EVIDENCE FOR SYNTHECEL® DURA REPAIR

Introduction

This value analysis brief presents evidence for SYNTHECEL® Dura Repair in the repair of dura mater (duraplasty) during cranial surgery, following traumatic, neoplastic, or inflammatory destruction. Materials used for dura replacement include human tissues, animal tissues, polymers, and biosynthetics. The ideal material should prevent CSF leakage, be biocompatible, be free of potential risk of infection, have excellent intra-operative handling, and be readily available. An ideal dura substitute should also have no harmful foreign body reaction, have mechanical properties similar to human dura, and be storable.

The search for the most suitable dura mater substitute continues because of the various disadvantages of the many materials used to date. Native autologous tissue grafts can perform well because they do not provoke severe inflammatory or immunological reactions, but potential drawbacks such as difficulty in achieving a watertight closure, formation of scar tissue, insufficiently accessible graft materials to close large dural defects, and additional incisions for harvesting the graft remain problematic. Off-the-shelf dural substitutes have been developed as alternatives to autologous transplantation and various xenografts have been studied, however these xenografts may be associated with adverse effects such as graft dissolution, encapsulation, foreign body reaction, scarring, and adhesion formation.

Methods

We conducted a review of peer-reviewed published literature using EMBASE, Medline, Google Scholar, PubMed and Scopus databases. Clinical and laboratory studies evaluating outcomes associated with the use of SYNTHECEL Dura Repair were evaluated. The search terms used were SYNTHECEL Dura Repair ‘biosynthesized cellulose’, ‘acellular graft’ and ‘(Synthes or Xylos) and dura’, and the search was limited to articles published in the past 10 years. Reference lists of selected studies were also reviewed for possible additional articles.
Executive Summary

Results across studies showed:
- No risk of disease transmission, superior device strength, and superior seal quality with SYNTHECEL Dura Repair (Table 1)\(^9,10\)
- SYNTHECEL Dura Repair thickness is similar to human dura and conforms to the brain\(^9,22,23\)
- SYNTHECEL Dura Repair is immunologically inert and has demonstrated minimal foreign body response\(^8\)

Table 1: Primary and Secondary Endpoints from Studies of SYNTHECEL Dura Repair

<table>
<thead>
<tr>
<th>SYNTHECEL Dura Repair Clinical Evidence</th>
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<tr>
<td>Biosynthesized cellulose</td>
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<td>• Unique construction of non-woven, interconnected cellulose fibers, which creates its strength(^9)</td>
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<td>• Functions as a mechanical layer to cover and repair dural defect while preventing further</td>
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<td>CSF leakage(^9)</td>
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<tr>
<td>• Demonstrated minimal foreign body response and immunologically inert(^8)</td>
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<tr>
<td>No Risk of Disease Transmission</td>
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<tr>
<td>Non-animal derived, no risk of transmissible diseases(^9)</td>
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<td>Sutureability</td>
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<tr>
<td>SYNTHECEL Dura Repair ranked as excellent in sutureability in 30% of cases vs 5.1% of cases in the</td>
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<td>control group(^9)</td>
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<td>Strength of Device</td>
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<tr>
<td>SYNTHECEL Dura Repair exhibited superior device strength compared to control (P&lt;0.0001)(^10)</td>
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<tr>
<td>Seal Quality</td>
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<td>SYNTHECEL Dura Repair exhibited superior seal quality compared to control (P=0.032)(^10)</td>
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Unmet Need in Dura Repair

**Autografts**

Autologous human connective tissue (pericranium, fascia lata) is material taken from the same individual and remains the benchmark material to repair defects in the dura mater. However, surgeons sometimes avoid using autografts because there are instances where there is not enough local replacement material of sufficient quality to fill the dural defect, and therefore they may have to take material from another area of the body (most commonly the fascia lata), requiring a second surgical site.\(^11,12,13\) This increases morbidity to the patient.

**Allografts, Xenografts, and Synthetic Materials**

Allograft dural tissue from human cadavers is not often used by surgeons and more recently has been associated with the transmission of viral infections, including Creutzfeldt-Jakob disease (CJD).\(^14,15,16\) Xenografts and synthetics are the two most commonly used dural graft materials, however, both materials present concerns for patients and surgeons. Synthetics have been associated with deep wound infections.\(^17\) Xenografts have been associated with the transmission of viral infections and have shown risk of hydrodynamic complications. This includes persistent CSF leakage, development of pseudomeningocele, noninfectious or aseptic meningitis, and delayed hydrocephalus.\(^18\)
A timeline of the evolution of technological advancement, research, and practice patterns in dura replacement is presented in figure 1.2,15,16,17,19,20,21

**Figure 1: Timeline of the Technological advancement, Research, and practice pattern Evolution in Dura Replacement**

- Rubber Tissue Implantation by Abbe
- Freeze-dried Vacuum-Stored Human Dural Tissue by Campbell
- PRECLUDE synthetic polymer from WL Gore received FDA approval
- Epidemic of bovine spongiform encephalopathy in cattle and emergence of a new variant of Creutzfeldt-Jakob disease
- Human cadaveric dural tissue associated with transmission of viral infections, including Creutzfeldt-Jakob disease, placed under special controls by the FDA
- Found that polymers may become chronically colonized, microorganisms, necessitating removal to eradicate promoting continued growth of infection
- Animal tissues are the most widely-used materials
- 2014 Synthes launches SYNTHECEL Dura Repair – Biosynthesized Cellulose Dural Replacement

**Results**

**Clinical Studies of SYNTHECEL Dura Repair**

Rosen et al. (2011) conducted a 6-month prospective randomized controlled trial (RCT) to establish that SYNTHECEL Dura Repair was not inferior compared with other commercially-available dural replacement products (made of bovine collagen (97.3%) and synthetic material (2.7%) (N=99).

**Overall Effectiveness**

The primary hypothesis, non-inferiority of SYNTHECEL Dura Repair was confirmed (p = 0.0206). No significant difference was revealed between groups for surgical site infection (p = 1.0000), wound healing assessment (p ≥ 0.3685), or radiologic endpoints (absence of pseudomeningocele and CSF fistula) (p ≥ 0.4061).
**Handling Qualities**

Superior handling qualities were evident with SYNTHECEL Dura Repair in the RCT. Ease of use was similar among products; however, device strength, sutureability, and seal quality favored SYNTHECEL Dura Repair. A statistically significant difference in favor of patients implanted with SYNTHECEL Dura Repair over control was observed for both device strength ($p<0.0001$) and device seal quality ($p=0.032$).

Figures 2-5 illustrate the secondary endpoints of the surgeon’s assessment of device handling characteristics across the patients treated ($n=62$ SYNTHECEL Dura Repair, $n=37$ for control; the number of implants was used as the denominator to compute all percentages and patients may have had more than 1 implant).

Figure 2: Ease of Use was Similar Among Products

Figure 3: SYNTHECEL Dura Repair Exhibited Superior Device Strength Compared to Control

Figure 4: SYNTHECEL Dura Repair Ranked Excellent in 30% of Cases vs. 5.1% in the Control Group in Sutureability

Figure 5: SYNTHECEL Dura Repair Exhibited Superior Seal Quality Compared to Control

*N/A= Not Applicable; A comparative analysis was not completed since the sample sizes across groups were too low for comparison*
Laboratory Studies of SYNTHECEL Dura Repair

An in vivo laboratory study of 36 New Zealand rabbits evaluated the local response and the efficacy of SYNTHECEL Dura Repair as compared to commercially available dural membranes DuraGen® (Integra LifeSciences Corporation) and Dura-Guard® Dural Repair Patch (Synovis Surgical Innovations). Gross evaluation and histopathologic evaluation in the rabbit craniotomy model at the implant sites at 2, 4, and 13 weeks post implantation demonstrated that SYNTHECEL Dura Repair was equivalent to DuraGen and Dura-Guard Dural Repair Patch when used to replace the dural membrane. The local inflammation response to SYNTHECEL Dura Repair two weeks after implantation was similar to that of DuraGen and less than that of Dura-Guard Dural Repair Patch (Figure 6).

Figure 6: Local inflammatory response to SYNTHECEL Dura Repair, DuraGen, and Dura-Guard Dural Repair two weeks after implantation*

Conformable

SYNTHECEL Dura Repair is similar in thickness to human dura and conforms to the brain (SYNTHECEL Dura Repair is 0.26 mm and human dura is 0.35-0.58 mm).\textsuperscript{9,22,23}

Hospital Inventory Management

Handling, moving, and processing of materials constitute about 35% to 40% of total supply chain costs in hospitals.\textsuperscript{24,25} Improving medical and medical supply inventory management provides a great opportunity to improve hospital savings.\textsuperscript{24,25} SYNTHECEL Dura Repair is one product choice for excellent onlay or suture performance.

Discussion

Based on these results, use of SYNTHECEL Dura Repair is expected to result in no risk of disease transmission and excellent sutureability, seal quality, and strength.
More About SYNTHECEL Dura Repair

SYNTHECEL Dura Repair is an assured and versatile solution for dura reconstruction needs:

• Clinically proven efficacy and favorable safety profile\textsuperscript{10}
• One product choice for excellent onlay or suture performance
• Excellent handling
• Non-animal derived, no risk of transmissible diseases
• Non-progenetic
• MR Safe

References

8 SYNTHECEL Dura Repair Instructions for Use GP2715-B 6/14.
9 Mechanical test data on file at DePuy Synthes. Mechanical test results are not necessarily indicative of clinical performance.
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