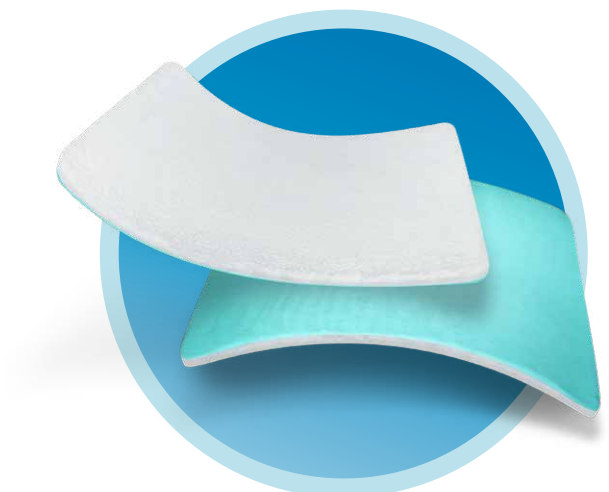
LIQOSEAL®

CERTAINTY IN WATERTIGHT DURAL CLOSURE



EVIDENCE-BASED PERFORMANCE

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LIQOSEAL®

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Cerebrospinal fluid (CSF) leakage is a widely recognized complication after neurosurgical procedures. It represents a significant patient burden, resulting in increased morbidity, prolonged hospital stays, possible surgical revisions, and enhanced costs.[1,2] Incidence rates vary depending on age, indication, location of surgery and underlying pathology, but in total CSF leakage occurs in 4-32% of surgical cases.[3,4]

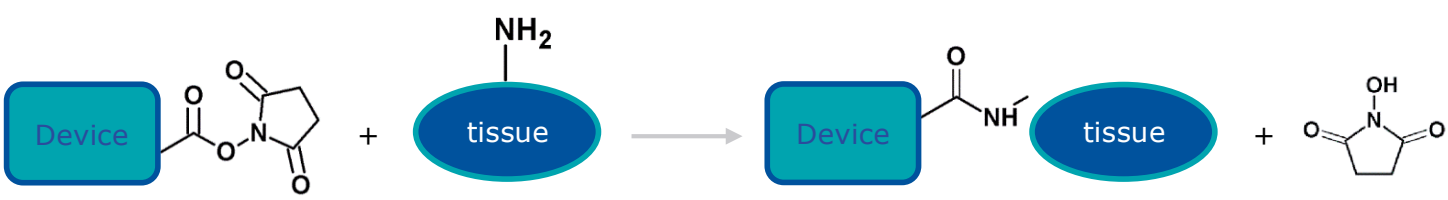
Achieving **watertight dural closure** to provide effective control of CSF leakage is a challenge. A puncture from a single needle is sufficient to cause leakage, and during prolonged operative procedures, the fragile dura mater shrinks due to dehydration, further complicating closure.

Effective dural sealants should reduce the risk of CSF leakage after cranial surgery by enhancing dural closure. However, a recent review showed that existing commercially available **dural sealants have not proven to significantly reduce post-operative CSF leakage** compared to suturing alone (8.2% versus 8.4% respectively).[3]

LIQOSEAL® provides certainty in watertight dural closure after cranial surgery. Our dural sealant patch was developed using an evidence-based approach. The data underlining its design and performance in comparison to existing market leaders is outlined below.

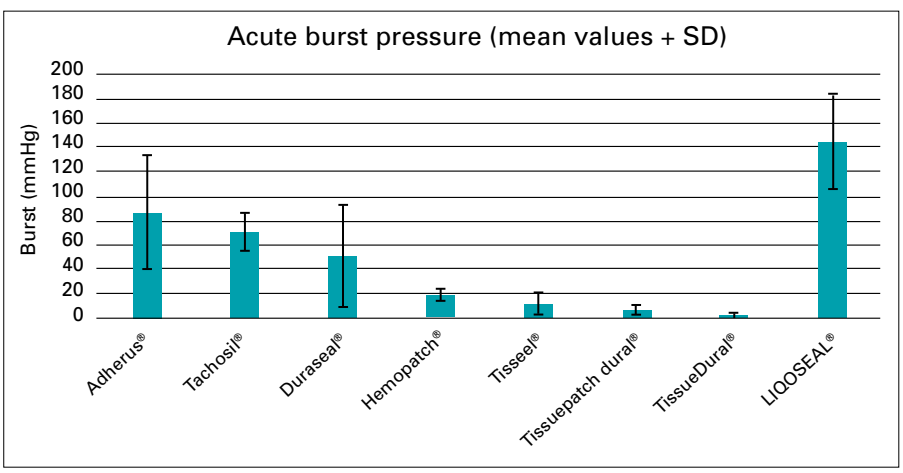
LIQOSEAL® - BASED ON PROVEN TECHNOLOGY

LIQOSEAL® uses Polyganics' proprietary bioresorbable polymer technology, which is already applied worldwide in multiple clinical areas. LIQOSEAL® is indicated for use as an adjunct to standard methods of cranial dural repair to provide a water-tight closure of the dura mater and reduce CSF leakage. The mode of action is explained in the graphic below.



LIQOSEAL® - EFFECTIVE AND ENDURING

LIQOSEAL® shows strong acute tissue adhesion[a] and is able to resist a higher acute burst pressure[b] (145 mm Hg)[6]. In case of chronic burst pressure testing[c] LIQOSEAL® compares favorably to existing available products when compared with existing sealants.[4,6] LIQOSEAL® maintains attached, whereas Tachosil® failed after 1,4 hours.[4,6]



a. in-house evaluation according to the ASTM standard F2392-4

b. pressure increase measurements immediately after application

c. pressure measurement during a period of 72 hours after application with 3-phase intracranial pressure fluctuations; test method is ASTM modified but developed by the Brain Technology Institute, BTI

LIQOSEAL®

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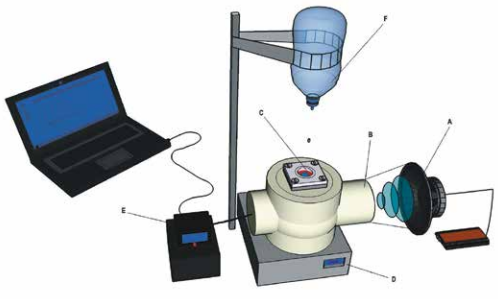
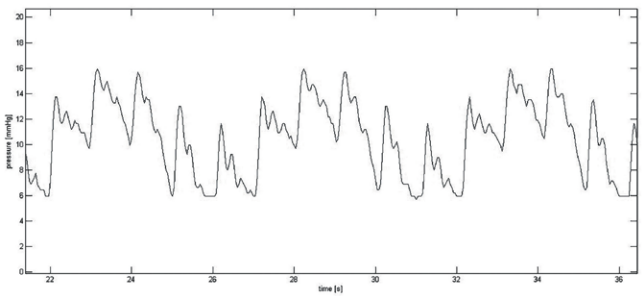
A



A: speaker with generated wave
B: Membrane in container filled with (artificial) cerebrospinal fluid connected to the speaker (a)
C: Dura
D: Temperature controller
E: Pressure meter connected to computer
F: Dropper

B



3-phase intracranial pressure fluctuation test-set-up

(Van Doormaal et al. 2017)

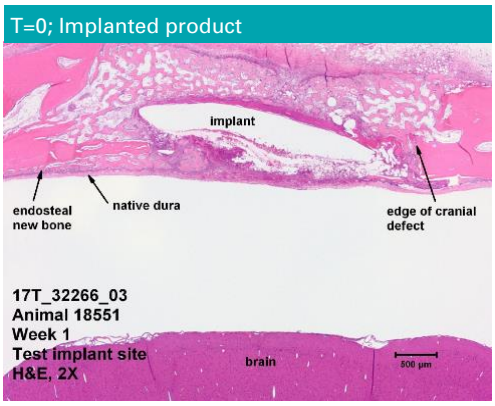
LIQOSEAL® - PROLONGED WATERTIGHT DURAL CLOSURE

In the international, multi-centered ENCASE clinical study[8] (Utrecht, The Netherlands, Zurich, Switzerland, Tilburg, The Netherlands), ***all patients met the primary endpoints: no CSF leakage after a period of 3 months***, strongly confirming watertight closure. Additionally, no clinically significant swelling was observed and no device related adverse events were reported. Safety end-points will continue to be collected for a period of 12 months.

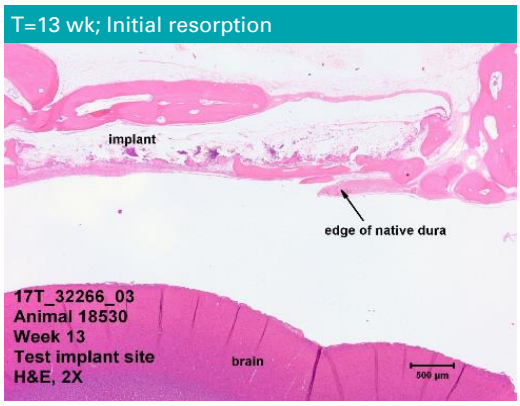
LIQOSEAL® - SAFE AND SUPPORTS HEALING

Histological data indicate a minimal foreign body response to LIQOSEAL®, as is anticipated to occur with implanted devices. A small number of macrophages and giant cells are observed (granulomatous reaction) followed by local formation of fibrotic tissue related to formation of 'neodura' between the patch and the brain. No to minimal local reaction is elicited by the device. An additional study confirms that LIQOSEAL® supports regeneration of the dura mater by acting as a scaffold for formation of the new fibrotic layer 'neodura'[5,7]. Resorption and integration of LIQOSEAL® is considered to be complete at 31 weeks, after which it shows a steady stage.

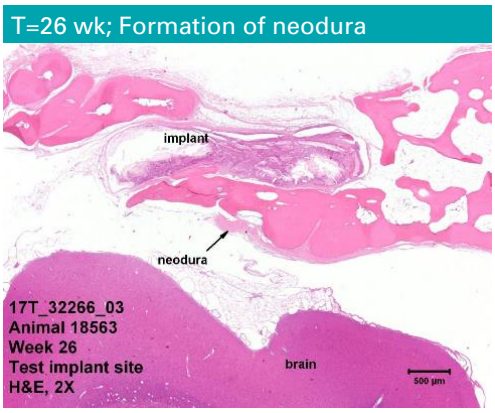
T=0; Implanted product



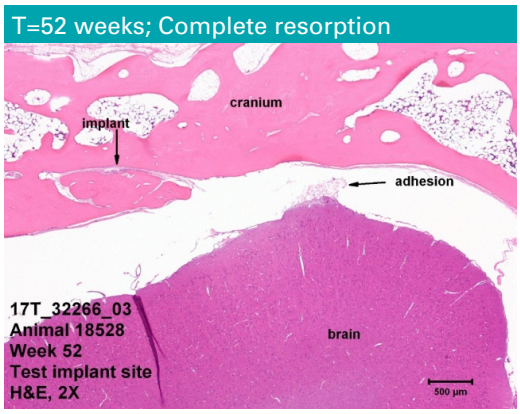
T=13 wk; Initial resorption



T=26 wk; Formation of neodura



T=52 weeks; Complete resorption



Histological analyses at different time points. LIQOSEAL® is tightly adhered to the dura and is infiltrated with inflammatory cells. A thin fibrotic layer neodura forms on the LIQOSEAL® scaffold.

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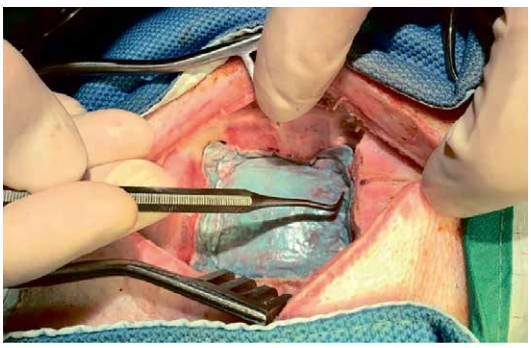
LIQOSEAL® - EASY TO USE

The soft and pliable patch is easy to apply and ready to use.
It requires no time-consuming preparation, or applicators, does not swell, is impermeable and is safely resorbed after use.[5]



LIQOSEAL® - DEDICATED DEVELOPMENT

LIQOSEAL® is developed in close collaboration with the Brain Technology Institute (BTI), Utrecht, The Netherlands, a consortium of internationally renowned institutes focused on clinical and research aspects of neurosurgery.

ORDERING INFORMATION

Article number	Size
DS01-024/08	8x8cm

LIQOSEAL® is supplied as 1 unit per box. It is packed in a Tyvek blister and subsequently placed in an aluminum pouch and carton box. LIQOSEAL® is a double-layered patch (white color site and green-blue fluid barrier) and is indicated for single use. It is supplied sterile. It should be stored in the freezer (< -15 C/0°F). The shelf life is at least 18 months. Within 8 months the device is considered to be essentially resorbed and integrated (based on animal data)[5]

References

1- Hutter G, von Felten S, Sailer M, Schulz M, Mariani L. Risk factors for postoperative CSF leakage after elective craniotomy and the efficacy of fleece bound tissue sealing against dural suturing alone: a randomized controlled trial. J. Neurosurgery. 2014. Sep; 121:724-744

2- Grotenhuis J. Costs of postoperative cerebrospinal fluid leakage: 1-year, retrospective analysis of 412 consecutive nontrauma cases. Surg Neurol. 2005, Dec; 64(6)l:490-3

3- Kinaci A, Algra A, Heuts S, O'Donnell D, van der Zwan A, van Doormaal T. Effectiveness of Dural Sealants in Prevention of Cerebrospinal Fluid Leakage After Craniotomy: A Systematic Review. World Neurosurg. 2018 Oct;118:368-376

4- Van Doormaal T, Kinaci A, van Thoor S, Redegeld S, Bergmann W, van der Zwan A. Usefullness of sealants for dural closure: evaluation in an in vitro model. Operative neurosurgery. 2017 Volume 0, Number 0:1-8

5- Kinaci A, van der Zwan A, van Doormaal T. EANS2018 Brussels, poster: Evaluation of a new dural sealant patch in a porcine craniotomy model

6- Kinaci A, van der Zwan A, van Doormaal T. EANS2018 Brussels, poster: Development of a dural sealant patch preventing cerebrospinal fluid leakage after cranial surgery

7- Van Doormaal T, Kinaci A, van Thoor S, Redegeld S, van der Zwan A. AANS 2018 New Orleans . poster. Cerebrospinal fluid prevention using a dural sealant; evaluation of current possibilities and design of a new synthetic patch.

8- ENCASE-1: Single-arm, open-label, multi-center (Zurich, CH; Utrecht, NL; Tilburg, NL) study to evaluate the safety and performance of Dura Sealant Patch in reducing CSF leakage following elective cranial surgery. Objective: Clinically assess the safety and performance of the Dura Sealant Patch as a means of reducing intra-as well as post-operative CSF leakage in patients (n=40) undergoing elective cranial intradural surgery with a dural repair closure procedure (clinicaltrial.gov identifier: NCT03566602)

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