Proposing Novel Biological Scaffolds for the Regeneration of the Dura Mater

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Introduction

The dura mater (DM), a protective membrane that envelops the brain and spinal cord, is crucial for maintaining cerebrospinal fluid (CSF) integrity and preventing infections. Damage to the dura—caused by trauma, surgery, or degenerative conditions—exposes neural tissues to pathogens like Streptococcus pneumoniae and necessitates urgent repair. Current strategies employ biological scaffolds, particularly decellularized tissues, to promote regeneration while minimizing immune rejection. This review examines next-generation biological scaffolds for DM repair, focusing on their mechanical properties, biocompatibility, and clinical translation. Decellularized scaffolds preserve extracellular matrix (ECM) components, thereby supporting cell growth, angiogenesis, and reducing inflammation. Advancements in tissue engineering and personalized medicine hold promise for improving neurosurgical outcomes.

Aims

1. Examine literature on biomimetic characteristics for DM scaffold fabrication.
2. Overview of approaches for dural regeneration, with a focus on biological scaffolds and material innovations.
3. Propose novel scaffolds, recommend context-specific materials (e.g., high-tension vs. low-tension sites), and highlight emerging methodologies to guide researchers and neurosurgeons.

Methods

This comprehensive review analyzed literature on dural substitutes: natural, synthetic, and composite grafts. We assessed their properties, efficacy, and therapeutic applications. Fabrication methods included validated decellularization techniques (chemical, enzymatic, physical) and advanced processing (electrospinning, 3D bioprinting). Evaluation criteria encompassed mechanical strength, biochemical composition, residual DNA content (<50 ng/mg), degradation kinetics, and biocompatibility. Clinical outcomes, complication rates, and host responses in preclinical/clinical studies were compared. Selection factors for surgical scenarios (defect size/location, patient comorbidities) were evaluated.

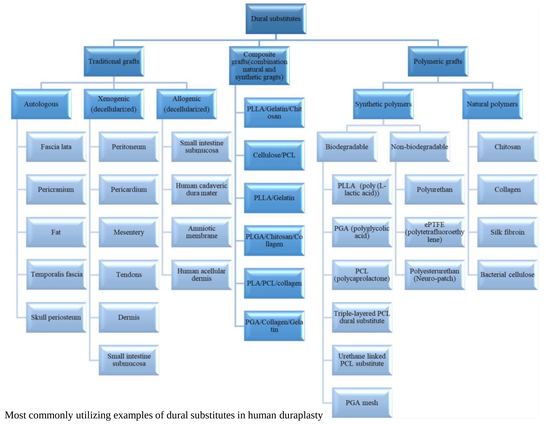
Results

Decellularized ECM (dECM) scaffolds effectively address limitations of current DM substitutes (e.g., immunogenicity, mechanical mismatch). Derived from xenogeneic sources (porcine/bovine pericardium, amniotic membrane), dECM preserves native ECM architecture (collagen, glycosaminoglycans), enhancing biocompatibility and integration. Preclinically, decellularized porcine DM promotes fibroblast proliferation and reduces inflammation vs. synthetics, with tensile strength (7–22 MPa) matching human DM (7.2 MPa). Multilayered composites (e.g., PCL/chitosan/gelatin) exhibit superior mechanics (>20 MPa) and prevent CSF leakage.

Clinically, commercial dECM products (DuraGen, TissuDura) achieve a watertight closure in spinal and cranial repairs with a complication rate of ≤3.1%. However, protocol variability (detergent concentration, sterilization) compromises scaffold consistency, potentially risking batch-to-batch variability, underscoring the need for standardization. Recent studies demonstrate that dECM scaffolds support enhanced angiogenesis and neural regeneration compared to synthetic alternatives, leading to improved functional neurological outcomes in animal models. Innovations like 3D-bioprinted dECM hydrogels with tailored pore structures and antibacterial composites (oxidized guar gum-crosslinked pericardium) enable personalized repair, offering anti-adhesion and neovascularization support. Key challenges include optimizing autologous recellularization and ensuring long-term biomechanical stability. Additionally, ongoing clinical trials are further validating these findings in diverse patient populations, with early results indicating favorable long-term safety and integration.

Demanded feature	Positive	Negative
Leakage blockade (water tightness)	PLA, PGA, PLGA, PGC, PEG hydrogel, quaternized guar gum	Alginate hydrogels, bacterial cellulose, collagen, chitosan, fibrinogen, gelatin, human amniotic membrane, and silk fibroin
Adhesion prevention	Freeze-dried gelatin, Alginate, Chitosan, Hyaluronic acid, Pullulan, Dextran, and derivative, Cellulose and derivative, PCL, PLA, PLGA, PVA, PEG	
Antibacterial property	Chitosan, oxidized quaternized guar gum	
Dura reconstruction (mimic the natural dura)	Gelatin, chitosan	
Appropriate biocompatibility	Alginate hydrogels, bacterial cellulose, collagen, chitosan, fibrinogen, gelatin, human amniotic membrane, and silk fibroin, quaternized guar gum	
Postsurgical complication		PLA, PGA, PLGA, PGC, PEG hydrogel, PCL

Investigation of materials and methods for novel biological scaffolding for dural substitute based on positive and negative features. PCL, polycaprolactone; PEG, poly(ethylene glycol); PGA, polyglycolic acid; PGC, poly(Glycolic Acid); PLA, polylactic acid; PLGA, poly lactic-co- Glycolic acid; PVA, polyvinyl alcohol.



Most commonly utilizing examples of dural substitutes in human duraplasty

Conclusions

Functional tissue reconstitution represents an innovative approach in tissue engineering and regenerative medicine, focusing on curing and replacing damaged or non-functional tissues. This emerging field, known as TERM (Tissue Engineering and Regenerative Medicine), integrates materials science, biology, and medical practices to develop advanced solutions for tissue repair and regeneration. Recent findings highlight novel strategies that provide creative solutions to significant challenges in the TERM industry, potentially leading to groundbreaking innovations.

One of the key advancements is the mass production of bioactive temporary implants designed with customized porosity and structure, addressing the complexities of personalized medicine. The use of three-dimensional (3D) scaffolding and hydrogel-based matrices enables effective treatment delivery for various diseases. Hydrogel matrices are particularly notable due to their high-water content, rigidity, and structural similarities to the natural extracellular matrix (ECM), making them ideal for tissue scaffolding applications. Moreover, 3D bioprinted hydrogels serve as precise biomimetic matrices for developing high-throughput in vitro models, enhancing research capabilities.

Decellularized ECM (dECM) has gained prominence in TERM, as it retains the original ECM's structure and biomolecules. dECM can be utilized as scaffolds, hydrogels, or bioinks, either independently or in combination with other materials, to support diverse tissue types. However, challenges remain, particularly regarding the consistency of results across studies, which can be improved through standardized decellularization methods. Despite the limited number of clinically approved tissue-engineered products, there is a marked shift towards targeted therapies facilitated by 3D technology, especially in cellular scaffold techniques. Composites, combining polymer and ceramic biomaterials, show promise for creating durable, biocompatible, and biodegradable structures. To translate these findings into clinical applications, further long-term research is essential to ensure effective implant-tissue interactions and structural integrity.

While considerable progress has been made, the development of an ideal dural replacement that mimics the native dura mater remains a priority. Future advancements in composite materials, 3D printing, and regenerative techniques are crucial for enhancing dural repair treatments. Ongoing research will provide valuable insights for clinicians and manufacturers, paving the way for improved patient outcomes in tissue engineering.