Value Analysis Brief

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.1 An ideal dura substitute should also have no harmful foreign body reaction, have mechanical properties similar to human dura, and be storable.2

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.3 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.3,4,5

SYNTHECEL Dura Repair is an implant based on biosynthesized cellulose technology. Biosynthesized cellulose technology has been used as a wound dressing.6 The organism Gluconacetobacter xylinus (formally Acetobacter xylinum) is propagated in a nutritive culture media and forms a cellulose pellicle of a specified weight and cellulose content (g cellulose/cm²).7 SYNTHECEL Dura Repair has a unique construction of non-woven, interconnected cellulose fibers, which creates its strength. It functions as a mechanical layer to protect and repair the dural defect while preventing further cerebrospinal fluid (CSF) leakage. SYNTHECEL Dura Repair is immunologically inert and has demonstrated minimal foreign body response. It is a non-resorbable dural graft with no adhesion formations, as demonstrated in a clinical trial, and is magnetic resonance (MR) safe. SYNTHECEL Dura Repair is packaged wet and ready to use as one product for either onlay or suture application.

Methods

We conducted a systematic 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 ‘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.
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Executive Summary

Aggregated results across studies showed no adhesions, no risk of disease transmission, superior device strength, and superior seal quality with SYNTHECEL Dura Repair (Table 1).8,9 SYNTHECEL Dura Repair thickness is similar to human dura and conforms to the brain.8,23,24

Table 1: Summary of Results for SYNTHECEL Dura Repair

<table>
<thead>
<tr>
<th>SYNTHECEL Dura Repair Clinical Evidence</th>
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<tbody>
<tr>
<td><strong>Biosynthesized cellulose</strong></td>
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<tr>
<td>• Unique construction of non-woven, interconnected cellulose fibers, which creates its strength8</td>
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<tr>
<td>• Functions as a mechanical layer to protect and repair dural defect while preventing further CSF leakage8</td>
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<tr>
<td>• Demonstrated minimal foreign body response and immunologically inert9</td>
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<td><strong>No Adhesions</strong></td>
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<td>No adhesion formations were observed in the 6-month randomized clinical study9</td>
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<td><strong>No Risk of Disease Transmission</strong></td>
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<td>Non-animal derived, no risk of transmissible diseases8</td>
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<tr>
<td><strong>Sutureability</strong></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 control group9</td>
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<tr>
<td><strong>Strength of Device</strong></td>
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<tr>
<td>SYNTHECEL Dura Repair exhibited superior device strength compared to control (P&lt;0.0001)9</td>
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<td><strong>Seal Quality</strong></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. Autologous tissue does not induce an immunologic or severe inflammatory response and there is no risk of transmissible diseases.10 Surgeons sometimes avoid using autograft 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.10,11,12 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).13,14,15 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.16 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.17
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A timeline of the evolution of technological advancement, research, and practice patterns in dura replacement is presented in Figure 1.2,14,15,16,18,19,20

**Figure 1:** Timeline of the Technological Advancement, Research, and Practice Pattern Evolution in Dura Replacement

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**Adhesion Formation**

Adhesion formation between dura mater and cortex and the overlying temporalis muscle and galea following decompressive craniectomy, can make subsequent cranioplasty difficult and adds to the risks of the procedure.21 Adhesions between graft and cortex may also be clinically significant because they might act as an epileptic focus.4 Thus, graft material to be used for dural repair should either not produce cortical adhesions or form minimal ones.

**Results**

**Clinical Studies of SYNTHECCEL Dura Repair**

Rosen et al. (2011)9 conducted a 6-month prospective randomized controlled trial (RCT) to establish that SYNTHECCEL 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 SYNTHECCEL Dura Repair was confirmed (P = 0.0206).9 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).9 A statistically significant difference in favor of patients implanted with SYNTHECCEL Dura Repair over control was observed for both device strength (P<0.0001) and device seal quality (P =0.032).9

**Handling Qualities**

Superior handling qualities were evident with SYNTHECCEL Dura Repair in the RCT.8 Ease of use was similar among products; however device strength, sutureability, and seal quality favored SYNTHECCEL Dura Repair.9
Figures 2-5 illustrate 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).^{9}

**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
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 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 was equivalent to DuraGen and Dura-Guard Dural Repair Patch when used to replace the dural membrane. The local inflammation response to SYNTHECEL 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).

Hospital Inventory Management

Handling, moving, and processing of materials constitute about 35% to 40% of total supply chain costs in hospitals. Improving medical and medical supply inventory management provides a great opportunity to improve hospital savings. 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 adhesions, no risk of disease transmission, superior device strength, and superior seal quality.
More About SYNTHECEL Dura Repair

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

- Clinically proven
- One product choice for excellent onlay or suture performance
- Superior handling
- No adhesions*
- Non-animal derived, no risk of transmissible diseases
- Non-progenic
- MR Safe

*Observed in clinical study.

References

15. Data on file. Depuy Synthes Test bench testing and charts from IDE.
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Rx Only

Not all products are currently available in all markets.