mole)	160340	211278
PDI (Polydispersity Index)	2.355	1.904
Glass transition temperature (°C)	57.26	53.13
Melting temperature (°C)	187.36	187.46
% Crystallinity	64.30	68.50
Radial strength of BRS flow diverter	9.25 N, 9.17 N, 10.96 N	

Tab. 2. Material properties after elastomeric coating of BRS flow diverter.

Material Properties after Elastomeric Coating of BRS Flow Diverter		
Sample Details	Sample-1	Sample-2
Molecular weight (gm/mole)	345856	335633
Number of molecular weight (gm/mole)	145567	133464
PDI (Polydispersity Index)	2.376	2.515
Glass transition temperature (°C)	60.19	50.71
Melting temperature (°C)	187.35	187.16
% Crystallinity	62.30	63.40
Radial strength of BRS flow diverter	84.73 N, 87.90 N, 67.76 N	

Chart. 5. Molecular weight (gm/mole).

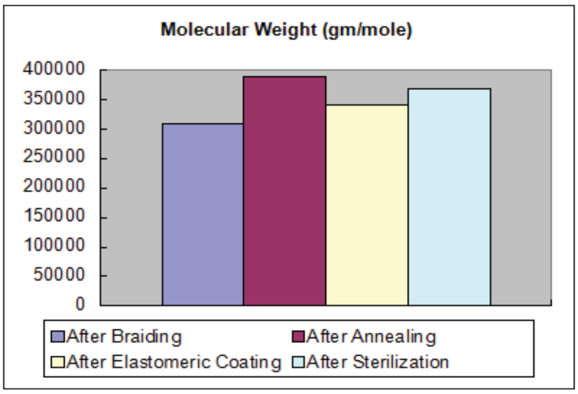


Chart. 6. Num. of molecular weight (gm/mole).

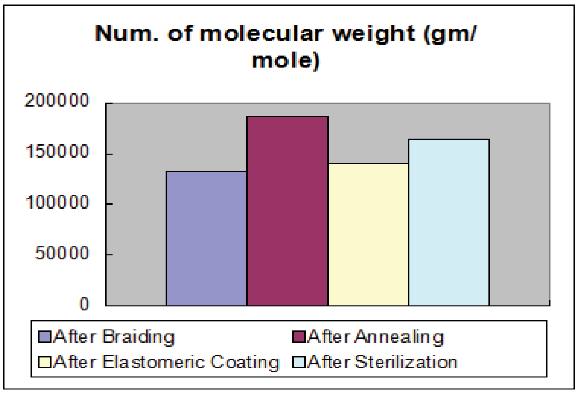


Chart. 7. Polydispersity index (%).

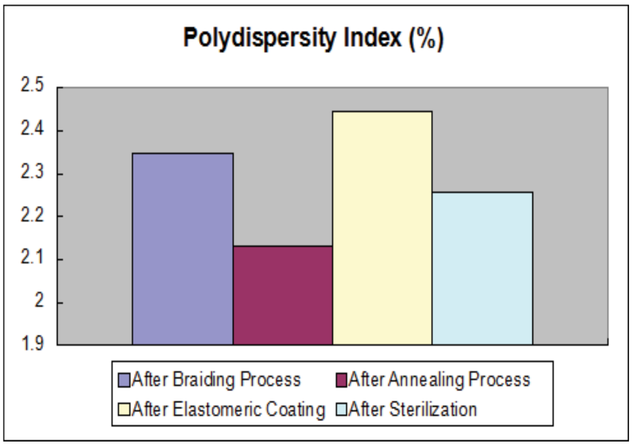


Chart. 8. Glass transition, melting temp and % crystallinity.

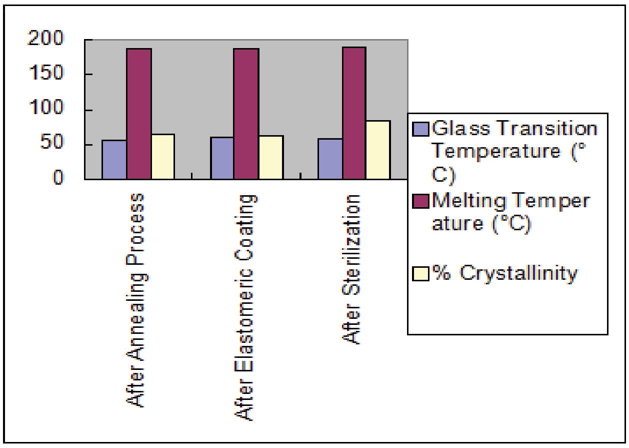


Chart. 9. Glass transition temperature (°C)

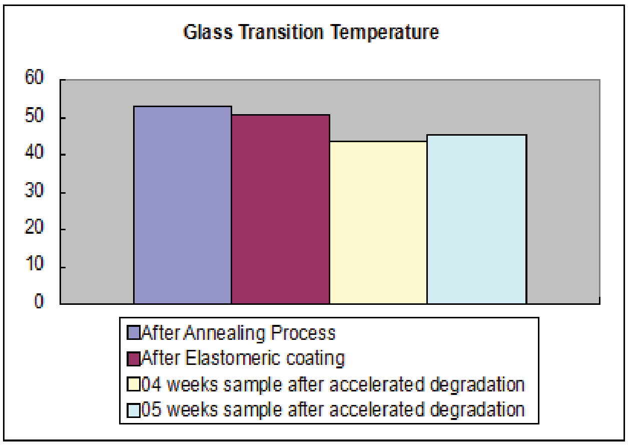


Chart. 10. Melting temperature (°C).

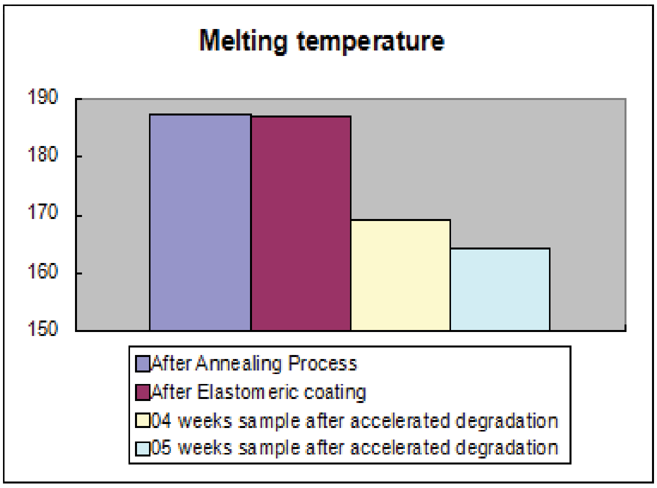
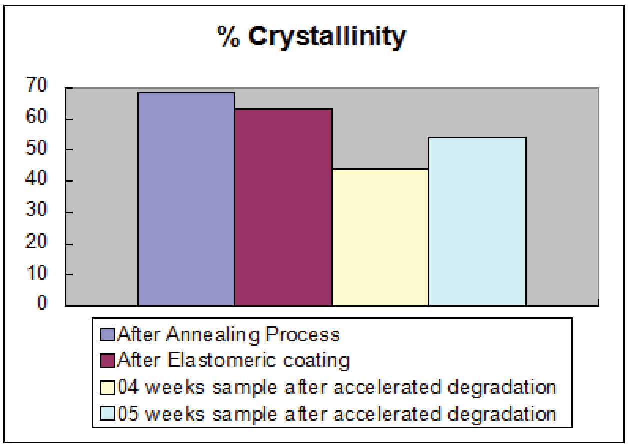


Chart. 11. % crystallinity.



New degradation data in *in vitro* condition

The following chart shows the accelerated *in vitro* simulation study at 70°C interval days.

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 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.

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