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The MynxGrip™ Vascular Closure Device

Initial experience with active extravascular arteriotomy closure.

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An estimated 7 million endovascular procedures are performed worldwide each year, including a large proportion to evaluate and treat atherosclerotic disease.[1] With increasing pressure on hospitals to reduce costs, effective arterial hemostasis techniques are essential for good clinical outcomes and a provision of safe, efficient, and cost-effective care in the catheterization laboratory. With vascular access site complications ranging from 3% to 6% for hemostasis achieved by manual compression,[1] many physicians have adopted the use of vascular closure devices (VCDs) in an effort to reduce complications, shorten time to hemostasis and ambulation, and minimize bed rest time and patient discomfort after catheterization.

VCDs can be categorized as either active closure (those that engage the vessel wall with sutures, clips, or plugs) or passive closure (those that introduce only thrombosing agents or sealants to seal the arterial wall).[2,3] Historically, physicians have been forced to choose between an active or a passive closure device. Although few data exist on the effectiveness of active versus passive devices, the added security of engaging the arterial wall appears to be the preference, particularly for fully anticoagulated patients undergoing interventional procedures and in those with morphologic features (eg, body habitus) suggesting an increased risk for vascular access site bleeding. The tradeoff for this added security, however, has meant leaving clips, plugs, or sutures in the artery lumen or vessel wall, which can potentially obstruct flow, become a nidus for infection, and/or impede future access attempts. Conversely, although passive closure devices have no intravascular components, they are not anchored to the arteriotomy site, leading some to doubt their effectiveness in high-risk patient populations.

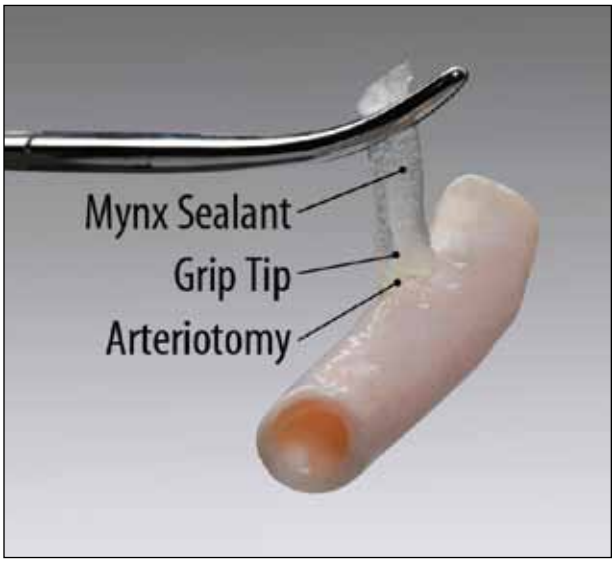

Figure 1. Bovine vessel suspended by MynxGrip Sealant.

The MynxGrip™ Vascular Closure Device (AccessClosure, Inc., Mountain View, CA) is redefining active closure by incorporating an active closure mechanism into the Mynx™ Vascular Closure Device, a historically passive closure solution. MynxGrip* provides the added advantage of active closure while maintaining all of the advantages of the original Mynx platform, which include an extravascular design, patient comfort, and complete resorption within 30 days.[4] Although the original Mynx's classification as a passive closure device may have limited its use in interventional cases and other populations at high risk for access site bleeding, MynxGrip provides the opportunity to extend utilization into these challenging patient populations and procedures.

**The product referred to as MynxGrip in this article is inclusive of MynxGrip™ Vascular Closure Device and Mynx™ Vascular Closure Device with Grip Technology.*

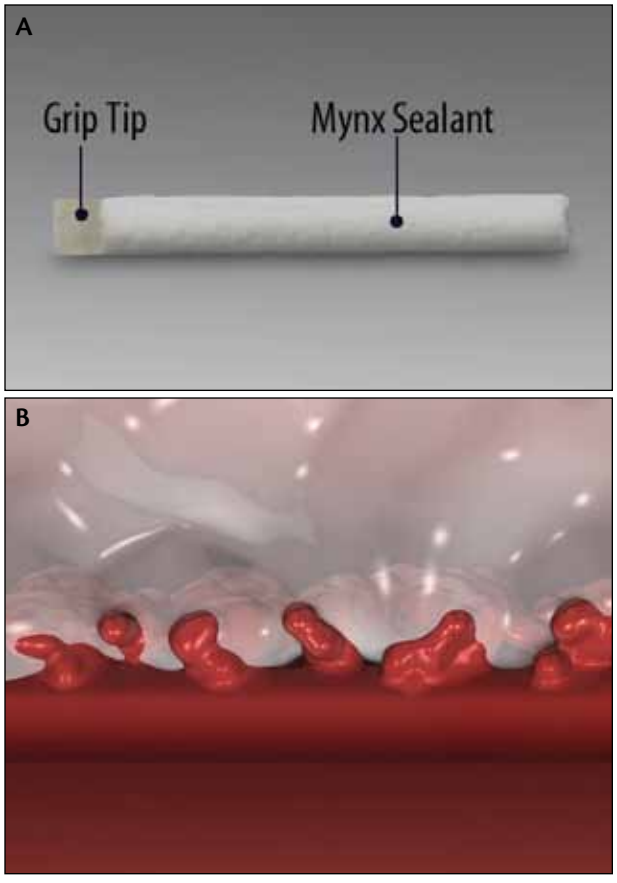

Figure 2. The MynxGrip Sealant technology (A). Grip Tip technology (white) interlocking with vessel wall tissues (red) (B).

THE SCIENCE BEHIND THE GRIP TECHNOLOGY™ SEALANT

MynxGrip was developed by adding the proprietary Grip Technology to the distal end of the original Mynx sealant (Figure 1). The Grip Tip is a new configuration of the original Mynx polyethylene glycol (PEG) sealant, a water-soluble, bioinert, nonthrombogenic polymer. The Grip Tip and Mynx Sealant are fused together to make the MynxGrip sealant (Figure 2). In the original Mynx sealant, the PEG components are reacted and cross-linked during the manufacturing process, and the cross-linked mixture is then freeze dried, creating the porous structure that absorbs blood and subcutaneous fluids and filling the tissue tract by expanding three to four times its original size. In the Grip Tip segment, the PEG components are combined in an unreacted state without cross-linking during manufacturing. Once inside the body, the components react and cross-link in response to the pH level and higher temperature of the body. This cross-linking action causes the Grip Tip to soften and interlock with the contours of the vessel wall (Figure 2), which anchors the sealant on the arterial wall. The result is a sealant that actively grips to the artery while expanding and filling the tissue tract to provide durable hemostasis.

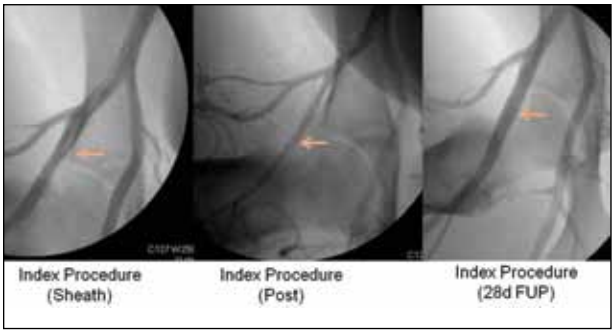

Figure 3. Serial angiograms of MynxGrip Technology in a porcine femoral artery. Note: the pig experienced vasospasm during postprocedure angiography.

PRECLINICAL EXPERIENCE WITH MYNXGRIP

A porcine study was conducted to provide angiographic evaluation, tissue responses, and bioabsorption profiles at the arteriotomy site after femoral artery closure with MynxGrip. In this study, Yorkshire pigs (n = 11) underwent femoral catheterization and closure in which a total of 12 femoral arteriotomies (6 F) were closed using Grip Technology. Successful hemostasis in all 12 arteriotomies was verified by clinical assessment, postclosure transcarotid angiography, and transcutaneous ultrasound. Serial angiographic images (Figure 3) during and after the index procedure and at 28-day follow-up showed smooth vessel wall contours. In addition, a smooth flow profile was demonstrated on ultrasound (not shown), and clinical assessment confirmed the absence of bleeding, bruits, or thrills.

Tissue response and absorption patterns of the Grip Technology sealant at 3 days and 28 days postclosure are shown in Figure 4. At 3 days, histologic examination shows a fibrinocellular cap filling the arterial wall breach with masses of sealant in the extravascular space, as well as perivascular hemorrhage. At higher magnification, neutrophilic infiltration at the arteriotomy site is evident, with beginning fibroplasia indicating initiation of the wound-healing process. At 28 days, the previous arterial wall breach is closed, with evidence of focal fibrous healing, patchy areas of fibrous scarring, and minimal scars in the adventitia. The cell types are lymphoplasmacytic, indicating normal wound healing. The absence of sealant material and the presence of granulomatous inflammatory infiltrate indicate complete absorption of the sealant and demonstrate that the tissue reactions after closure

TABLE 1. PATIENT AND PROCEDURAL CHARACTERISTICS IN THE MYNXGRIP EARLY USER EVALUATION[a]

	Patients N = 774[b]
Diagnostic cases, n/N (%)	392/717 (55%)
Interventional cases, n/N (%)	325/717 (45%)
Age, years (mean ± SD)	65 ± 12
Male sex, n/N (%)	442/760 (58%)
BMI, mg/kg^2 (mean ± SD)	31 ± 6.9
History of PVD, n/N (%)	212/735 (29%)
Prior catheterization, n/N (%)	429/687 (62%)
Preexisting hematoma, n/N (%)	13/755 (2%)
Vessel size, mm (mean ± SD)	7 ± 1
PVD or calcium at access site, n/N (%)	92/687 (13%)
Sheath size, n/N (%)	
5 F[c]	15/769 (2%)
6 F[d]	666/769 (87%)
7 F	86/769 (11%)
8 F	2/769 (0.3%)
Puncture location, n/N (%)	
CFA	650/695 (94%)
Bifurcation	28/695 (4%)
Superficial femoral artery	14/695 (2%)
Brachial (n = 1) or profunda (n = 2)	3/695 (0.4%)
Major complications, n/N (%)	2/774 (0.26%)
Minor complications, n/N (%)	5/774 (0.65%)

[a]Early User Evaluation forms were collected during the period of October 11, 2011, and February 14, 2012.
[b]Denominators reflect the number of data points available for each endpoint.
[c]Two 5-F sheaths were upsized to 6 F during the procedure.
[d]Two 6-F sheaths were upsized to 7 F during the procedure.

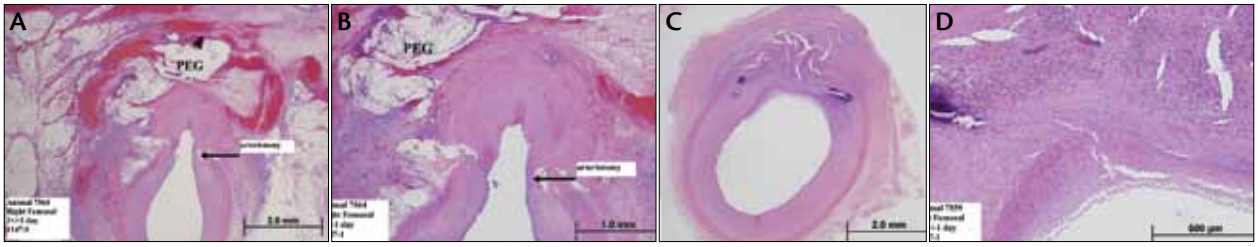

Figure 4. Porcine histology at 3 days after MynxGrip closure (A, B): The arterial wall breach is filled with fibrinocellular blood clot integrated and surrounded by mixed acute reaction. The cells are neutrophilic, which is indicative of early fibroplasia. Masses of sealant are present in the extravascular space. Twenty-eight days after closure (C, D): The previous arterial wall breach is closed with focal fibrous healing/scar. The cells are fibrous and lymphoplasmacytic, with minimal granulomatous inflammatory infiltrate (macrophages). There is no evidence of sealant present.

with MynxGrip are consistent with the normal wound-healing process.

EARLY CLINICAL EXPERIENCE WITH MYNXGRIP

In early user experiences, MynxGrip performed effectively in diagnostic and interventional procedures, including higher-risk patients. Data were collected during the Early User Evaluation of 774 patients who were treated at 22 centers in the United States, in which 45% of patients underwent interventional catheterization procedures. The majority of these procedures used 6- (87%) or 7-F (11%) sheaths. In this population, clinical success was 99% (freedom from any major or minor clinical complications), and device success (hemostasis achieved) was 98%.

Patient selection for this evaluation followed the criteria outlined in the instructions for use. As shown in Table 1, MynxGrip was used in patients with a mean age of 65 years and a mean body mass index (BMI) of 31 mg/kg^2 (16.7–57.7 ± 6.9). One percent of the patients were underweight (BMI < 18.5), 40% were obese (BMI = 30–39.99), and 10% were morbidly obese (BMI ≥ 40). A majority of patients (62%) had undergone previous catheterizations, 13% had peripheral vascular disease (PVD) or calcium in the vicinity of the puncture location, and 6% had a puncture location outside of the common femoral artery (4% bifurcation, 2% superficial femoral artery, 0.3% profunda). Mean systolic blood pressure before closure was 136 mm Hg (82–222 ± 23.12 mm Hg), with 4% over 180 mm Hg. As shown in Figure 5, procedural anticoagulation was achieved alone or in combination with aspirin (64%), clopidogrel (39%), bivalirudin (40%), heparin (27%), prasugrel (4%), and low-molecular-weight heparin (2%). Some instances of more intensive anticoagulation occurred, including glycoprotein IIb/IIIa inhibitors (3%) and warfarin (3%).

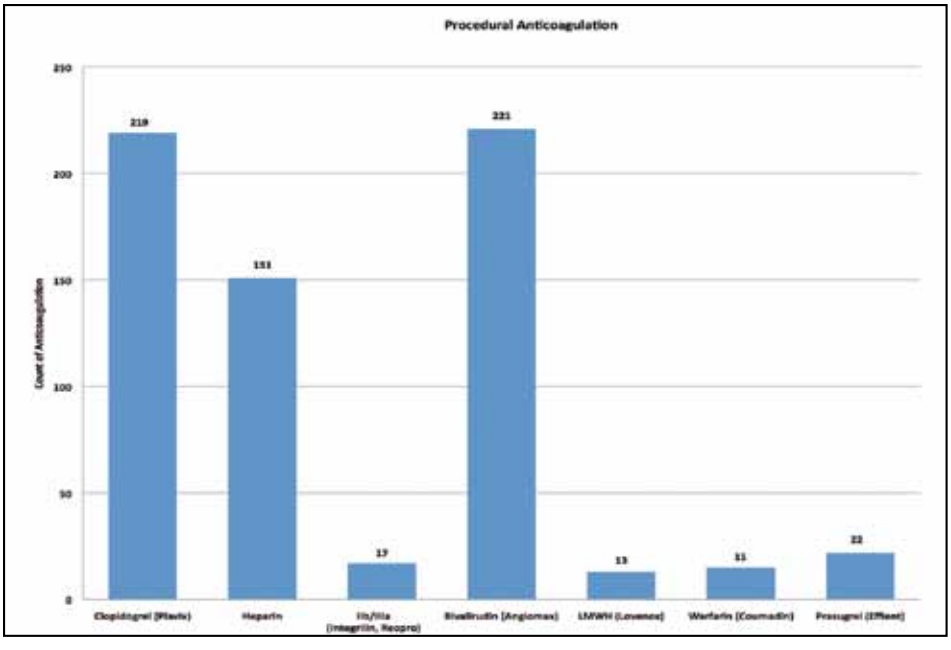

Figure 5. Anticoagulation usage in the Early User Evaluation study (N = 557). Note: procedural anticoagulation was achieved alone or in combination.

Major complications occurred in two of 774 cases (0.26%), including a hematoma in a heavily anticoagulated patient after coronary stenting and a femoral pseudoaneurysm. Both cases resulted in surgical repair. There

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were five minor complications (0.65%) reported in this study, including two hematomas that were approximately 6 cm in size and required additional compression, two cases of access site bleeding that required additional compression, and one retroperitoneal bleed that resolved with application of a compression-assist device.

The successful use of MynxGrip is highly encouraging given the challenging patient population, which included underweight and obese patients, patients with uncontrolled high blood pressure, patients with PVD in the vicinity of the puncture location, and patients with a puncture location outside of the common femoral artery (CFA). Additionally, patients with extensive anticoagulation were not excluded. Overall, < 1% of deployments using MynxGrip were associated with a major or minor complication, thereby demonstrating the potential for use of this device in very challenging patient populations.

CASE REPORT

MynxGrip in a Complex Interventional Procedure With Aggressive Anticoagulation

In a case study from Orlando Regional Medical Center, a 74-year-old man with a history of severe, multivessel coronary artery disease and previous multivessel bypass surgery presented to the emergency department with acute myocardial infarction due to thrombotic occlusion of the distal limb of the sequential saphenous vein graft supplying the first and third obtuse marginal branches. This patient also had a known total occlusion of the vein graft to the right coronary artery and was known to have atresia of the left internal mammary artery graft to the left anterior descending artery. A complex, interventional catheterization procedure involving thrombectomy and aggressive anticoagulation with eptifibatide was undertaken.

The distal limb of the sequential vein graft to the third obtuse marginal branch was treated with aspiration thrombectomy for thrombotic total occlusion, which restored TIMI grade 3 flow. After placement of a drug-eluting stent, 0% residual stenosis was achieved with TIMI grade 3 flow. The ostial and proximal segment of the second obtuse marginal branch, which had stenosis of up to 90%, was stented using two overlapping drug-eluting stents, resulting in a 0% residual stenosis with brisk TIMI grade 3 flow. The patient received additional boluses of heparin during the procedure to maintain an activated clotting time of 275 seconds. Intravenous nitroglycerin was discontinued during the procedure, but an eptifibatide drip was continued from the emergency department. After the procedure, the patient was treated with aspirin and prasugrel, as well as an 18-hour infusion of intravenous eptifibatide. The interventional catheterization system was removed after femoral angiography confirmed the introducer sheath position in the right CFA above the bifurcation. MynxGrip was deployed with satisfactory hemostasis.

MynxGrip successfully achieved femoral arteriotomy hemostasis after removal of a 7-F sheath in this patient with acute myocardial infarction after a complex interventional procedure involving thrombectomy and aggressive anticoagulation including intravenous eptifibatide. The effectiveness of this new device in a challenging interventional case illustrates how the addition of Grip Technology to the Mynx sealant combines the advantages of an extravascular closure device with the security of engaging the artery wall to achieve hemostasis.

EXPANDING THE MYNX PLATFORM

The original Mynx device is an established arteriotomy closure option that has been used in more than 1 million patients in the 4 years that the device has been commercially available. Two advantages of the original Mynx device are its extravascular deployment, in which nothing is left behind, inside, or on the artery, and the 100% resorbable nature of the polyethylene glycol sealant. In a retrospective, single-center evaluation of the need for surgical repair of vascular closure complications, Noor et al[5] reported significantly fewer surgical procedures secondary to vascular closure complications after closure with Mynx compared with Angio-Seal (St. Jude Medical, Inc., St. Paul, MN) (0.06% vs 0.61%; $P < .0001$), which is composed of a resorbable anchor inside the vessel and an extravascular collagen plug that are tethered together by sutures. Surgical vascular repair rates were statistically comparable between Mynx (0.06%) and manual compression (0.19%; $P = .14$).

Another apparent advantage of the Mynx is its attractive patient comfort profile. In a blinded, randomized, controlled trial (N = 64) comparing patient-reported pain associated with Mynx and the Angio-Seal

Evolution device, Fargen et al[6] reported significantly greater pain at closure and greater increase in pain from baseline to closure in the Angio-Seal group ($P = .009$ and $P = .002$, respectively). Closure was reported as the most painful part of the procedure by 88% of patients receiving Angio-Seal compared with 34% of patients receiving Mynx ($P < .001$). The MynxGrip Vascular Closure Device builds on these advantages that have made it the most widely used passive closure solution in the United States.

DISCUSSION

The early experience with MynxGrip has provided valuable insights into this new approach to vascular closure (ie, the addition of active closure properties to a passive closure device). The results from the preclinical porcine study verified complete absorption of the Grip Technology sealant after 28 days, and tissue reactions were consistent with the normal wound-healing process. The 99% clinical success rate in a cohort of 774 patients that included a high percentage of interventional procedures in anticoagulated patients, as well as many patients with various risk factors for closure device failure (eg, CFA calcification and/or atherosclerosis, obese body habitus, non-CFA sheath entry site), suggests a potential broader utility for MynxGrip in complex patients. In addition, physicians using MynxGrip in the Early User Evaluation have reported more definitive closure with less oozing, leading to greater confidence in the technology and higher usage in interventional and high-risk patient populations.

In the current health care arena, excellent patient outcomes and high patient satisfaction must be achieved with treatments that are cost and time efficient. By reducing demands on nursing staff, decreasing time to ambulation, and minimizing complications stemming from arteriotomy closure, the use of VCDs can contribute to cost effectiveness, time efficiency, and perhaps most importantly, patient satisfaction. Five large, broadly inclusive observational and multicenter registries, each involving more than 10,000 patients, have consistently demonstrated fewer bleeding complications with the use of VCDs compared to manual compression.[7-11] For physicians who use VCDs, there has historically been a choice between active and passive closure. The introduction of the MynxGrip Vascular Closure Device provides a new option: an extravascular, patient-friendly closure device with the added security of active closure. The initial experience with MynxGrip has demonstrated the potential for this innovative closure technology to provide the ensurance of active closure in a previously passive device with an existing track record for patient comfort. ■

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Early User Evaluation Participating Sites (partial list): Community Regional Medical Center, Fresno, California; Deborah Heart and Lung Center, Browns Mills, New Jersey; Orlando Regional Medical Center, Orlando, Florida; Baptist Memorial Hospital-Memphis, Memphis, Tennessee; Baptist Memorial Hospital-De Soto, Southhaven, Mississippi; St. John Macomb-Oakland Hospital, Warren, Michigan; Alexian Brothers Medical Center, Elk Grove Village, Illinois; DMC Harper University Hospital, Detroit, Michigan; Englewood Hospital and Medical Center, Englewood, New Jersey; Hutchinson Regional Medical Center, Hutchinson, Kansas; MacNeal Hospital, Berwyn, Illinois; Regional Hospital of Jackson, Jackson, Tennessee.

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