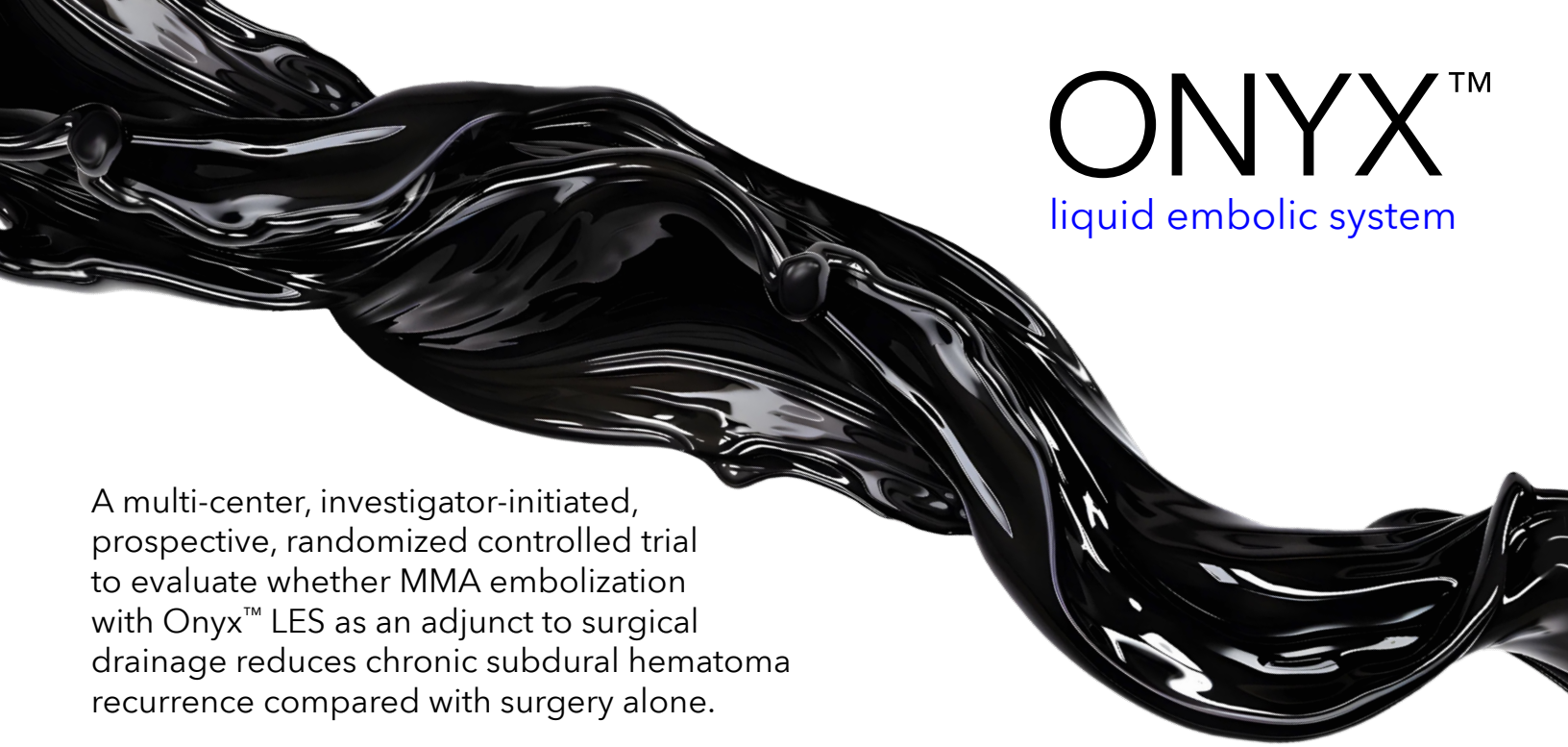

ONYX™
liquid embolic system

A multi-center, investigator-initiated, prospective, randomized controlled trial to evaluate whether MMA embolization with Onyx™ LES as an adjunct to surgical drainage reduces chronic subdural hematoma recurrence compared with surgery alone.

EMMA-Can Key Findings

From August 2021-April 2025, 192 patients were randomized across 9 tertiary care centers in Canada: 98 to the interventional group (surgery + Onyx™ LES embolization) and 94 to the control group (surgery alone). The final analysis included 186 participants with 93 in each group.

Patients embolized within 72 hours after surgical drainage.

84.6% reduction in symptomatic recurrence when combined with surgery (28% vs 4.3%).

0% (0/93) deaths or SAEs related to the embolization procedure.

100%

Onyx™ 18 LES

0% 100%

used in this study

Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population)*

Characteristic	Interventional Group (N=93)	Control Group (N=93)
Age – yr	71.8 ± 10.6	71.9 ± 10.9
Male sex – no. (%)	69 (74.2)	67 (72.0)
Anticoagulant use – no. (%)**	18 (19.4)	10 (10.8)
Subdural hematoma on both sides – no. (%)	2 (2.2)	6 (6.5)
Hematoma volume, mean ± SD, mL	132.2 ± 44.4	131.4 ± 48.6
Hematoma thickness at screening – mm Mean ± SD	22.6 ± 6.0	23.9 ± 5.7
Midline shift at screening – mm Mean ± SD	10.0 ± 4.0	9.4 ± 3.8

* Plus-minus values are mean ±SD. The intention-to-treat population included all the patients who provided informed consent and underwent randomization to undergo middle meningeal artery embolization plus surgery (treatment group) or surgery alone (control group). Some patients excluded due to withdrawn consent, were found to be ineligible, or lost to follow-up. Site reported data.

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In this multicenter randomized trial, adjunctive middle meningeal artery embolization using Onyx™ LES after surgical drainage of unilateral symptomatic chronic subdural hematoma reduced symptomatic recurrence on CT scan. The reduction in recurrence rates observed across multiple contemporary RCTs support MMAe as a promising adjunctive strategy. Larger, pooled analyses and longer-term follow-up are needed to determine its impact on functional recovery, quality of life, and health care utilization.

Onyx™ Liquid Embolic System (LES): Essential Prescribing Information

Complete indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician. This device should be used by physicians with a thorough understanding of angiographic and percutaneous neurointerventional procedures.

Indications for use
1. Onyx™ LES is indicated for presurgical embolization of brain arteriovenous malformations (bAVMs).
2. Onyx™ LES is indicated for embolization of the middle meningeal artery (MMA) as an adjunct to surgery for the treatment of symptomatic subacute or chronic subdural hematoma (SDH).

Contraindications
The use of the Onyx™ LES is contraindicated when any of the following conditions exist: • When optimal catheter placement is not possible. • When provocative testing indicates intolerance to the occlusion procedure. • When vasospasm stops blood flow.

Warnings
• Due to the possibility of electrical arcing with the tantalum metal in the Onyx™ LES material, use of monopolar electrocautery devices for surgical resection of bAVMs embolized with the Onyx™ LES should be avoided. Bipolar devices should be used with caution. • Verify that adequate sedation is used throughout the embolization procedure. Insufficient sedation may result in patient discomfort or movement. Patient movement during embolic agent injection may result in embolization of an unintended vessel. • Failure to continuously mix the Onyx™ LES for the required time (at least 1 minute) may result in inadequate suspension of the tantalum, resulting in inadequate fluoroscopic visualization during delivery. • Use only Medtronic/ev3 Onyx™ LES/DMSO compatible microcatheters indicated for use in the neurovasculature and Medtronic/ev3 Onyx™ LES/DMSO compatible syringes. Other microcatheters or syringes may not be compatible with DMSO and their use can result in thromboembolic events due to catheter degradation. • Use only 1 mL syringe to inject DMSO and the Onyx™ LES. Other syringes may not be compatible with DMSO. • Premature solidification of the Onyx™ LES may occur if microcatheter luer contacts saline, blood or contrast of any amount. • Inject Onyx™ LES immediately after mixing. If the Onyx™ LES injection is delayed, tantalum settling can occur within the syringe resulting in poor visualization of Onyx™ LES during injection. • Do not exceed 0.3 mL/minute injection rate. Animal studies have shown that rapid injection of DMSO into the vasculature may lead to vasospasm and/or angionecrosis. • Only use thumb pressure to inject the Onyx™ LES at the recommended rate of 0.16 mL/minute. Using palm of hand to advance plunger may result in catheter rupture due to over-pressurization in the event of catheter occlusion. • Adequate fluoroscopic visualization must be maintained during the Onyx™ LES delivery to avoid non-target vessel embolization. If visualization is lost at any time during the embolization procedure, STOP the Onyx™ LES delivery until adequate visualization is re-established. • Onyx™ LES can lead to increased procedural risk of unintended embolization when encountering an anatomic variation (e.g., ophthalmic collateral). • Do not allow more than 1 cm of the Onyx™ LES to reflux back over catheter tip. • Angioarchitecture, vasospasm, excessive Onyx™ LES reflux, or prolonged injection time may result in difficult catheter removal and potential entrapment. • Excessive force to remove an entrapped catheter may cause serious intracranial hemorrhage. • The long-term effects of an entrapped catheter that is left in a patient are unknown, but potentially could include clot formation, infection, or catheter migration. • After using a microcatheter with the Onyx™ LES, do not attempt to clear or inject any material through it. Such attempts may lead to embolus or embolization of an unintended area. • STOP injection if the Onyx™ LES is not visualized exiting catheter tip. If the catheter becomes occluded, over-pressurization can occur. During the Onyx™ LES injection, continuously verify that the Onyx™ LES is exiting the catheter tip. Testing has shown that over-pressurization and rupture can occur if 0.05 mL of the Onyx™ LES is injected and is not visualized exiting the catheter tip. • STOP injection if increased resistance to the Onyx™ LES injection is observed. If increased resistance occurs, determine the cause (e.g., the Onyx™ LES occlusion in catheter lumen) and replace the catheter. Do not attempt to clear or overcome resistance by applying increased injection pressure, as use of excessive pressure may result in catheter rupture and embolization of unintended areas. • DO NOT interrupt the Onyx™ LES injection for longer than two minutes prior to re-injection. Solidification of the Onyx™ LES may occur at the catheter tip resulting in catheter occlusion, and use of excessive pressure to clear the catheter may result in catheter rupture. • This device is supplied STERILE for single use only. Do not reprocess or resterilize. Reprocessing and re-sterilization increases the risks of patient infection and compromises device performance. • The safety and effectiveness of the Onyx™ LES as a long term implant has not been established. • Not for use with premature infants (<1500 g) or individuals with significant liver and kidney function impairment. • Performing embolization to occlude blood vessels is a high-risk procedure. This device should be used only by physicians with neurointerventional training and a thorough knowledge of the pathology to be treated, angiographic techniques, and super-selective embolization. • After Onyx™ LES embolization of the arteries, feeding bAVM or target branch/es of the MMA may be subject to increased pressures as a result of changes in hemodynamics. Increased arterial pressures could result in hemorrhagic complications. • Animal experimentation has shown that when the Onyx™ LES escapes outside the vascular space, as might occur if the vessel wall is compromised, a subacute inflammatory response to the material may occur. Increased intracranial pressure due to unresorbed Onyx™ LES material in this space may cause tissue damage. • DMSO can initiate the liberation of histamine and there has been an occasional hypersensitivity reaction with topical administration of DMSO. This hypersensitivity has been reported in one patient being treated for interstitial cystitis. If anaphylactoid symptoms develop, appropriate therapy should be instituted. • DMSO may interact with other embolic agents, such as polymer coated coils, e.g., gel coatings and suture material coated coils. • Therapeutic embolization should not be performed when high blood flow precludes safe infusion of the embolic agent. • The microcatheter tip should be placed so that embolization of the bAVM occurs distal to any arterial vessels that may supply normal brain tissue or cranial nerves. • For additional Materials of Concern information such as REACH, CA Prop 65 or other product stewardship programs, go to www.medtronic.com/productstewardship. • The safety and effectiveness of this device for radial neurovasculature access in direct comparison to a transfemoral approach has not been demonstrated. The risks and benefits for radial access against a transfemoral approach should be carefully weighed and considered for each patient.

Precautions
• The safety and effectiveness have not been studied in the following patient populations: ○ Pregnant and nursing women ○ Individuals less than 18 years old ○ Individuals with aneurysms not associated with a bAVM nidus, or distal feeders to a bAVM nidus ○ Individuals not diagnosed with subacute or chronic subdural hematoma ○ Individuals with significant contraindication to angiography ○ Individuals identified with potentially dangerous anatomical variations leading to increased procedural risk. • Some data indicate that DMSO potentiates other concomitantly administered medications. • A garlic-like taste may be noted by the patient with use of the Onyx™ LES due to the DMSO component. This taste may last several hours. An odor on the breath and skin may be present. • Inspect product packaging prior to use. Do not use if sterile barrier is open or damaged. • Use the Onyx™ LES prior to the "Use-by date" printed on the package. • If using radial artery access, perform a screening examination of the radial artery per institutional practices to ensure that radial access is appropriate for the patient. • If using a guide sheath or introducer sheath, ensure the radial artery lumen diameter is larger than the outer diameter of the guide sheath or introducer sheath. • Operators should take all necessary precautions to limit X-ray radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors where possible. • Verify that the catheters and accessories (see directions for use) used in direct contact with the Onyx™ LES polymer are clean and compatible with the material and do not trigger polymerization or degrade with contact. Use only Medtronic/ ev3 Onyx™ LES/DMSO compatible microcatheters indicated for use in the neurovasculature and Medtronic/ev3 Onyx™ LES/DMSO compatible syringes. Other microcatheters or syringes may not be compatible with DMSO and their use can result in thromboembolic events due to catheter degradation. Refer to the Warnings and Directions for Use sections. • Wait a few seconds following completion of the Onyx™ LES injection before attempting catheter retrieval. Failure to wait a few seconds to retrieve the microcatheter after the Onyx™ LES injection may result in fragmentation of the Onyx™ LES into non-target vessels. • To reduce the risk of catheter entrapment, carefully select catheter placement and manage reflux to minimize the following: ○ Angioarchitecture ○ Vasospasm ○ Reflux ○ Injection time • If catheter entrapment is suspected (with any embolic agent), a fast catheter retrieval technique may result in catheter shaft separation, and potential for vascular damage, embolism, and thromboembolism. Follow catheter retrieval instructions at the end of the DIRECTIONS FOR USE section. • If significant traction is required to remove an entrapped catheter, it may be safer to leave the microcatheter in the vasculature.

Adverse Events
Two prospective, randomized, multi-center clinical trials were conducted on the Onyx™ LES. Refer to CLINICAL STUDY RESULTS – SUBACUTE / CHRONIC SDH section for adverse events reported in the EMBOLISE trial evaluating patients with subacute or chronic SDH. Refer to CLINICAL STUDY RESULTS – BRAIN AVM section for adverse events reported in the Onyx™ LES vs. TRUFILL™ n-BCA trial evaluating patients with brain AVMs.

Potential Complications
Potential complications of the device and the embolization procedure, include or are synonymous with, but may not be limited to the following: • Access site complications such as fistula, pseudo-aneurysm, pain and tenderness, inflammation, necrosis, granuloma, pathological hand cold intolerance, amputation, hematoma or hemorrhage, compartment syndrome, hand dysfunction • Allergic reaction • Arrhythmia • Catheter entrapment • Catheter rupture • Complications of radiation exposure (e.g. alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia) increases as the procedure time and the number of procedures increase • Contrast related complications including but not limited to burning sensation, nausea, contrast nephropathy • Death • Device migration and cast movement • Headache • Infection • Intracranial hemorrhage or hemorrhage in another vascular location • Ischemic events: TIA/stroke • Myocardial infarction • Nerve damage or cranial nerve palsy • Neurological deficits/ dysfunctions • Pulmonary embolism • Seizures • Thrombocytopenia • Thromboembolic events • Vascular complications including but not limited to dissection, perforation, rupture, occlusion, vasospasm, hypotension • Visual complications related to anatomical variants (ophthalmic collateral)

*If a serious incident related to the device occurs, contact your Medtronic representative and the competent authority in your respective country/region.

Training
Serious, including fatal, consequences could result with the use of the Onyx™ LES without adequate training. Onyx™ LES implantation should only be performed by physicians who have successfully completed training in the use of Onyx™ LES. Contact your Medtronic sales representative for information on training courses. If any technical assistance is required, contact Medtronic at the telephone number on the back cover of this Instructions for Use.

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See the device manual for detailed information regarding the instructions for use, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative.