2019

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Weizuo Wang
Department of Tissue Engineering, China Medical University, Shenyang 110122, Liaoning, China

Qiang Ao
Department of Tissue Engineering, China Medical University, Shenyang 110122, Liaoning, China

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Recommended Citation
Weizuo Wang, Qiang Ao. Research and application progress on dural substitutes. Journal of Neurorestoratology 2019, 07(04): 161-170.

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Research and application progress on dural substitutes

Weizuo Wang, Qiang Ao

Department of Tissue Engineering, China Medical University, Shenyang 110122, Liaoning, China

ABSTRACT
Dural defects are a common problem in clinical practice, and various types of dural substitutes have been used to deal with dural defects. These play an important role in dural repair. Dural substitutes have gradually reached researchers, neurosurgeons, and patients for approval. This article summarizes the structural characteristics of the dura mater and its regeneration after injury, and reviews the state of progress in research and application. It will provide a reference for the development and application of dural substitutes.

1 Introduction
Tumor erosion, neurosurgical operations, and severe trauma can cause dural defects in the central nervous system. During the dural repair process, it is necessary to prevent cerebrospinal fluid leakage, intracranial infection, adhesion, and other complications. Since the last century, scientists have been trying to create better dural substitutes to improve the repair process and reduce complications. Dozens of dural substitutes have been reported in the literature; these can be divided into four categories: autologous tissue materials, allogeneic tissue materials, xenogeneic materials, and macromolecular polymer materials. Each dural substitute has its own advantages and disadvantages. As there is no definitive evidence to prove that one type has absolute predominance over other types, the optimal choice of materials for use in dural repair procedures remains unclear. In order to describe the structure and characteristics of the human dura mater, this paper reviews the research progress and application of dural substitutes along with their basic mechanism after implantation. It will serve as a reference for the selection of dural substitutes in clinical practice and the development of new-generation materials.

2 Structural characteristics of dura mater and its regeneration after injury

2.1 Structure of dura mater
The dura mater is an opaque and tough fibrous...
membrane that covers the brain and spinal cord. On the basis of its location, the dura mater is divided into the cerebral dura mater and spinal dura mater.

The dura mater consists primarily of collagen fibers arranged in layers, which are generally divided into two parts. The outer layer is called the endosteal layer, which is the periosteum of the inner surface of the skull. This layer is loosely attached to the inner surface of the skull but is more difficult to strip from cranial sutures and the skull base. The inner layer of the dura mater is called the meningeal layer and is thicker, tougher, and more durable than the endosteal layer. In addition to being separated at the dural sinus, the two meningeal layers are fused at other parts, and there are blood vessels and nerves running through them [1]. In 2015, Louveau reported lymphatic vessels parallel to the dural sinus, which was the first report of the meningeal lymphatic vessels [2]. The structure of the dura mater is mainly composed of collagen fibers with elastic fibers. There are a few fibroblasts in the dura mater and osteoblasts in the periosteum. Kegel reported that the average thickness of human dura mater is $1.06 \pm 0.22$ mm [3]. Noort examined the dura mater of 16 fresh human cadavers who died at 20 to 77 years of age. The average failure stress of the human dura mater was 4.70 MPa (range: 3.28 MPa–7.86 MPa), and the average failure strain was 18.4% (range: 16.0%–21.1%) [4]. Chauvet found that the amount of collagen fibers in the dura mater decreased gradually from the inner layer to the outer layer, whereas the amount of elastic fibers increased. It was also observed under scanning electron microscopy that the dura mater of human beings had a multi-layered structure. On the basis of the results of scanning electron microscopy [5], Protasoni further divided human dura mater into five different layers—the bone surface layer, external median layer, vascular layer, internal median layer, and arachnoid layer—based on the 3D architecture, disposition, and orientation of the collagen fibers. The change in direction of the collagen fibers is mostly visible between the vascular and internal median layers, where they are subjected to the highest stretching forces. This allows neurosurgeons to distinguish the two layers of the dura mater [6].

Spinal dura mater is the outer layer of the spinal cord capsule, covering the arachnoid membrane, the pia mater, and the spinal cord, which corresponds to the dura mater’s inner layer and continues to the dura mater at the foramen magnum [7]. Spinal dura mater can be divided into three layers: an outer layer consisting of collagen fibers and elastic fibers with an average thickness of about 2 μm; a median layer that is thick and strong, with blood vessels but no innervation; and an inner layer that is connected with the arachnoid membrane, with an average thickness of about 8 μm [8]. As the location of spinal dura mater is lower than that of the cerebral dura mater, it bears higher hydrostatic pressure, so it must be more watertight.

2.2 Repair and regeneration of the dura mater

The function of the dura mater is to support and protect the central nervous system and create relatively closed conditions for the circulation of cerebrospinal fluid. When a dural defect is small, it can be repaired by suture. When a dural defect caused by trauma, surgical breakage, or tumor infiltration is large, it must be repaired by dural substitutes. Dural substitutes can prevent the injured area of the brain or spinal cord from reaching other tissues and effectively recover the watertightness of the original structure. The repair of dura mater with dural substitutes can effectively reduce the incidence of epilepsy, cerebrospinal fluid leakage, infection, and other complications.
After implantation of the dural substitute, the reconstruction of regenerated dura mater is synchronized with the degradation of the graft. Fibroblasts are the key cells in these two processes. The implanted dural substitute provides a scaffold for the migration and implantation of fibroblasts, lymphocytes, macrophages, and other cells that secrete collagen fibers, elastic fibers, reticular fibers, proteoglycan, and glycoprotein in the process of dural reconstruction. At the same time, the matrix metalloproteinases (MMPs) secreted by fibroblasts and other cells degrade the implanted collagen-based dural substitute, together with some non-specific proteases and peptidases. MMPs are a group of zinc-dependent enzymes that regulate cell matrix composition. MMPs-1, 8, and 13 are human endogenous enzymes known to decompose fibrous collagen in vivo [9]. In type-I collagen, which is the main component of most dural substitutes, each triple-helical unit is composed of two α1 chains and one α2 chain. MMP-mediated collagen degradation preferentially occurs at the site on the α2 chain, breaking the chain into three quarter- and one quarter-length fragments (molecular weights of about 75,000 and 250,000, respectively). Consequently, these two fragments are degraded into oligopeptides or amino acids by a variety of non-specific proteases [10]. The degradation time of a dural substitute is related to the composition, size, and thickness of the material, preparation processing, the location of the graft, and other factors. Laun et al. reported that fibroblasts and histocytes began to migrate to the dural substitute implanted into a patient on the fourth day after operation and entered the graft through pores in the fibers [11]. Three months after the operation, the thickness of a graft made of bovine pericardium was reduced by half, and the thick collagen fibers on the surface of the graft were replaced by new, slim fibers. At 24 months after the operation, the thickness of the graft was only about 1/10. Good vascularization could be seen in the transition region between the new tissue and implanted dural substitutes [11]. In addition, it has been reported that dural substitutes made of pure collagen extracted from equine Achilles tendon are completely degraded 1 year after implantation in the patient’s body and that the regenerated dura mater has an ideal structure [12]. However, the degradation process of macromolecular polymer material used in dural substitutes has rarely been reported in detail.

3 Development and application of dural substitutes

In the last hundred years, scholars from all over the world have used hundreds of different materials to prepare dural substitutes: Abbe first reported using rubber patches to repair dura mater in 1895 [13]. Craig and Ellis first reported the use of animal-derived materials to repair the dura mater in 1905. The dural substitute used in the operation, which was made from bovine peritoneum, was called Cargile membrane [14]. Subsequently, scholars in various countries have tried to repair the dura mater with materials obtained from animal pericardium, allantoic membrane, amniotic membrane, and other animal sources. In 1926, Dandy successfully repaired the dura mater with autologous fascia lata for the first time [15]. In 1958, Campbell and Sharkey reported that freeze-dried allogenic dura mater could be used as a dural substitute and achieved clinical success for the first time [16, 17]. Over the next three decades, this type of material was commercialized and widely used in duraplasty in various countries. In 1991, Gortler verified the feasibility of expanded polytetrafluoroethylene as a synthetic polymer material for dural transplantation in animal experiments for the first time, and its clinical effect was confirmed [18]. In this century, polyglycolic acid (PGA), L-lactic acid
and epsilon-caprolactone copolymers, polyglactin 910 copolymers, and polydioxycyclohexanone blended fabrics have been used clinically. There are dozens of raw materials available for the preparation of dural substitute. On the basis of the sources of these raw materials, dural substitutes can be divided into four categories. Here we introduce the development and application of each type.

### 3.1 Autologous tissue materials

This type of dural substitute is taken from the patient's skull periosteum, fascia lata, cap aponeurosis, or temporal muscle fascia before or during the operation to repair the dural defect [19, 20]. In duraplasty, the cranial periosteum can be obtained directly and easily without a second operation, so it is more popular than other autologous tissues for dural repair. Autologous materials can effectively avoid the risk of immune rejection and potential transmission of pathogenic microorganisms and reduce medical costs. However, the size and shape of autologous tissue are often limited, so it is not suitable for repairing large dural defects.

### 3.2 Allogeneic tissue materials

In 1957, freeze-dried human cadaveric dura mater was successfully applied to repair a patient's dural defect [17]. This kind of artificial dura mater became popular all over the world in the next 30 years and was widely applied in clinical use [21]. In 1988, however, a report revealed a case of progressive dementia, convulsions, and other clinical symptoms, as well as pathological features of amyloid plaques and spongiform degeneration in brain tissue, which were consistent with the characteristics of Creutzfeldt–Jakob disease (CJD) [22]. Since that time, similar cases have been found all over the world. Most of the dural substitutes involved are Lyodura brand products. It was reported that the dura mater of CJD patients was used after their death to prepare the dural substitute, which caused the spread of this disease. Considering the use of dural substitutes involved, this disease is named dura mater graft-associated CJD (dCJD). Prions are the pathogen involved in dCJD, which are distorted proteins encoded by the genes of normal host cells. Although they do not contain nucleic acid, they are self-proliferating and infectious. The titer of prions in the central nervous system is much higher than that in other parts, and there is no simple and reliable detection method for prions [23]. Therefore, dural substitutes made from allogeneic dura mater were gradually withdrawn from the historical stage when the source of the dura mater was insufficient and the transmission of prions could not be completely avoided [24, 25]. Domestic and foreign scholars have also tried to use amniotic membrane, dermis, and other allogenic materials to prepare dural substitutes and have achieved some positive results [26–28]. However, owing to the lack of sources of allogenic materials, this type of material has not been widely used.

### 3.3 Xenogeneic materials

The use of porcine, bovine, equine, and other animal tissues to prepare dural substitutes has a history of more than 100 years, and this type of artificial dura mater is the most commonly used in clinics at present [29]. On the basis of their preparation methods, these types of dural substitutes can be divided into two subtypes: one that keeps the original morphology of animal tissues and a second that is prepared using extracted animal collagen. The former maintains the structure of fibrous scaffolds in the extracellular matrix of animal tissues (such as bovine or porcine heart capsule, dermis, and small intestinal submucosa) and is prepared by freeze-drying, cross-linking, or decellularized treatment [30, 31]. The latter
is extracted from tissues rich in collagen (such as bovine or equine Achilles tendon) to form collagen-based dural substitutes [32]. Type I collagen is the main component of the artificial dura mater that is created, and the scaffold structure formed by crisscrossing collagen fibers provides a favorable microenvironment for reconstruction of the dura mater. Some scholars believe, however, that the use of animal-derived materials such as bovine or porcine tissue might increase the risk of disease transmission, so they have attempted to use fish tissue to prepare dural substitutes [33, 34].

3.4 Macromolecular polymer materials
In order to avoid the spread of pathogens caused by the use of allogeneic or xenogeneic materials, improve clinical efficacy, and reduce costs, researchers have attempted to use various synthetic polymers to prepare dural substitutes. On the basis of their degradation after implantation, synthetic substitutes can be subdivided into two subtypes: nonabsorbable materials and absorbable materials. The former is represented by expanded polytetrafluoroethylene and polyurethane dural substitute, and the latter is composed of PGA, copolymer of L-lactic acid and epsilon-caprolactone, or copolymer of lactide and polydioxanone. Absorbable materials are difficult to degrade in vivo, which can lead to foreign body reactions, friction with the cerebral cortex or spinal cord, and other postoperative complications, and the advent of absorbable materials to a certain extent results in the deficiencies above [35–37].

Polymers are stretched into filaments by electrospinning, and a three-dimensional structure similar to the natural dural structure is formed. This bionic and porous scaffold provides holes or cracks, which is beneficial to the migration of patient’s autologous cells. The migration of cells is important for the degradation of implanted materials and the reconstruction of the dura mater [38]. In addition, by changing the composition and concentration of each polymer, the toughness of the fibers can be adjusted, and the appropriate level of mechanical strength of the synthetic dural substitute can be obtained [39]. However, ensuring the watertightness of the material is an important issue for its clinical application and is particularly critical for repairing spinal dura mater (spinal dura mater bears higher hydrostatic pressure than cerebral dura mater). Some scholars have tried to improve the watertightness of dural substitutes by controlling the size of fiber pores and adding hydrophobic material to the surface of synthetic substitutes [40].

Another important question is how to adjust the degradation rate of the synthetic dural substitute to an ideal range and obtain biological activity similar to that of collagen. Combining a polymer with other components for the preparation of synthetic dural substitutes is a good way to ensure watertightness. For example, the poly (lactic-co-glycolic acid) (PLGA) is nontoxic and is widely used in many fields such as biological scaffold materials, drug delivery systems, and surgical sutures. The degradation of the material can be controlled by changing the ratio of lactic acid to glycolic acid. A dural substitute made of PLGA and polydioxanone has both proper degradability and watertightness [39]. It was approved by the Food and Drug Administration of the United States in 2016 and has good clinical results. Compared with collagen-based dural substitutes, synthetic macromolecular materials lack the biological functions of inducing cell migration and promoting the secretion of related cytokines. Some researchers have attempted to prepare dural substitutes by adding gelatin or silk fibroin into the polymer. This method not only ensures the bionic structure of the dural substitute but also increases the biological function and improves the surface properties of the material, thereby enhancing its repair effects [38].
4 Preparation of dural repair materials

The major function of dura mater is to form a central, airtight system. Trauma or surgery often results in the absence of arachnoid and pia mater. Thus, the dural substitutes contact the cerebral cortex or spinal cord directly after the duraplasty operation. This direct contact might lead to friction between the graft and nervous tissue when the intracranial pressure changes greatly, which can damage the delicate cerebral cortex or spinal cord. Therefore, dural substitutes not only should have good watertightness to prevent cerebrospinal fluid leakage but also should be smooth and flexible to avoid the damage of nerve tissue caused by friction. Therefore, the question of how to reasonably prepare dural substitutes that meet the requirements is the subject of continuing research. The preparation of dural substitutes often involves the following techniques.

4.1 Vacuum freeze-drying technology

This refers to a technology that freezes water-bearing materials into solids. Ice in biomaterials sublimes directly from a solid form to a gas under low temperature and pressure conditions, thereby achieving the purpose of drying. After freeze-drying treatment, the structure of the material is porous, like a fluffy porous sponge, and the volume of the material is basically the same or slightly larger than that of the original [33]. It has been reported that after freeze-drying of animal tissues, the structure of fibrous scaffolds in the extracellular matrix remains basically unchanged, some proteins can maintain good biological activity, and the structure of the cell membrane is destroyed, which reduces the antigenicity of this material [41, 42]. Freeze-dried dural substitute is conducive to long-term preservation. It can be rehydrated and restored to its original flexible texture by immersion in sterile saline for several minutes before use. Furthermore, the porous structure generated in dural substitutes after vacuum freeze-drying treatment creates better conditions for the patient’s autologous cells to migrate and multiply, which is conducive to the reconstruction of the dura mater [34].

4.2 Acellular technology

Acellular treatment is a technology that removes cells from human or animal tissues and organs. It has been reported that acellular tissue can reduce the immunogenicity of allogenic or xenogenic materials [42]. SDS is one of the ideal and widely used methods in the acellular process, but the residual surfactant in the material has an impact on tissue regeneration. Therefore, scholars in various countries are exploring more physical methods such as gamma ray, repeated freeze-thaw, and enzymatic methods to remove cell components in the preparation of artificial dura mater in order to obtain materials without surfactant residues [42, 43]. Furthermore, in the process of acellularization, the fibrous scaffold of the extracellular matrix can be destroyed, which decreases the mechanical strength of the material. Therefore, one study used different freeze-thaw temperatures, chemical detergents, and incubation times in order to determine the optimal method for cell removal. The authors found that a porcine decellularization method including a freeze-thaw in liquid nitrogen, an ionic detergent (0.1% SDS), and a 24 h incubation period resulted in a scaffold that retained the necessary components, the ultrastructure of the extracellular matrix (ECM), and the biomechanical properties. This method could greatly reduce the immunogenicity of the material as well [44].

4.3 Cross-link technology

Cross-linking refers to the process in which polymers (natural or synthetic) are linked to other
polymers through covalent or ionic bonds. The technology of physical or chemical cross-linking is widely used in the preparation of dural substitutes and can improve the chemical and biomechanical properties of the original materials. One common method is the use of glutaric dialdehyde to increase the mechanical strength and anti-degradation ability of the dural substitute. However, the remaining glutaraldehyde or other aldehyde cross-linking agents, to some extent, prevent the migration and proliferation of a patient’s cells into the dural substitute, which restricts the regeneration and repair of the dura mater. In order to overcome these shortcomings, physical cross-linking methods and other cross-linking agents with lower toxicity such as carbodiimide have been used in recent years [43, 45]. Synthetic polymer materials lack specific cell recognition signals and cannot induce cell migration and adhesion effectively, and some collagen-based substitutes are limited by low mechanical properties and excessive degradation speed in vivo. Therefore, obtaining higher biocompatibility and proper mechanical properties of high-polymer materials or even a collagen-based matrix is a great challenge. Polydopamine (PDA) coated cross-linking strategies provide a possibility. Owing to PDA’s robust capacity to deposit onto the various surfaces via the oxidative self-polymerization of dopamine, collagen is immobilized onto dural substitutes, possibly leading to enhancement of the efficiency and effectiveness of the duraplasty [46, 47].

4.4 Electrospinning technology

This is a special fiber manufacturing technology that uses an electric field to weave filaments formed by polymer solutions into dural substitutes. With the development of electrospinning technology, filaments can be knitted into multi-layer scaffolds similar to natural dural fibers by controlling the direction of the fibers [46, 48]. By changing the composition of the biomimetic material polymer, biological activity can be added to dural substitutes, allowing control of the degradation, watertightness, and mechanical strength of the grafts [46, 49, 50].

5 Dura mater and meningeal lymphatic vessels

Louveau et al. first discovered the presence of lymphatic vessels in the dura mater in 2015, overturning the long-standing misconception that there are no lymphatic vessels in the central nervous system [2]. Meningeal lymphatic vessels are an important part of the lymphatic circulation of the central nervous system. They play a crucial role in the discharge of metabolic wastes in the brain, regulation of intracranial tissue fluid volume, and communication of the peripheral immune system [51, 52]. Some scholars have reported that the loss of meningeal lymphatic function can affect the prognosis of Alzheimer’s disease, stroke, and other neurological diseases [53–55]. With our deepened understanding of meningeal lymphatic function, higher requirements for the recovery of lymphatic structure and function are needed urgently in duraplasty. The question of how to promote better reconstruction of meningeal lymphatic vessels may become a significant issue in the field of dural substitutes.

6 Conclusions and prospects

Much progress in dural repair has been achieved over the past hundred years, but dural substitutes still cannot completely avoid the occurrence of immune rejection, cerebrospinal fluid leakage, and other complications. Currently, dural substitutes lack the properties of perfect biomimetic structure, ideal tissue compatibility, and degradation in accordance with the remodeling process. Each
dural substitute has its own shortcomings, and there is room for further improvement. It is urgent that we develop a new generation of dural substitutes with better clinical effects. Therefore, the mechanism of dural replacement repair needs to be further studied and explored, and new raw materials also need to be explored. With the rapid development of materials science and an effective combination of basic research and clinical study, we believe that the problem of dural defect repair will be solved successfully.

**Conflict of interests**

All contributing authors have no conflicts of interest in this paper.

**References**

[1] Standring S. Gray’s anatomy: the anatomical basis of clinical practice. 41st ed. Elsevier, 2016.

[2] Louveau A, Smirnov I, Keyes TJ, et al. Structural and functional features of central nervous system lymphatic vessels. Nature. 2015, 523(7560): 337–341.

[3] de Kegel D, Vastmans J, Feherway H, et al. Bio-mechanical characterization of human Dura mater. J Mech Behav Biomed Mater. 2018, 79: 122–134.

[4] van Noort R, Black MM, Martin TR, et al. A study of the uniaxial mechanical properties of human Dura mater preserved in glycerol. Biomaterials. 1981, 2(1): 41–45.

[5] Chauvet D, Carpentier A, Allain JM, et al. Histological and biomechanical study of Dura mater applied to the technique of Dura splitting decompression in Chiari type I malformation. Neurosurg Rev. 2010, 33(3): 287–294; discussion 295.

[6] Protasoni M, Sangiorgi S, Cividini A, et al. The collagenic architecture of human Dura mater. J Neurosurg. 2011, 114(6): 1723–1730.

[7] Ding WL, Liu XZ. Systematic Anatomy. 9th ed. Beijing: People’s Medical Publishing House, 2018.

[8] Vandenabeele F, Creemers J, Lambrichts I. Ultrastructure of the human spinal arachnoid mater and Dura mater. J Anat. 1996, 189( Pt 2): 417–430.

[9] Kapoor C, Vaidya S, Wadhwan V, et al. Seesaw of matrix metalloproteinases (MMPs). J Can Res Ther. 2016, 12(1): 28–35.

[10] Lu KG, Stultz CM. Insight into the degradation of type-I collagen fibrils by MMP-8. J Mol Biol. 2013, 425(10): 1815–1825.

[11] Laun A, Tonn JC, Jerusalem C. Comparative study of lyophilized human Dura mater and lyophilized bovine pericardium as dural substitutes in neurosurgery. Acta Neurochir (Wien). 1990, 107(1/2): 16–21.

[12] Centonze R, Agostini E, Massaccesi S, et al. A novel equine-derived pericardium membrane for dural repair: A preliminary, short-term investigation. Asian J Neurosurg. 2016, 11(3): 201–205.

[13] Abbe R. Rubber tissue for meningeal adhesions. Trans Am Surg Assoc. 1895, 13: 490–491.

[14] Craig AB, Ellis AG. I. an experimental and histological study of cagile membrane: with reference to (1) its efficacy in preventing adhesion in the abdominal and cranial cavities and around nerves and tendons, and (2) its ultimate fate in the tissues. Ann Surg. 1905, 41(6): 801–822.

[15] Dandy WE. Pneumocephalus (intracranial pneumatocele or aerocele). Arch Surg. 1926, 12(5): 949–982.

[16] Campbell JB, Bassett CAL, Robertson JW. Clinical use of freeze-dried human Dura mater. J Neurosurg. 1958, 15(2): 207–214.

[17] Sharkey PC, Usher FC, Robertson RC, et al. Lyophilized human Dura mater as a dural substitute. J Neurosurg. 1958, 15(2): 192–198.

[18] Görtlér M, Braun M, Becker I, et al. Animal experiments with a new Dura graft (polytetrafluorethylene)—results. Neurochirurgia (Stuttg). 1991, 34(4): 103–106.

[19] Perrini P. Technical nuances of autologous pericranium harvesting for dural closure in Chiari malformation surgery. J Neurol Surg B Skull Base. 2015, 76(2): 90–93.

[20] Chen JC, Li YN, Wang T, et al. Comparison of posterior Fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation type I in adult patients: A retrospective analysis of 103 patients. Medicine (Baltimore). 2017, 96(4): e5945.

[21] Rosomoff HL, Malinin TI. Freeze-dried allografts of Dura mater - 20 years’ experience. Transplant Proc. 1976, 8(2 Suppl 1): 133–138.
[22] Thadani V, Penar PL, Partington J, et al. Creutzfeldt-Jakob disease probably acquired from a cadaveric dura mater graft. Case report. J Neurosurg. 1988, 69(5): 766–769.

[23] Kobayashi A, Kitamoto T, Mizusawa H. Iatrogenic creutzfeldt-Jakob disease. In: Human Prion Diseases. Elsevier, 2018.

[24] Ae R, Hamaguchi T, Nakamura Y, et al. Update: Dura mater graft-associated Creutzfeldt-Jakob disease - Japan, 1975-2017. MMWR Morb Mortal Wkly Rep. 2018, 67(9): 274–278.

[25] Shijo M, Honda H, Koyama S, et al. Dura mater graft-associated Creutzfeldt-Jakob disease with 30-year incubation period. Neuropathology. 2017, 37(3): 275–281.

[26] Marton E, Giordan E, Gioffrè G, et al. Homologous cryopreserved amniotic membrane in the repair of myelomeningocele: preliminary experience. Acta Neurochir (Wien). 2018, 160(8): 1625–1631.

[27] Tomita T, Hayashi N, Okabe M, et al. New dried human amniotic membrane is useful as a substitute for dural repair after skull base surgery. J Neurol Surg B Skull Base. 2012, 73(5): 302–307.

[28] Lee JH, Choi SK, Kang SY. Reconstruction of chronic complicated scalp and dural defects using acellular human dermis and latissimus dorsi myocutaneous free flap. Arch Craniofac Surg. 2015, 16(2): 80–83.

[29] Azzam D, Romiyo P, Nguyen T, et al. Dural repair in cranial surgery is associated with moderate rates of complications with both autologous and nonautologous dural substitutes. World Neurosurg. 2018, 113: 244–248.

[30] Seo Y, Kim JW, Dho YS, et al. Evaluation of the safety and effectiveness of an alternative dural substitute using Porcine pericardium for duraplasty in a large animal model. J Clin Neurosci. 2018, 58: 187–191.

[31] Sun HT, Wang HD, Diao YF, et al. Large retrospective study of artificial Dura substitute in patients with traumatic brain injury undergo decompressive craniectomy. Brain Behav. 2018, 8(5): e00907.

[32] Lee CK, Mokhtari T, Connolly ID, et al. Comparison of Porcine and bovine collagen dural substitutes in posterior fossa decompression for Chiari I malformation in adults. World Neurosurg. 2017, 108: 33–40.

[33] Li Q, Mu LL, Zhang FH, et al. A novel fish collagen scaffold as dural substitute. Mater Sci Eng: C. 2017, 80: 346–351.

[34] Li Q, Zhang FH, Wang HM, et al. Preparation and characterization of a novel acellular swim bladder as dura mater substitute. Neurol Res. 2019, 41(3): 242–249.

[35] Pierson M, Birinyi PV, Bhimireddy S, et al. Analysis of decompressive craniectomies with subsequent cranioplasties in the presence of collagen matrix dural substitute and polytetrafluoroethylene as an adhesion preventative material. World Neurosurg. 2016, 86: 153–160.

[36] Xiong NX, Tan DA, Fu P, et al. Healing of deep wound infection without removal of non-absorbable Dura mater (neuro-patch®): A case report. J Long Term Eff Med Implants. 2016, 26(1): 43–48.

[37] Huang YH, Lee TC, Chen WF, et al. Safety of the nonabsorbable dural substitute in decompressive craniectomy for severe traumatic brain injury. J Trauma. 2011, 71(3): 533–537.

[38] Deng KX, Yang YY, Ke YQ, et al. A novel biomimetic composite substitute of PLLA/gelatin nanofiber membrane for Dura repairing. Neurol Res. 2017, 39(9): 819–829.

[39] Schmalz P, Griessenauer C, Ogilvy CS, et al. Use of an absorbable synthetic polymer dural substitute for repair of dural defects: A technical note. Cureus. 2018, 10(1): e2127.

[40] Suwanprateeb J, Luangwattanawilai T, Theeranattapong T, et al. Bilayer oxidized regenerated cellulose/poly ε-caprolactone knitted fabric-reinforced composite for use as an artificial dural substitute. J Mater Sci Mater Med. 2016, 27(7): 122.

[41] Chi YY, Le YJ, Liu XZ, et al. Biological properties, degradation and absorption of collagen sponges in vivo (in Chinese). Chin J Tissue Eng Res. 2014, 18: 5515–5519.

[42] Zhang YL, Zeng YL, Zou LJ, et al. Antigenicity of freeze-dried irradiated pig dura mater (in Chinese). J Clin Rehabilitative Tissue Eng Res. 2008, 12(53): 9950–9952.

[43] Zhang YL, Zeng YL, Xin GH. Determination of freeze-dried and irradiated porc dural resistant ability to collagenase digestion and biomechanics. J Clin Rehabilitative Tissue Eng Res. 2010, 14(53): 9950–9952.

[44] Wu LC, Kuo YJ, Sun FW, et al. Optimized decellularization protocol including α-Gal epitope
reduction for fabrication of an acellular Porcine annulus fibrosus scaffold. *Cell Tissue Bank.* 2017, 18(3): 383–396.

[45] Han L, Zhang ZW, Wang BH, et al. Construction and biocompatibility of a thin type I/II collagen composite scaffold. *Cell Tissue Bank.* 2018, 19(1): 47–59.

[46] Xu Y, Cui WG, Zhang YX, et al. Hierarchical micro/nanofibrous bioscaffolds for structural tissue regeneration. *Adv Healthcare Mater.* 2017, 6(13): 1601457.

[47] Hu Y, Dan WH, Xiong SB, et al. Development of collagen/polydopamine complexed matrix as mechanically enhanced and highly biocompatible semi-natural tissue engineering scaffold. *Acta Biomater.* 2017, 47: 135–148.

[48] Lv FY, Dong RH, Li ZJ, et al. In situ precise electrospinning of medical glue fibers as nonsuture dural repair with high sealing capability and flexibility. *Int J Nanomedicine.* 2016, 11: 4213–4220.

[49] Kurpinski K, Patel S. Dura mater regeneration with a novel synthetic, bilayered nanofibrous dural substitute: an experimental study. *Nanomedicine (Lond).* 2011, 6(2): 325–337.

[50] Flanagan KE, Tien LW, Elia R, et al. Development of a sutureless dural substitute from Bombyx mori silk fibroin. *J Biomed Mater Res Part B Appl Biomater.* 2015, 103(3): 485–494.

[51] Visanji NP, Lang AE, Munoz DG. Lymphatic vasculature in human dural superior sagittal sinus: Implications for neurodegenerative proteinopathies. *Neurosci Lett.* 2018, 665: 18–21.

[52] Lohrberg M, Wilting J. The lymphatic vascular system of the mouse head. *Cell Tissue Res.* 2016, 366(3): 667–677.

[53] Patel TK, Habimana-Griffin L, Gao XF, et al. Dural lymphatics regulate clearance of extracellular tau from the CNS. *Mol Neurodegener.* 2019, 14(1): 11.

[54] Yanev P, Poinsette K, Hominick D, et al. Impaired meningeal lymphatic vessel development worsens stroke outcome. *J Cereb Blood Flow Metab.* 2019: 0271678X1882292.

[55] Wen YR, Yang JH, Wang X, et al. Induced dural lymphangiogenesis facilitates soluble amyloid-beta clearance from brain in a transgenic mouse model of Alzheimer’s disease. *Neural Regen Res.* 2018, 13(4): 709–716.

**Qiang Ao** received his M.D. degree from Dalian Medical University, China (2003) and then received his postdoctoral training in Tsinghua University. He was an associate professor of neuroscience in Tsinghua University (2007–2014), then a professor of China Medical University (2014–2019), and is now a professor in School of Biomedical Engineering, Sichuan University, China. He has published more than 100 papers on journals including *Biomaterials, Brain Stimulation, Acta Biomaterialia.* His current research interests include the biomaterials and stem cells related regeneration and reconstruction of tissues and organs. E-mail: aoqiang@tsinghua.edu.cn

**Weizuo Wang** received his Master’s degree on Neurosurgery from China Medical University in July 2014. Now he is a Ph.D. candidate in the Department of Tissue Engineering, China Medical University. He is an attending doctor of Neurosurgery in the Fourth Affiliated Hospital of China Medical University, China. His research focuses on evaluation and preparation of dural substitutes, repair and functional reconstruction of central nervous system. E-mail: wzwang@cmu.edu.cn