CLINICAL INVESTIGATION PLAN

A PROSPECTIVE, RANDOMIZED, CONTROLLED MULTI-CENTER STUDY OF ARTIFASCIA® DURAL REPAIR PATCH COMPARED WITH COMMERCIALLY AVAILABLE DURAL SUBSTITUTES

NEOART STUDY

Protocol Number: CLN-01-1011

Revision 05

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Title	A Prospective, randomized, controlled multi-center study of ArtiFascia® Dural repair patch compared with commercially available dural substitutes- **NEOART Study.**
Device	ArtiFascia®
Intended Use	ArtiFascia® is indicated as a dural substitute for the repair of dura matter.
Study Design	Prospective, randomized, multi-center, two-arm, single blind, parallel group clinical study.
Study Objective	To evaluate the safety and effectiveness of ArtiFascia® in comparison with commercially available dural substitutes in subjects requiring Dural repair following neurosurgery.
Study Population	Men and women scheduled for an elective cranial surgery that requires Dural repair, that meet the inclusion/exclusion criteria and can provide written Informed Consent.
Enrollment	A total of 90 subjects (81 + 9 to account for 10% loss to follow-up rate) will be enrolled and implanted with test or control device. To account for an assumed 10% loss to follow-up rate, additional 9 subjects will be enrolled (60 in the ArtiFascia® group and 30 in the control group).
Study Groups	Subject will randomly be allocated into one of the following two groups in a 2:1 allocation ratio of ArtiFascia and control groups: • *Experimental group*: ArtiFascia® device • *Control group:* Other commercially available suturable dural substitutes (e.g. Duraform, Duragen, Durepair)
Randomization	Study population will be randomized using 2:1 ratio of experimental group (ArtiFascia device recipients) to control group (commercially available dural replacement recipients) respectively and preoperatively blinded.
Duration of Study	Completion of active enrolment is anticipated to last approximately 2 years. The primary endpoint will be achieved when the final study subject has completed a 6-months follow-up. The entire duration of the study is anticipated to require a total of 2.5 years.

Study Enrollment Start Date: November 2019

Estimated Study Enrollment End Date: November 2021

Estimated Study Follow Up Completion: May 2022

Investigational sites	Up to 10 centers in Europe and Israel are planned to participate in this study.
Duration of Subject Participation	Each subject will be followed from pre-treatment to 6 months. After discharge, subjects will come for a clinic visit at 4-6 weeks and at 6 months post implantation.
Primary Endpoint	Absence of CSF fistula (drainage from wound or sinus) and pseudo-meningocele within 6 months post-operative as evaluated by MRI imaging.
Secondary Endpoints	1. Wound healing assessment 2. Device Handling Characteristics (i.e., Ease of Use, strength Suturability, Seal Quality) 3. Magnetic Resonance Imaging at the 6-month follow-up, to determine the presence or absence of the following measures: • Adhesion formation • New tissue formation • Brain edema adjacent to device implant site
Inclusion Criteria	1. Subject between the ages of 18-75 2. Subject is scheduled for an elective cranial surgery with a dural damage that can be completely repaired/closed by a suturable dural substitute (ArtiFascia device or other commercially available dural substitutes) 3. Subject has undergone imaging (such as, MRI) in the past 6 months before enrolment 4. Surgical wound is expected to be Class I/clean 5. Subject understands the study requirements and the treatment procedures and provides written Informed Consent before any study-specific tests or procedures

are performed

6. Subject is able and willing to adhere to the required follow-up visits and testing

Exclusion Criteria

1. Pregnant women or interest in becoming pregnant during the duration of the study
2. Subject has known hydrocephalus
3. Subject is unable to undergo MRI after the surgery
4. Subject's life expectancy is less than 12 months
5. Subject has a local or systemic infection (e.g. urinary tract infection (UTI), active pneumonia) or evidence of any surgical site infection, fever > 38.3°C, positive blood culture and/or a positive chest x-ray for acute infectious process
6. Subject will require use of dural adhesive or sealant
7. Subject is intended to undergo craniectomy wherein bone flap will not be returned
8. Subject with suspected low success in wound healing due to past treatments (e.g. chemotherapy, radiation therapy, severe diabetes etc.) or other conditions (e.g. severe peripheral vascular disease, long standing steroids treatment)
9. Subject has been clinically diagnosed with malignancy (other than basal cell carcinoma or low-grade glioma), uncontrolled diabetes (A1C>6.5%), sepsis, systemic collagen disease.
10. Subject had chemotherapy and/or radiotherapy in the past 12 weeks before surgery or is planned to have chemotherapy or radiotherapy less than 12 weeks after surgery.
11. Subject is an acute cranial trauma surgical case
12. Subjects with a concurrent disease that would place the patient in excessive risk to the planned surgery
13. Subject had a previous neurosurgery in the same

anatomical site

14. Subject with other undesirable symptoms defined by the principal investigator
15. Patient has clinically significant coagulopathy as determined by the surgeon
16. Subject is participating in another clinical trial using similar investigational devices/drugs

Visits and Procedures

Baseline: The baseline visit will include an assessment of subject qualifications for inclusion in the study according to the inclusion/exclusion criteria. Informed consent must be signed. Medical data will be taken including subject's medical complaints, medical history, neurological assessment, and medications use. Blood tests will include CBC and chemistry (according to site standards).

Randomization and Procedure: Vital signs (blood pressure, temperature, pulse rate), as well as height and weight will be measured prior procedure.

The subject will be randomized during the index procedure after the physician confirmation that the subject fulfills all inclusion criteria. If found eligible, subject will be enrolled and randomized to one of the 2 groups: experimental group (ArtiFascia device recipients) or control group (commercially available suturable dural substitutes recipients). In addition, recruitment of subjects planned to undergo surgery in posterior fossa area will be limited to 15% of the total study sample size to ensure comparability to common rates of this procedure reported in the literature.

Procedure will be performed under general anesthesia. ArtiFascia® or the control device will be implanted and sutured according to device IFU. Immediately post procedure essential data will be recorded including procedural details, surgeon's opinion on device ease of use and suture-ability, and other procedure related complications and medications prescribed.

Post operation the subject will stay at the hospital according

to site standards and physician discretion.

Follow-up: After discharge, all subjects will have regular follow-up visits at 4-6 weeks and at 6 months post procedure.

At discharge and at 4-6 weeks and 6-month visits, the following examinations may be performed:

Physical examination of the surgical site to test CSF leakage
Vital signs (blood pressure, temperature, pulse rate)– only at discharge and at 4-6 weeks
Standard assessment of general neurological health
Physical examination of the surgical site to test wound healing
Adverse events will be assessed on a continuous basis from the baseline through the study completion at 6 months, and all events whether related or not related will be reported.
Magnetic Resonance Imaging will be performed 6 months post operation in all subjects.
During the follow-up period MRI may be performed if deemed necessary. In case MRI is performed, the presence of pseudo-meningocele or other internal CSF leakage in the implant area, will be evaluated. If MRI is performed more than 3 months post operation and does not indicate presence of a leak, this data will be used to determine the leak rate and the subject will not be required to undergo an additional MRI at 6 months.