HEMOSTASIS UPDATE

The Cleveland Regional Medical Center: Experience with the Neptune Pad

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Closure Devices and the Cath Lab of the 21st Century

It has been close to a decade since the first vascular hemostasis device was approved by the FDA for commercial use. The adoption and use of closure devices following catheterization and interventional procedures is becoming routine.

Data from a recently conducted 58-center closure device study notes that on average, more than half of the centers used closure devices following diagnostic cases and more than 40% used closure devices following interventional cases. Interestingly, close to two-thirds of the facilities reported using hemostatic pads, of which nearly a fifth indicated using hemostatic pads in greater than 51% of cases. And, of this, 70% indicated that hemostatic pads were the most frequently used closure method employed to achieve vascular access site hemostasis. Furthermore, of those centers that indicated using other closure methods, such as manual compression, suture-mediated devices, collagen plugs, or mechanical compression most frequently, nearly 60% indicated being "light users" of hemostatic pads or using hemostatic pads in 10 to 50% of cases. [1]

Although the popularity of closure devices appears to be increasing, the main concern atop many users' lists are the complications associated with using closure devices, particularly invasive or vascular closure devices. These include suture-mediated devices like Perclose ® (Abbott Vascular Devices, Redwood City, CA) and collagen plug devices, such as AngioSeal™ (St. Jude Medical, Minnetonka, MN) and VasoSeal ® (Datascope Corporation, Mahwah, NJ). Non-invasive closure devices, or those that do not penetrate the surface of the skin, such as mechanical closure devices, include C-clamps and FemoStop ® (RADI Medical Systems, Inc., Reading, MA). However, more recently, this category has expanded to include various topical hemostatic pads and patches, which include:

- SyvekPatch ® (Marine Polymer Technologies, Inc., Danvers, MA);
- Chito-Seal (Abbott Vascular Devices, Redwood City, CA),
- Clo-Sur P.A.D. (Scion Cardio-Vascular, Miami, FL)
- D -Stat Dry (Vascular Solutions, Minneapolis, MN)
- Neptune Pad (TZ Medical Inc., Portland, OR).

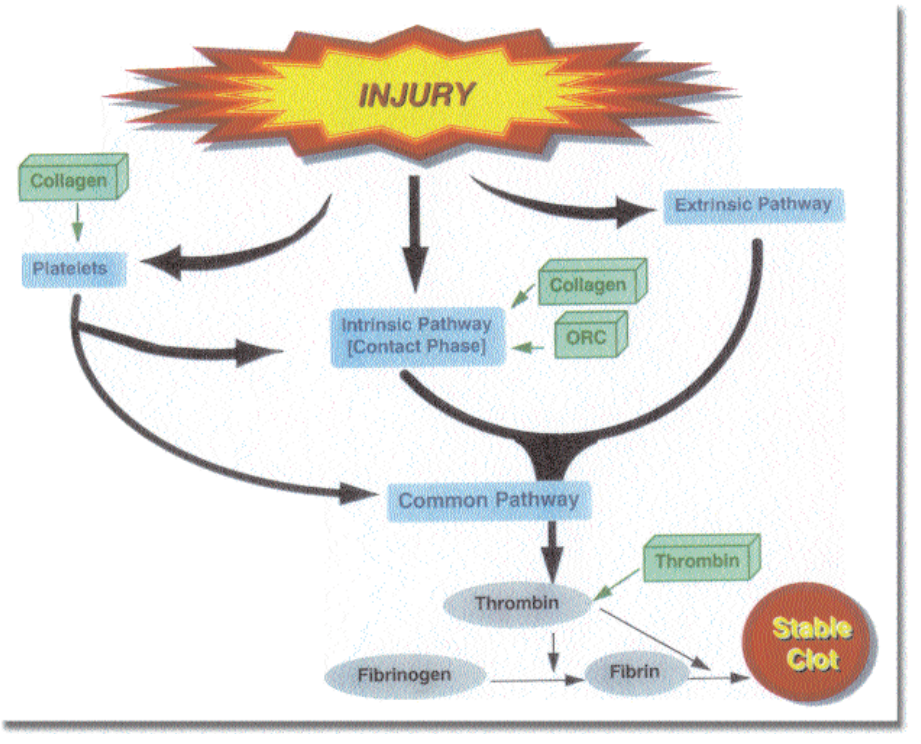

Figure 1. A reproduction of the clotting cascade.

Hemostatic pads and patches are less likely to directly cause a complication than the act of performing manual compression or using a vascular closure device. This is because hemostatic pads are used at the skin's surface at the puncture site in conjunction with manual compression to arrest bleeding, unlike vascular closure devices that penetrate the skin surface and leave a component of the device "behind," for example, a suture or plug, at the arteriotomy. These components can cause complications such as infection.

Some medical literature comparing closure methods may be misleading. For instance, in a 2002 meeting abstract presented at the annual Society for Cardiovascular Angiography and Interventions (SCA&I) course, Meyers and colleagues reported a pseudoaneurysm in the "Syvek" arm. [2] Pseudoaneurysms are usually associated with injury to the vessel as opposed to being the result of using a topical hemostasis pad (THP) on a patient. Other studies comparing THP to manual compression indicated that complications were observed in the THP groups, such as hematomas, or that overall "significant complications" were insignificant in the THP groups, but again these complications, such as hematomas, were more likely the result of manual compression techniques rather than being directly associated with THPs. [3-4] A study conducted by Nader et al of 1,000 patients that had undergone diagnostic and interventional procedures concluded that assisted compression with the Syvek patch had a "benign complication profile." [5]

In this article, we will share on one center's experience with the Neptune calcium alginate pad, Cleveland Regional Medical Center in Shelby, North Carolina.

Non-invasive devices: How are they different?

The mechanism of action between invasive closure devices and non-invasive closure devices is as different as the devices themselves. Simply put, invasive closure devices seal or close off the arteriotomy, while topical hemostatic pads are used at the skin surface in conjunction with manual compression, creating a barrier between the operator's hand and the skin surface at the access site. Hemostatic pads are more than a sterile dressing, such as a gauze 2x4 or 4x4, because hemostatic pads contain active ingredients that interact with the body's ability to clot.

Effectiveness, as measured in terms of time to hemostasis, is dependent on the active ingredient and how the hemostatic pad's active

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ingredient interacts with the clotting cascade (see Figure 1). Products containing thrombin trigger the clotting process by converting fibrinogen to a fibrin clot. Other products, such as the Neptune Pad, affect hemostasis at the contact phase.

There is another significant difference between invasive and non-invasive closure devices: price. Whereas the list price of vascular closure devices ranges from $200 to $300 per unit, the list price of hemostatic pads varies significantly less, ranging from $30 to $80 per unit. But there are distinct differences between the commercially available hemostatic pads and patches, not only between active ingredients and how these ingredients interact with the clotting cascade, but also the material from which they are made, all affecting the price. Table 1 presents a side-by-side comparison of commercially available hemostatic pads and patches.

The Neptune Pad

The technology behind the Neptune Pad is based on a marine calcium alginate biopolymer. The pad resembles an absorbent off-white "woolly" fibrous pad, which in one non-scientific test by the company, absorbed and "locked-in" a teaspoon of grape juice in a matter of seconds. The grape juice did not seep through the pad, leaving the unexposed side relatively dry. Alginates are used widely in the food, bakery, pharmaceutical, cosmetic and textile industries, primarily because of alginates' stabilizing properties.

Alginates have been tested extensively both in animal models and in humans as a wound and surgical dressing. The alginate fibers that make up the Neptune Pad have been found, according to a clinical paper by Scherr, [6] to be "non-antigenic, sterilizable by heat, [and] hemostatic." Furthermore, when blood comes into contact with the alginate fabric it "forms an alginate-blood gel," which resembles a paste, according to Scherr.

Scherr states that hemostasis might also be accelerated by the use of alginates, because the alginates may promote the "release of free calcium ions from the tissue." Additionally, alginates plus blood are thought to form a "homogenous 'plastic' film which covers the wound," protecting the wound to promote healing. Other experiences like those of Oliver and Blaine, [7] who studied the use of alginate wool following neurosurgeries, indicated that alginate wool-like pads could be left in situ. They also found that the alginate wool could be used effectively dry or moistened in saline, and the pad would not lose its absorbency. According to Scherr, "alginate is a very poor medium for microbial growth," suggesting it can be left in place for long periods of time and removed simply by remoistening the pad with saline.

The Neptune Pad can be useful, particularly following interventional procedures, when oozing occurs, whether an invasive closure device was used or some other closure method is employed to achieve vascular access hemostasis. The fact that the alginate in the Neptune Pad is a poor medium for microbial growth suggests fewer chances for microbial infection. This means a patient undergoing an interventional procedure — even if the patient has been anticoagulated — could be administered a pad that could be left in place, for example, for a period of 24 hours, to absorb any oozing or fluid discharge, without a high risk of infection.

Table 1. A SIDE-BY-SIDE COMPARISON OF TOPICAL HEMOSTASIS PADS AND PATCHES

Device name	Chito-Seal	Clo-Sur^{PLUS} P.A.D.	D-Stat Dry	Neptune Pad	Syvek NT Patch
Manufacturer	Abbott Vascular Devices	SCION Cardio-Vascular	Vascular Solutions	TZ Medical	Marine Polymer Technologies
Marketer	Same	Medtronic Vascular	Same	Same	Same
Web site	www.abbottvascular.com	www.medtronic.com	www.vascularsolutions.com	www.tzmedical.com	N/A
Device characteristic based on 510(k)	Chito-Seal is made from Abbott's proprietary chitosan gel, which is derived from chitin, a marine biopolymer.	Non-woven pad consisting of a proprietary formulation of poly-D-glucosamine and poly-N-acetylglucosamine derived from chitosan.	Lyophilized pad consisting of thrombin, sodium cardoxymethylcellulose (CMC) and calcium chloride.	Calcium alginate fiber pad.	Non-woven pad of cellulosic polymer, poly-N-Acetylglucosamine, isolated from a marine microalgae
Time to hemostasis*					
■ *in vitro* testing	10.8 min.[8]	8.8 min.[8]	0.25 min.[8]	4 to 8 min.[9]	10.8 min.[8]
■ Real-world	N/A	~10 min.[3]†‡	<5 min.[10]†	<10 min.[9]†	~10 min.†‡
List price	Approx. $79/unit	*Contact Medtronic*	Approx. $59/unit	Approx. $30/unit	$79 each
Additional comments	Markets its proprietary chitosan gel as being "twice as chemically active as chitin," indicating that hemostasis is achieved by positively charged chitosan attracting negatively charged RBCs and platelets.	The Clo-Sur^{PLUS} P.A.D. is the latest version and is the only FDA-cleared product with a bacterial barrier. Hemostasis is achieved by attracting negatively charged RBCs to the positively charged "polyprolate" biopolymer.	D-Stat Dry's thrombin component interacts with the clotting cascade to "speed up" the fibrinogen conversion process. The company also offers a D-Stat Radial product, consisting of the same lyophilized components in D-Stat Dry and is non-woven gauze.	Calcium alginates used for medical dressing are also used in other medical applications, such as dentistry and surgery. Calcium alginate pads are also poor mediums for microbial growth. The pad can remain in place up to 24 hours. TZ Medical markets a line of complementary products including a radial version called the Comfort Band.	By far, Syvek has the most clinical studies under its belt as it was the first FDA-cleared THP. It has been used in both diagnostic and interventional procedures.

** Time to hemostasis was selected for the comparison chart based on the factor "effectiveness" as explained in the accompanying article. Effectiveness appeared to be the only statistically significant factor between both heavy and light THP users as being the most important factor influencing THP choice based on five factors that are believed to be good predictors of closure device choice that were evaluated by 35 THP users.[1]*

† Time to hemostasis is based on the time it took to achieve hemostasis for the majority of the patients under study.

‡ Time to hemostasis for patients undergoing diagnostic and interventional procedures.

Single-Center Experience

Cleveland Regional Medical Center (CRMC), located in Shelby, NC, is a dedicated diagnostic catheterization laboratory that performs approximately 700 cases per year. Of their cases, about 50% are sent on for interventional procedures outside the hospital. Of the remaining cases, approximately 70% are administered closure devices. Half of this 70% are administered an invasive closure device, while the other half get the Neptune Pad.

According to Dr. Eusebio, the CRMC's cath lab director, invasive closure devices are used on more high-risk patients. These patients are typically overweight and have deep groin sticks that are likely to rebleed. However, Dr. Eusebio did indicate using Neptune in heavier patients successfully, keeping them for longer observation periods before ambulating and discharging them from the hospital. This facility primarily uses

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5Fr catheters to perform diagnostic caths, but occasionally used 4Fr catheters where there was a greater tendency to use Neptune.

Dr. Eusebio indicated that manual compression times were shortened when the Neptune Pad was used. "When pads weren't being used, 15 to 20 minutes of manual compression was required." Now, according to the cath lab manager, they are averaging 6- to 10-minute hold-times.

Dr. Eusebio also noted that patients can be ambulated sooner, within a couple of hours, when Neptune is used. "With the [Neptune] pad, ambulation time is better when compared to manual compression alone." Although he finds that the Neptune Pad works well, Dr. Eusebio did indicate that rebleeds can occur, especially in overweight patients.

According to Dr. Eusebio, a key factor in CRMC's use of Neptune is that it can be used with complementary devices, such as the EZ-Hold manual-assist compression device can be used alone or with the Neptune Disc that comprises a plastic base — the "disc" — packaged with a calcium alginate wound dressing, or the Neptune Pad. According to the company, the EZ-Hold was developed and patented by a registered nurse who sought to reduce hand fatigue and direct contact with bodily fluids. Resembling a "pill on a stick," it is meant to relieve pressure from the fingers while applying manual compression. It also permits the healthcare provider, usually a non-physician cath lab member, to comfortably hold pressure with one hand while freeing up the other hand for other things, such as palpating for a pulse or sheath removal.

The EZ-Hold has become a standard of care in the CRMC cath lab when manual compression is performed and has been in use since 2000. "We liked the concept of it," said Beth Mayer, EMT-P, CVT, Manager of the Heart Center at CRMC. CRMC actually started using the EZ-Hold prior to adopting the Neptune Pad. The three CRMC cath lab members that are trained to use the EZ-Hold, including Mayer, indicated that they found it more efficient to use when holding manual pressure than when performing manual compression alone. The EZ-Hold "operators" also believe that in combination with the Neptune Pad, hold times are reduced and hemostasis is achieved more rapidly (e.g., perceived time to hemostasis is approximately 6 to 10 minutes). Where once the cath lab staff was required to perform the arduous task of a 20 to 30-minute manual hold, adoption of the EZ-Hold also reduced physical exertion. "It really saves your hand from cramping up," explained Mayer.

According to Henderson, they have observed fewer rebleeds overall with the Neptune Pad than they had with the previous product they stocked. Julie McMurry, RN, who is responsible for patient Quality Management (QM) in the cath lab, indicated that she prefers the Neptune Pad to the other hemostatic pads the lab use to stock. One of McMurry's responsibilities in the cath lab is to tend to patients with hematomas and rebleeds. When she used other hemostatic pads, particularly in patients on aspirin therapy or Plavix, the patients tended to ooze. According to McMurry, "They don't with the Neptune." Mayer and her staff have noticed a difference in patients taking aspirin and Plavix, because in the past, it was hard to get the bleeding under control. "It was quite a lengthy compression," Mayer stated, "but, with Neptune, we're having a lot of success." According to the Neptune Pad's FDA indications for use, "Neptune products are used to promote the rapid control of bleeding and hemostasis…at arterial/vascular sites and in patients on anticoagulation therapy."

"Sometimes we have to hold over the eight minutes, but generally we're reaching hemostasis by fifteen minutes, and no rebleeds," commented Mayer. "We want the patient to do well. We don't want to see

Cleveland Regional Medical Center's cath lab staff

L to R: Beth Mayer, EMT-P, CVT, Manager of the Heart Center and Dr. Eusebio, the CRMC's cath lab director

Table 2. CLEVELAND REGIONAL MEDICAL CENTER NEPTUNE PAD EXPERIENCE FOLLOWING DIAGNOSTIC CATHERIZATION IN 76 PATIENTS

Sheath size:	5F = 69 patients
	6F = 2 patients
	7F = 5 patients
Pre-Medications :	None = 40 patients
	Chronic aspirin = 33 patients
	Chronic aspirin and blood thinners = 2 patients
	Blood thinners = 1 patient
Procedural Medications:	None = 69 patients
	Plavix = 5 patients
	Lovenox = 1 patient
	UHF = 1 patient
Time to hemostasis	< 5 minutes = 3 patients
(hold times in minutes)	6-10 minutes = 52 patients
	11-15 minutes = 14 patients
	*16-20 minutes = 5
	*20-25 minutes = 2
Complications:	76 patients experience no complications, rebleeds, or hematomas
**Comments:*	One patient did not follow instructions by bending knees and rolling on to side. No re-bleeding was experienced, but longer hold-time (~17 minutes) was required due to non-compliancy.
	A longer hold time (~22 minutes) was required for a patient on aspirin therapy

Source: TZ Medical, Inc. Data used with permission from TZ Medical, Inc.

Table 3. QUICK FACTS ON CLEVELAND REGIONAL MEDICAL CENTER (CRMC)

Location:	Shelby, NC
Inception:	In 1993, CRMC began offering diagnostic catherization services through the radiology department. In 2000, a stand alone diagnostic catherization laboratory was created within the CRMC Heart Center.
Case per year:	Approximately 700
Percent of diagnostic cases:	100%
Percent of interventional cases:	None, however, CRMC has been evaluating the possibility of offering interventional services.
Invasive closure device usage:	Approximately 50% of cases.
Neptune Pad usage:	Approximately 50% of cases.
Began using the Neptune Pad	August of 2003
Number of physicians on staff:	3
Number of non-physician cath lab staff:	5
Director, Cath Lab:	Dr. Eusebio, MD
Manager, Cath Lab:	Beth Mayer, EMT-P, CVT
Contact number:	704-487-3656

rebleeds. The patients become upset when they see blood."

Adopting Neptune, according to the CRMC cath lab staff, has enabled the CRMC to realize greater staff efficiencies both inside and outside the cath lab. Rebleeds caused staffing problems, particularly after the staff had moved on to a new case. Prior to adopting the Neptune Pad, rebleeds used to strain the small cath lab's human resources. "When we get rebleeds on the floor, we're expected to go up to and handle them," indicated Mayer. Although Mayer's staff was always able to respond quickly and effectively to this type of situation, it interfered nonetheless. Mayer commented that the low occurrence of rebleeds as a result of using the Neptune Pad has reduced the need of having an on-call cath lab member to tend to rebleeds when patients leave the cath lab.

Table 2 presents data for 76 patients that received the Neptune Pad following diagnostic catheterization at the Cleveland Regional Medical Center between May and September 2004. Even with more than half the patients on or receiving medication, 69 patients (or >90%) required hold times of less than 15 minutes with the Neptune Pad. The investigators from this experience concluded that the Neptune Pad is effective in achieving hemostasis with no complications, rebleeds, or hematomas.

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