A New Biomimetic Synthetic Absorbable Dural Substitute

By Medprin R&D Team

ABSTRACT

Background

Dural repair products are evolving from animal tissue derived materials to synthetic materials as well as from inert to absorbable features. Biomimicry inspired design will significantly improve growth and regeneration of dural cells and tissues for better repair effects and less complications. We have firstly developed the new absorbable Poly-L-lactide (PLLA) dural repair product ReDura based on biomimetic electrospun technology.

Objective

The new product would be characterized with mechanical properties and biocompatibility both *in vitro* and *in vivo* and proved to be safety and efficacy in animal and clinical research.

Methods

The microstructure, mechanical properties, and cytotoxicity were evaluated by SEM scanning, tensile testing, and MTT assay, respectively. For safety and efficacy evaluation, canine model was used for dural defect repair experiment and subsequent general and histological observations. One completed clinical case was reported here to further evaluate the safety and efficacy of ReDura.

Results

The ReDura patch exhibited unique 3D nonwoven microfibers structure with excellent mechanical strength and good flexibility as well as good biocompatibility. In animal study, complete defect closures and no CFS leakage or nervous system defect were found. Postoperative local inflammatory response was mild and similar to the control groups, indicating that ReDura has good tissue compatibility. In clinical research, there was no CSF leakage post-operation and other clinical observations were normal. The health recover of the patient was good.

Conclusions

The new biomimetic absorbable PLLA dural patch fabricated was confirmed safe and effective, and proved to be an ideal dural alternative substitute.

Keywords: biomimetic, synthetic, absorbable, microfibrous patch, dural repair

INTRODUCTION

Dural defect is a common problem during neurosurgery. Open craniocerebral injuries (industrial, traffic, or war-related), tumor invasion, congenital meninges defects, or other cranial diseases can lead to defects of the dura mater. Such defects need be repaired timely so as to prevent leakage of the cerebrospinal fluid (CSF), encephalocele, and stress from the barometric pressure. Otherwise, it can be life endangering.

Currently, there are a number of dural substitutes and the materials used can be generally classified into four types: autologous fascia, allograft, biological material (de-cellularized animal tissue, e.g. bovine pericardium, or animal tissue derived material, e.g. collagen), and synthetic material[1-3]. However, clinical applications of autologous fascia, allograft and biological material can lead to problems such as limited availability, transmission of animal pathogen, low mechanical strength, immulogical problems, etc[4-6]. Synthetic materials have no risk of transmitting disease or least causing immune response, and they are easy to be processed into required shapes and sizes. In general, they can be divided into non-absorbable and absorbable materials. The latter one can be gradually replaced by regenerated dural tissues during degradation process. At present, absorbable synthetic materials are widely applied in clinic including Ethisorb Vicryl (polygalactin910), Gunza polydioxanone (PDS) etc[7]. However, these products applied conventional polymer fabrication techniques lack of adequate flexibility difficult to handle and suture, as well as lack of biomimetic design less growth and regeneration of dural cells and tissues.

ReDura, a recently developed and CE-approved product by Medprin Co. Ltd., is made of biodegradable Poly-L-Lactide (PLLA) and fabricated by an emerging electrospinning technology. In this study, the safety and efficacy of ReDura was evaluated in the canine dural defect model. Meanwhile, the mechanical properties and biocompatibility of ReDura were characterized both *in vitro* and *in vivo*. To further confirm the safety and efficiency, a clinical case was studied. As controls, two major commercially available dural products, biological material patch （NormalGEN） and synthetic absorbable substitute (SEAMDURA) by using conventional fabrication methods, were chosen to compare with ReDura.

MATERIALS AND METHODS

Dural Substitutes

ReDura, provided by Medprin Biotech GmbH (Germany) is composed of absorbable materials PLLA manufactured by electrospinning technology. Two control groups are chosen, one is NormalGEN supplied by Grandhope Biotech. C. Ltd. (Guangzhou, China), a biological dural patch, whose material is obtained from porcine pericardium and vascular membrane. The other is SEAMDURA from Gunze Ltd. (Japan), an absorbable synthetic dural substitute made of a film from copolymer of L-Lactide and ε-Caprolactone (P(LA/CL)), and Polyglycolic acid (PGA)[8, 9]. It is made by using conventional weaving and/or coating methods and lacks of biomimetic design.

■ Characterization of ReDura

Microstructure

The microstructure of ReDura substitute was evaluated through Scanning Electron Microscope (SEM) (ESEM XL30 HY-3080, FEI, USA) by using a standard SEM sample preparation and scanning protocol.

Mechanical Testing

In the tensile test, the samples were cut into pieces about 10×10mm. The tensile strength and elongation at break were recorded. For the stitch tear strength, pieces 10mm wide were tested by suturing the sample at 2mm from its edge with No.4-0 silk suture. The maximum tensile strength when suture pulled out or samples wrecked were recorded. Both the tensile and stitch tear strengths were measured at room temperature, at a stretching speed of 200mm/minute by the mechanical testing instrument (HY-3080, Shanghai HengYi Co., Ltd., China).

In vitro Accelerated Biodegradation Test

To mimic *in-vivo* degradation process of material, an accelerated *in-vitro* degradation test was performed in Phosphate-buffered saline, 50°C set as accelerated temperature, and pH value adjusted as 7.4±0.2. The solution used in the test should not be less than 10ml and the ratio of solution volume (ml) to materials weight (g) should not be lower than 30:1. The samples were fully soaked in the solution and could not be taken out until reached end-time point at 1, 2, 3, and 4 weeks, respectively. The mechanical test was performed at different time points.

Cytotoxicity Test

According to *ISO10993.5-2009* standard, the cytotoxicity was evaluated with L929 mouse fibroblast cell line using the MTT assay[10, 11]. Sterile ReDura substitutes were cut into pieces 10mm wide. Six samples in total were prepared and respectively extracted in the DMEM culture medium without serum for 24 hours. The obtained extract liquid (1ml per one well) were separated into 24-well plates seeded by L929 cells. In individual well, 1×10^5 cells were seeded. At the same time, equivalent DMEM culture medium was added as blank and equivalent dilution of phenol (5%) was added as positive control. The plates were then put in the incubator (37±1°C, 5% CO^2) for 3 days. The MTT compound (1mg/ml) was added in each well with 0.5ml. After four hours of incubation, the supernatant culture medium was discarded from the plates. In each well, 200μl DMSO was then added in and stirred until dissolved fully. The 24-well plate was tested by microplate reader (BIO-RAD Model 550, BIO-RAD, USA) at a wavelength of 490nm and the absorbance for each well was recorded. The viability and cytotoxicity was expressed by the optical density (OD) value of treated samples versus OD values of positive control wells (untreated cells) both corrected by blank measurements of wells with no cells.

■ Animal Experiment

Animals Selection

Canine model animals were adult Chinese domestic dogs, provided by Suibei Medical Animal Testing Center (Guangzhou, China). All the animal experiments were approved by Institutional Animal Care and Use Committee of the Third Affiliated Hospital of Sun Yat-sen University (Guangzhou, China). The health and growth conditions of the experimental dogs were monitored at least 2 weeks before operation. 24 healthy adult dogs in total, weighted 15-20kg and aged 1.5-2 years were randomly divided into three groups with 8 dogs each for the short- and middle-term observation (up to 180 days): ReDura, biological material (NormalGEN), and synthetic material (SEAMDURA) groups. Another 3 dogs were chosen to be observed for the long-term study of 2 years with ReDura, NormalGEN and SEAMDUR implanted in both sides of dogs' head for dural repair.

Surgical Method

After intravenous anesthesia, the dog was shaved off hair and placed on the operation table in prone position. After top midst scalp was cut vertically, unipolar electrotome was used to cut laterally for 0.5cm along sagittal suture. Then headed muscle tissue on both sides was detached respectively, and periosteum was detached to expose skull plates (4×3

cm) on two sides of top skull. High-speed drill was used to grind the skull plates to form two bone windows (about 2.5×2 cm). Blood vessels of the exposed dura mater were ablated by bipolar coagulator, and then a piece of oval dura (2×1.5cm) on both sides was cut by microscopic scissor to generate a dural defect on top skull. Repair material was taken out from package, cut into proper size to cover the dural defect completely. The wound was seamed with 3/0 notched interrupted suture with one stitch on each side. Suture was knotted to eliminate gap between the patch and original dura. Then penicillin powder was scattered evenly into the cut to avoid infection. Muscle was sutured by a round pin and No.1 thread; rubber drains were placed on both right and left sides outside dura and scalp was discontinuously sutured by No.4 thread.

Post-operation Observation

At different time points up to 2 years after surgery, the animals were sacrificed and the implant samples were retrieved. Briefly, the skulls of the dogs were opened surgically and the implants and surrounding tissues were taken out. The retrieved samples were inspected carefully and two 10×10mm pieces were cut down. One was placed into a clean specimen bottle for followed mechanical test and the other was fixed in Formalin solution for histological analyses including H&E and Masson trichrome staining.

Tissue Biomechanics

To evaluate the mechanical change of the implant over the implantation, tensile strength of ReDura were tested before implantation and after implantation for 1, 4, 10, and 12 weeks, respectively. The testing method is the same as described previously.

■ Clinical Case Study

To further confirm the safety and efficacy of this new device, one clinical case was studied focusing on the applicability of ReDura with a patient needed for dural repair. This clinical case of using ReDura in neurosurgical procedures was approved by Chinese State Food Drug Administration (CFDA) and the medical ethics committee, Zhujiang Hospital of South Medical University on July, 2011.

Patient

The patient was female, 25 years old, with dura defect after brain tumor surgery. She was chosen and excluded the following severe conditions: diseases of heart, liver, kidney, blood system or other vital organs, unstable emotion, pregnant or lactating.

Before the surgery, the patient received radiation treatment for the astrocytic glioma in the right frontal and parietal lobe and recurred to be admitted to the hospital. The patient was scanned with computed tomography (CT) and the images revealed the focus volume and edema area were enlarged.

Surgical Procedure

The patient underwent surgery under general anesthesia. After removal of space-occupying tumors, one 4×6 cm ReDura patch was cut according to the dimension of the dural defect and sutured to the remaining dura mater to achieve satisfactory closure. The subcutaneous layer was rinsed with diluted povidone iodine solution and a drainage tube was used. Finally, the scalp was full thickness sutured.

Outcome measurements

After operation, the patient's conditions were routinely monitored at 1, 3, 5, 8, and 11 days including body temperature, meningeal irritatation sign, cerebrospinal fluid (CSF) leakage, hydrocephalus, nausea and vomiting, epilepsy, infection and wound healing. On the 11th day post-operation, the patient was arranged a CT scan with lumbar puncture to exam the ncurolymph condition and intracranial pressure. Then the patient was tested with routine clinical assays including blood test, liver and kidney function, cell-mediated immunity, and humoral immunity. The CT scan examined the conditions of CSF and hydrocephalus. After 90 and 180 days of operation, clinical follow-up was performed to check if any abnormal effect occurred.

Besides this clinical case, the multicenter clinical trial of this new product is in progress. We will report the results of the clinical trial later after the multicenter trial is completed.

■ Statistical Analysis

Statistical differences were performed by analysis of variance (ANOVA) followed by Tukey–Kamber multiple comparison test. Differences were regarded as significant at $P < 0.05$.

RESULTS

■ Characterization of ReDura

Gross and Microstructure Observation

As shown in Figure 1a, the ReDura substitute appears a white membrane with even thickness of about 0.3 μm. The ReDura provides 11 different

sizes ranging from 15×20mm to 150×150mm, which can meet most of actual dural defects in clinic. SEM scan (Figure 1b) shows that the ReDura is a non-woven fabric composed of electrospun PLLA fibers and the average diameter is about 0.7-2μm. The microstructure of ReDura resembles the extracellular matrix (ECM) of human dura mater, which may provide a beneficial environment for cells migration and proliferation and thus lead to rapid repair and regeneration of dural tissues.

Mechanical Test

The basic mechanical performance of ReDura is shown in Figure 2. Among transverse and longitudinal directions, the tensile strength had no significant difference (P=0.4716, n=8) and distributed from 2.8 to 4.3Mpa. Combined transverse and longitudinal results, the average tensile strength was 4.14±0.18 Mpa (n=8), the average stretching elongation 60.5±13.2 % (n=8), and the average stitch tear load 3.71±0.46 N (n=8) with all samples higher than 1N, which meet clinical suture requirement.

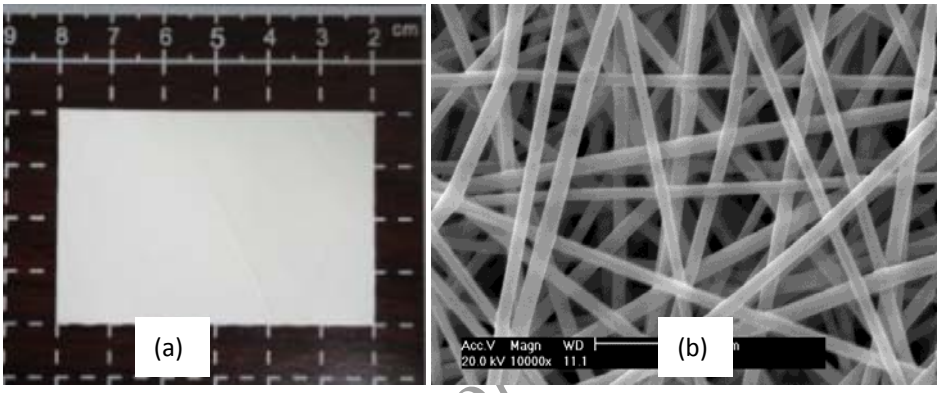

Figure 1. Gross observation (a) and SEM micrograph (b) of the ReDura substitute

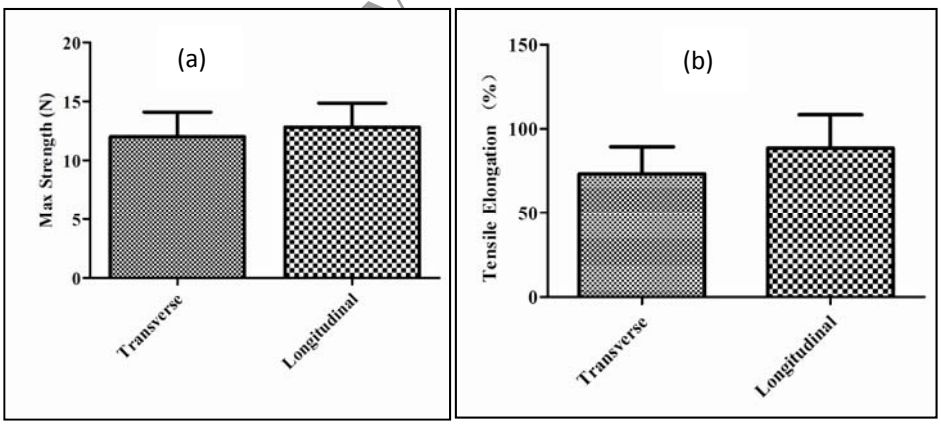

Figure 2. Tensile strength (a), elongation (b) and analyses of the ReDura patch

Accelerated Biodegradation Test

In the accelerated test, the material degradation was reflected by the decrease of tensile strength at different time points. As shown in Figure 3, the maximum load started about 12 N, was then steadily decreased, and finally reached to zero after 4 weeks of incubation. From gross observation, the patch appeared to be intact with the first two weeks and only very few cracks were found on the surface after 2 weeks. After 3 weeks of incubation, although the patch still maintained its integrity, the membrane became more brittle and a number of deep cracks were obvious on the surface. At the end of the 4th week, the patch suddenly lost its integrity and decomposed to a vast number of small pieces (about 1 mm or smaller in diameter).

According to Arrhenius theory and pre-designed testing conditions, the

4 weeks in the accelerated model is theoretically equal to about 2-3 months of the actual degradation of the ReDura material in the animal body. In another world, after 2-3 months the ReDura PLLA material itself degraded with full loss of mechanical properties and integrity and the whole patch of the product converted to a large number of PLLA tiny defragments, which subsequently have a complete degradation as shown below in the last-term implantation experiments.

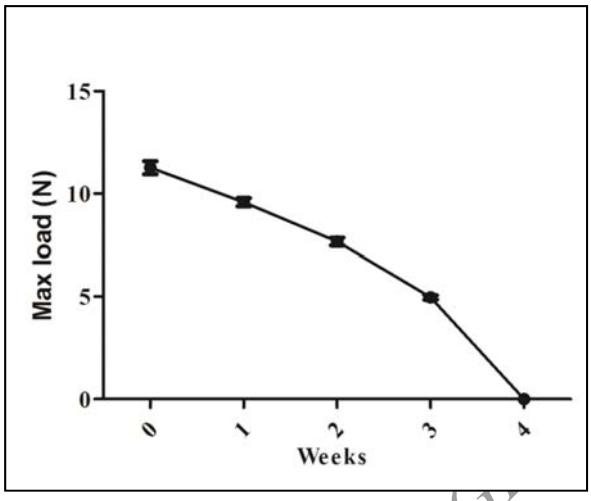

Figure 3. *In vitro* degradation trend analysis of the ReDura patch

Cytotoxicity Test

As shown in the Figure 4, the OD value and cell proliferation rate were 0.57 and 101.15% for ReDura liquid extracts, 0.58 and 105.55% for the standard tissue culture plate, and 0.1 and 17.87% for positive control. There was no significant difference between ReDura and blank (the standard tissue culture plate) ($P > 0.05$) and but significant difference between ReDura and positive control ($P < 0.05$). It could be concluded the ReDura mesh did not affect cell proliferation and had no obvious cytotoxicity.

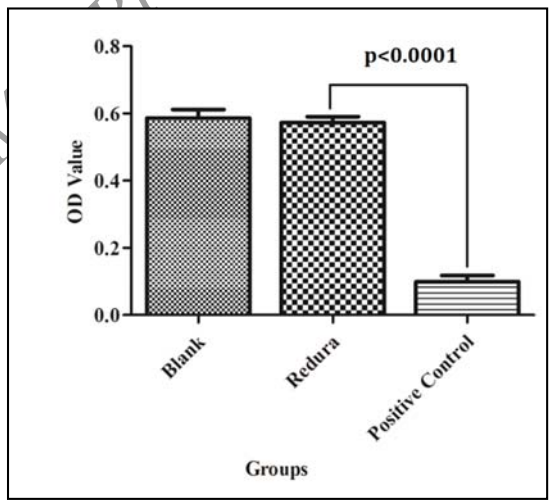

Figure 4. Cytotoxicity analysis of the ReDura patch

■ Animal Experiment Study

Short- or middle-term observations of the implants (up to 180 days)

After 90 and 180 days of implantation, the implants were retrieved. For gross observation, Figure 5 shows the repairing effect of the implants and Figure 6 shows the interfaces between the implant and cerebral cortex. For histological evaluation, Figure 7 and Figure 8 show the results of H&E staining and Masson trichrome staining, respectively.

After 90 and 180 days of implantation, all three groups demonstrated complete closures of the defects and no any CSF leakage was found (Figure 5). The ReDura and synthetic groups integrated well with surrounding tissues without obvious boundaries, but the biological group did not integrated and the boundary was clearly distinguished. To feel the stiffness of the implant, the samples of the three groups were tested by direct touching and the ReDura felt softer than the other two groups.

To investigate whether the patch adhered to brain tissues or not, the interfaces between the implant and cerebral cortex were observed. As shown in Figure 6, the most areas of the ReDura and synthetic implants had no adhesion with clear and smooth surface, only very few spots appeared mild adhesions. These adhesions could be easily separated by slightly detaching the implant from the brain tissue. However, the biological group demonstrated adhesions between the implant and cortex, and these adhesions are severe and in order to separate these adhesions can often result in the damage of the brain tissues.

For histological analyses, the implants with surrounding tissues were taken out. After 90 days of implantation, the ReDura implant was tightly enwrapped by surrounding tissues and infiltrated with a large number of fibroblasts and mass neovascularization. The biological samples were also tightly enwrapped by surrounding tissues but with less number of infiltrated fibroblasts due to its dense structure derived from bovine pericardium. In the synthetic group, the implanted materials were separated into lots of fragments and cavity left with visible fibroblast grown in. The inflammatory reactions of the three groups are similar all mild with only a few of lymphocytes and foreign giant cells. For Redura, about 30-40% residual fibers were maintained with no degradation. For both biological and synthetic groups, local calcification was found.

After 180 days of implantation, in all three groups, the number of inflammatory cells including macrophage and lymphocytes obviously reduced. For ReDura group, the PLLA material mostly degraded only 20-30% left and the degraded part were substituted by new grown fibrotic tissues. There was no adhesion between repairing patch and cerebral cortex. For biological group, more fibroblasts were grown into the dense structure but little material degradation. The adhesion between new fibrosis tissue and brain tissue were obvious. On the surface of brain tissue, cerebral pia mater defect was found and some cerebral pia integrated with new fibrosis tissue. For synthetic group, many material fragments were spread in the new dural tissues accompanied by a little calcification.

Masson trichrome staining shows all the three groups presented good collagen formation and the collagen fibers are mostly aligned. In particular, for the ReDura group, there was a collagen layer formed on the surface of cerebral pai mater and an orderly collagenous fibers structure was seen.

Long-term observations of the implants (up to 2 years)

Figure 9 shows the 2-year repairing effect of the three patches. After 2 years of implantation, the three groups maintained a complete closure of the defect and CSF leakage was still not found. Compared with the biological and synethic groups, the ReDura implant felt softer similar to native dura matter through direct touching. For biological group, there was filamentous adhesion between outer surface of the mesh and brain musculature, difficult to separate them. The white substitute seemed tougher than the ReDura by direct touching. For the synthetic group, mass of necrotic tissue and small amount of effusion were found in the musculature.

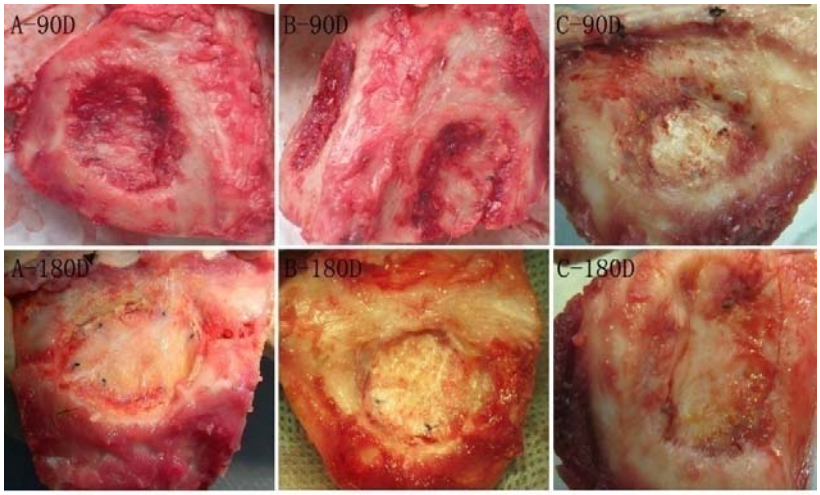

Figure 5. Gross observation of the retrieved implants after 90 and 180 days of implantationReDura: 90th day (A-90d) and 180th day (A-180d); the biological material group (NormalGEN): 90th day (B-90d) and 180th day (B-180d); the synthetic material group (SEAMDURA): 90th day (C-90d) and 180th day (C-180d).

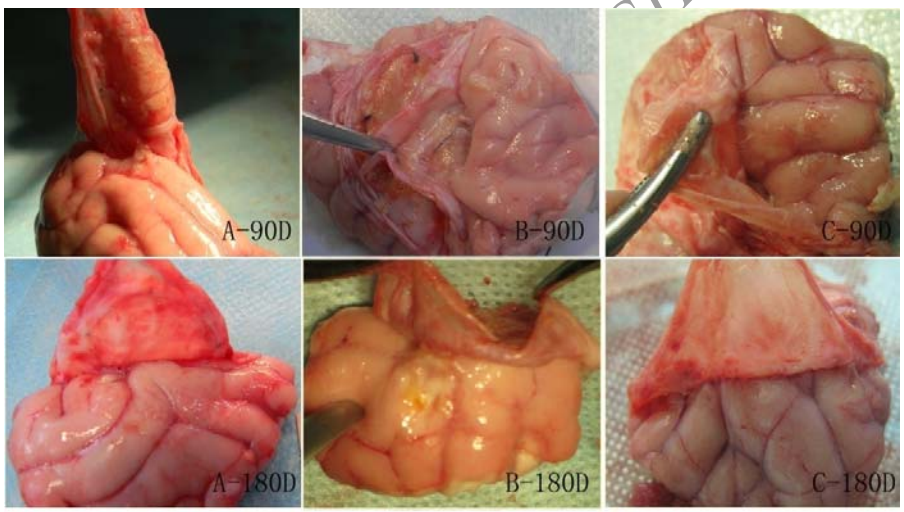

Figure 6. The interfaces between the implants and cerebral cortex after 90 and 180 days of implantation. ReDura: 90th day (A-90d) and 180th day (A-180d); the biological material group (NormalGEN): 90th day (B-90d) and 180th day (B-180d); the synthetic material group (SEAMDURA): 90th day (C-90d) and 180th day (C-180d).

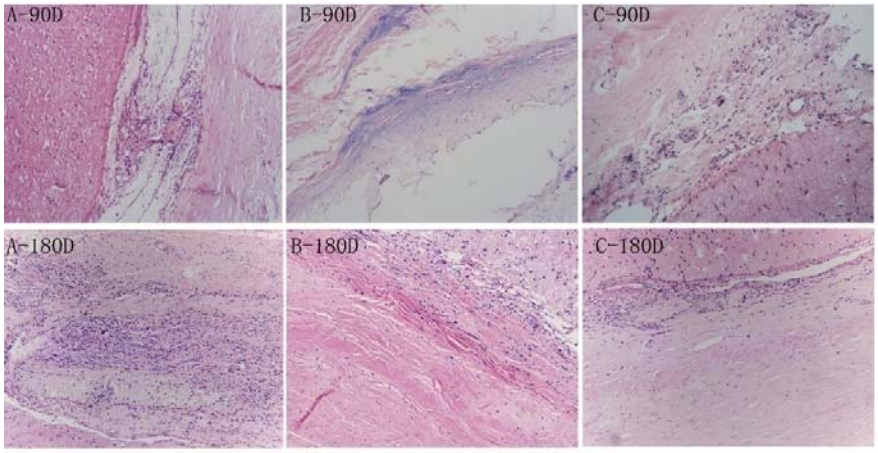

Figure 7. HE staining of the implants after 90 and 180 days of implantation. ReDura: 90th day (A-90d) and 180th day (A-180d); Biological material group (NormalGEN): 90th day (B-90d) and 180th day (B-180d); synthetic material group (SEAMDURA): 90th day (C-90d) and 180th day (C-180d). (Magnification: ×100)

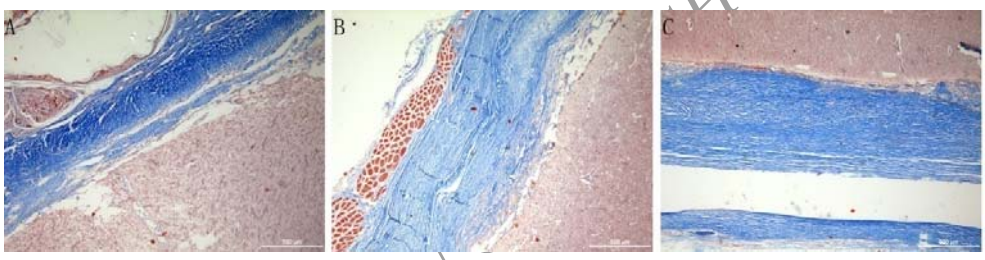

Figure 8. Masson trichrome staining of the implants 180 days after implantation: A—ReDura, B—Biological material group (NormalGEN), C-Synthetic material group (SEAMDURA) (Magnification: ×100)

Figure 10 shows the histological results of the long-term implantation. For the ReDura group, the materials were completely degraded and substituted by regular aligned fibroblast and collagen. The new dural tissue formed with a large amount of fibroblast, but the inflammatory cells were not clearly seen. For the biological group, the materials maintained most mass with slow degradation, and massive collagen belonged to the biological implant material (NormalGen is derived from porcine pericardium) was still left over with a few of newly deposited fibroblasts and collagen. Among the fibroblasts a little focal calcification and a few of cartilage cells were seen. The side of cerebral pia mater was infiltrated by a few inflammatory cells. For synthetic group, only little material was remained and the cerebral pia mater was intact with normal cerebral cortex. The materials were deposited massive fibroblasts and collagen without focal calcification.

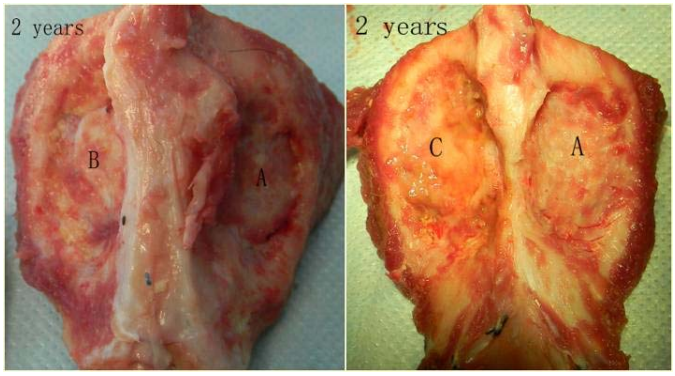

Figure 9. Gross observation of the retrieved implants for the long-term period up to 2 years (A—ReDura, B—biological material (NormalGEN), C-Synthetic material (SEAMDURA)

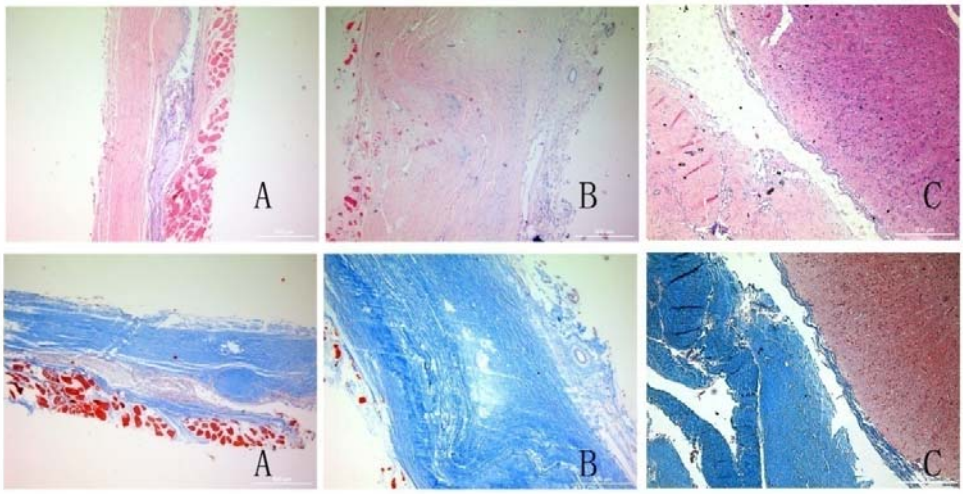

Figure 10. Histological observation for the long-term period (HE staining—upper, Masson trichrome staining-lower) of the repair patches at the 2 years (A—ReDura, B—NormalGEN, C--SEAMDURA) (Magnification: ×100)

Tissue biomechanics

To monitor the mechanical change of ReDura over the period of implantation, the tensile strength was compared before and after samples implanted at different time points. As shown in Figure 11, the maximum tensile load was 12N before implantation. With the material degradation, the maximum tensile load dropped to about 8N one week and four weeks after implantation, but with the formation of new tissues, the maximum load then gradually increased to 20N after eight weeks and 34N after twelve weeks of implantation.

This phenomenon that the strength dropped in the early phase of implantation then raised in the following stage was highly correlated with specific materials and structures which ReDura owns. ReDura is composed of biodegradable PLLA material which can initiate degradation once implanted in the body. The tensile strength decreased with the degradation of the PLLA material at the early stage (4 weeks), but rapidly was raised (after 8 weeks) to a higher level close to the strength of the native dural tissue. This requires that the degradation rate of the materials matched well with formation of new tissues. In this case, the unique 3D biomimetic structure of ReDura can result in the rapid growth of the new dural tissues, whose strength compensated for the mechanical loss due to material degradation. For ReDura, this can ensure that no CSF leakage occurred during and after the degradation of the ReDura material.

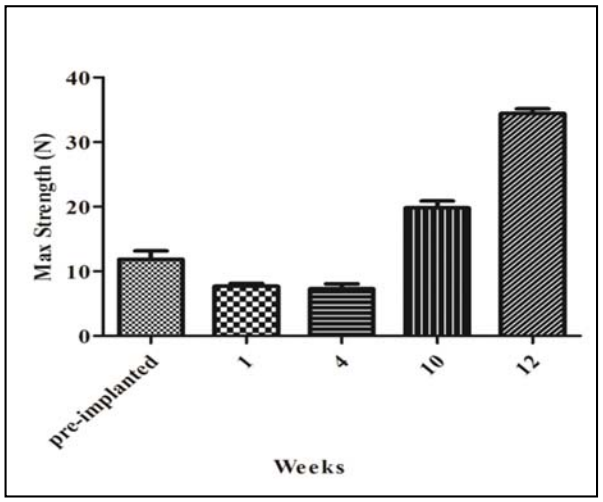

Figure 11. The mechanical analysis of the ReDura patch after implantation for different time points

■ Clinical research

One clinical case was studied with a 6-month follow up and the results were shown in Table 1. The body temperature was normal and there was no obvious infection or CSF observed after surgery. The CT image on the 3rd day confirmed that intracranial pneumatocele decreased markedly and the hematocele in right temporal lobe reduced compared with pre-operation (Figure 12-A). The right temporal lobe involving gray matter showed large lamellar low density shadow and the area was the same as pre-operation but with low density. The doubted brain infarction foci showed the same phenomenon. On the 3rd and11th day, no CSF leakage was found in CT scanning (Figure 12-C&D). The hematocele and edema in right temporal lobe focus absorbed and the doubted brain infarction foci changed for the better. The other situations were basically the same as before.

After 90 and 180 days of clinical follow-up, the patient had no fever and headache, no nausea and vomiting, no CSF observed, good healing, no meningeal irritatation sign, and no epilepsy.

Table 1 Clinical observation post-operation

Post-operation (days)	Headache	Fever	Nausea & vomiting	CSF & subcutaneous fluids	Wound heal
1	Mild	No	Felt	No	-
3	Slight	No	Felt	No	Good
5	No	No	No	No	Good
8	Intracranial pressure and CSF normal*				

* From lumbar puncture examination

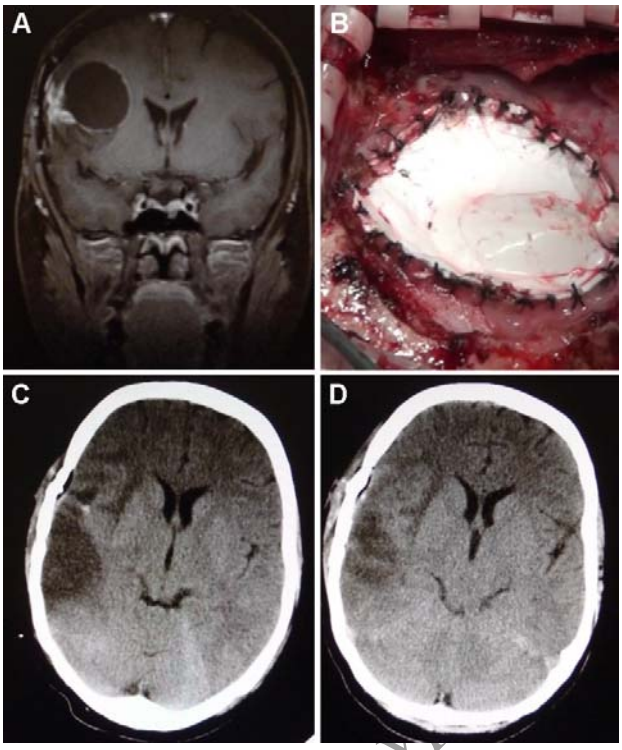

Figure 12. The CT scan and surgical operation of the patient (A: CT scan before operation; B: Surgical method; C: CT scan on the 3rd day post-operation; D: CT scan on the 11th day post-operation)

DISSCUTION

The dural substitutes are evolving from animal to synthetic materials to avoid the transmission of animal diseases, as well as from inert to biodegradable features to erase the chronic inflammatory reactions. Moreover, biomimicry-inspired design is becoming an important trend for tissue scaffolding including artificial dural substitutes to enhance formation of new tissues. In the last decade, although many efforts were used to develop synthetic biodegradable dural products with improved properties, these products are based on the conventional fabrication methods, such as weaving, knitting, coating, solvent casting, etc and still have limitations such as too stiff and tough for handling, less biocompatibility, etc. More importantly, these products lack of biomimetic design, which leads to less tissue repair and regeneration due to their microstructures far different from native dural tissues. To address these issues, new strategies and fabrication methods are needed.

Just recently, electrospinning has emerged as an important method in manufacturing nano- or micro-sized fibers out of synthetic or natural polymers. Such fibers can mimic the morphology and physical structure of components in the ECM to promote cell adhesion and growth[12]. For example, electrospun non-woven nanofiber membranes have been used for a variety of tissue constructs including nerve tubes[13, 14], cardiac grafts[15-18], and cartilages[19]. In addition to being able to mimic naonfibrous or microfibrous ECM features, electrospun biomaterials for dural tissue repair have other advantages, first, have a very high surface area-to-volume ratio and high porosity for better cell migration and perfusion. Second, the electrospun scaffolds should exhibit adequate strength and elasticity to endure the pressure and contour the soft brain tissue as well as allow surgically friendly implantation[16]. Third, by employing different techniques, it is possible to add drugs or growth factors, which allow the potential use of anti-infection or other functional dural substitutes[20].

Through our attempt, PLLA mesh manufactured by electrospinning was first applied in dura substitute as reported in this article. As demonstrated in this study, the electropsun PLLA implant exhibited 3D networks of micro-fibers with the ranging of 0.7 to 2μm, which highly similar to ECM environment of native dural tissues. The new product exhibits good high tensile strength (4Mpa or more), which ranks ReDura among one of the strongest commercially available dural products. ReDura also has

adequate flexibility (stretching elongation about 60.5%) as demonstrated good suture and conformability when implanted in animal and clinical research in this study. Moreover, the excellent biocompatibility was proven both in vitro cell cyototoxity and animal study. In the histological evaluation of implantation up to 2 years, the ReDura showed ideal repairing effect of dural defects as demonstrated by a complete closure of the defect and no CSF leakage. Moreover, similar to the biological and synthetic controls (two commercially available products), the ReDura demonstrated the low level of inflammatory reactions with very small amount of inflammatory cells at each stages of the implantation. After 2-years of implantation, the ReDura completely degraded and metabolized to safe by-products of CO_2 and H_2O, which indicate a long-term safety of the new product. The safety and effectiveness was further confirmed by one clinical application with the patient with removal of astrocytic glioma and subsequent repair of dural defect with ReDura. All major clinical observations, including no CSF leakage, local infection, and wound recovery are normal. So far this operation has been completed for more than 2 years and the patient is healthy and functional activities are normal.

CONCLUSIONS

We have firstly developed a new biomimetic synthetic absorbable dural substitute by using emerging electrospinning technology. This product exhibits excellent strength and flexibility and good biocompatibility. The animal study and clinical case study confirmed that the new biomimetic synthetic absorbable dural sustitutue is an ideal product for dural repair in neurosurgery because of its good tissue biocompatibility, no CFS leakage, proper degradation, and superior anti-adhesion property. No nervous system defect occurred among test animals and clinical case. Postoperative local inflammatory response was at lower level and similar to controls, which indicated this test material has good tissue compatibility. This product has a full degradation over a 2-year period for long-term safety. This product has recently obtained CE approval and launched in the market for clinical uses.

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