AccessClosure: FDA Clearance--Yes; Product Launch--Not Yet

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Summary:	Sometimes just getting FDA approval isn't enough. AccessClosure got FDA clearance of its PMA vascular closure device, only to delay the product's launch in order to develop an improved version. The company forestalled one-and-a-half years of revenue to address physicians' concerns and introduce an improved product. This was particularly wise in the field of vascular access closure devices, where previous devices have disappointed. The decision appears to be paying off as the company is seeing rapid adoption even though its product is priced at a premium.

Further Analysis:

Title	Magazine	Issue	Article ID
Interview with Amar Sawhney	*IN VIVO*	Jun. 2009	2009800107
Fred Khosravi & Amar Sawhney: Dynamic Device Development Duo	*IN VIVO*	Jun. 2009	2009800123
Vascular Access Closure Ten Years Later: Why Start-Ups Can't Seal the Deal	*Start-Up*	Dec. 2008	2008900249
An Open Market for Vascular Access Closure Devices	*Start-Up*	May 2004	2004900111

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Sometimes just getting FDA approval isn t enough. This start-up got FDA clearance of its PMA vascular closure device, only to delay the product s launch in order to develop an improved version. The risk appears to be paying off.

By Stephen Levin

For most device start-up companies, obtaining FDA clearance of a PMA product is a cause for celebration and leads to immediate US commercialization.

For AccessClosure, a vascular closure device company started by serial entrepreneurs Fred Khosravi and Amar Sawhney through their Incept development organization, FDA clearance presented a dilemma because physicians complained the product wasn t easy to use.

The company decided to delay the launch, forestalling one-and-a-half years of revenue, to address physicians concerns and introduce an improved product.

The decision appears to be paying off as the company is seeing rapid adoption even though its product is priced at a premium.

Of the nine companies that the company and product development organization Incept has launched in its 11 year history, **AccessClosure Inc.** lies at the intersection of the core skill-sets of co-founders Fred Khosravi and Amar Sawhney. (Khosravi and Sawhney dislike the word incubator, preferring to describe Incept as an enabler of new companies and technologies.) (*See interviews with Fred Khosravi and Amar Sawhney in this issue.* [*A*#2009800108] [A#2009800107].) Focused on vascular closure devices for cardiovascular procedures, AccessClosure combines Khosravi s background in interventional cardiology with Sawhney s hydrogel expertise.

While the company now looks extremely promising, based on initial sales and clinical experience with its current-generation device, it wasn t that long ago that, despite having an FDA-approved product, AccessClosure s prospects appeared dim, particularly to outsiders. That is because physician reaction in clinical trials was that the device worked but was hard to use never a good sign in terms of driving adoption.

As a result, the company made the decision not to commercialize the first version of the device even though it had received FDA clearance, a strategy pretty much unheard of among device start-ups and one that raised red flags among many company observers. Typically, device start-ups prefer to get their first product out on the US market once the FDA has given the green light, knowing there are improvements to be made, and then quickly address those concerns in a follow-on second-generation product. AccessClosure s decision to delay commercialization until it improved its product s ease of use flew in the face of conventional wisdom and sparked questions about the company s ability to bring its product to market, and raised concerns about its future. Company officials, however, insist that they knew all along they could address physicians concerns quickly enough so that the company could sustain the revenue loss resulting from the delayed product launch. In their view, the resulting improved product would better position AccessClosure to capture a larger market share once the new device became available.

The idea to develop a vascular closure device has its design roots in the product tree of hydrogel sealants that Amar Sawhney developed beginning with Incept s first company, **Confluent Surgical Inc.** (now part of **Covidien Ltd.**). Those initial products were designed for post-surgery ob/gyn and neuro applications. Upon witnessing the sealing capabilities of those products, several of Fred Khosravi s interventional cardiology colleagues suggested that if this material was so successful at sealing post-surgical wounds, it might also be able to seal post-interventional femoral artery punctures, which is a huge, currently underserved market.

Confluent started doing preclinical research using its liquid gel product for vascular closure and found that it worked quite well in sealing interventional punctures. The product was then used to treat a small number of patients successfully to establish proof-of-principle. At this point, Khosravi and Sawhney decided to take this product to the next stage, which for Incept means starting a company.

Time to Start a Company

Consistent with Incept s approach of launching separate companies to develop hydrogel applications in different clinical areas, the co-founders decided to move the vascular closure product out of Confluent and into its own company in 2002. "Looking at what Confluent was doing, especially since it was primarily looking at surgical uses of the technology, we knew that they could never effectively develop a cardiovascular interventional product," Fred Khosravi explains. "We knew we would either have to sell the vascular closure product or spin it off into an independent company where that was the focus, and particularly because of the huge market opportunity, we chose the latter and decided to launch AccessClosure."

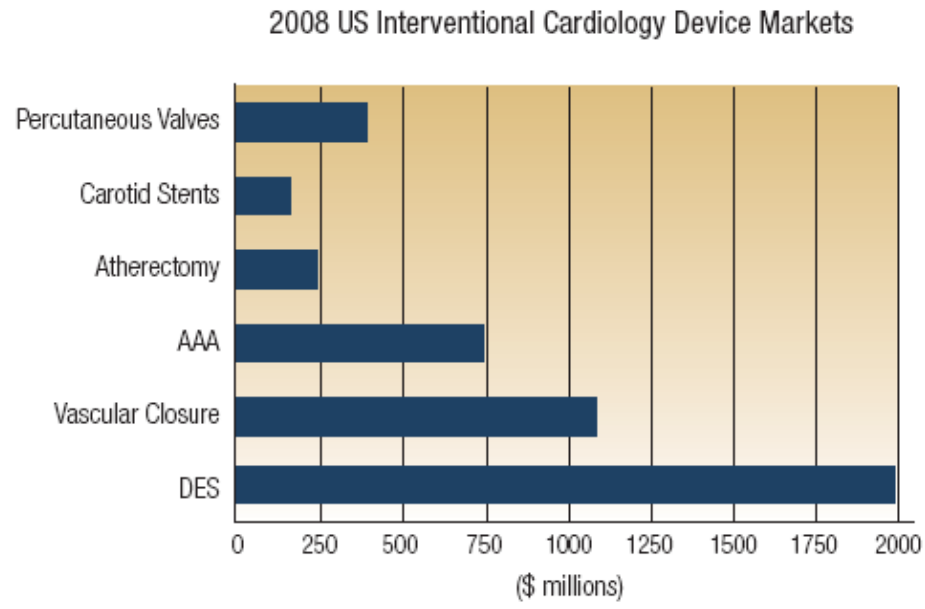
At the time, Khosravi was just exiting **Boston Scientific Corp.**, where he had worked as president of its embolic protection division for 18 months following the large company s acquisition of Embolic Protection Inc. (EPI) from Incept. [W#200110033] He then became co-founder, CEO, and employee number one of AccessClosure. The company s initial team consisted largely of former EPI employees who followed Khosravi to the new start-up in Mountain View, CA.

Within the device industry, Incept s decision to launch a vascular closure company was not universally well-received. Many of Khosravi s and Sawhney s physician friends and industry colleagues were surprised that Incept would get involved in a space that, while presenting a huge market opportunity and large unmet clinical need, had seen its share of previous failures.

Yet, the size of the potential opportunity was undeniable. Vascular closure represents a true billion-dollar market in the US alone (unlike so many other device opportunities that claim markets of that size). In terms of dollars, vascular closure is second only to drug-eluting stents in terms of US cardiovascular device product markets. (*See Exhibit 1.*)

Exhibit 1

Vascular Closure: Second Largest US CV Product Market



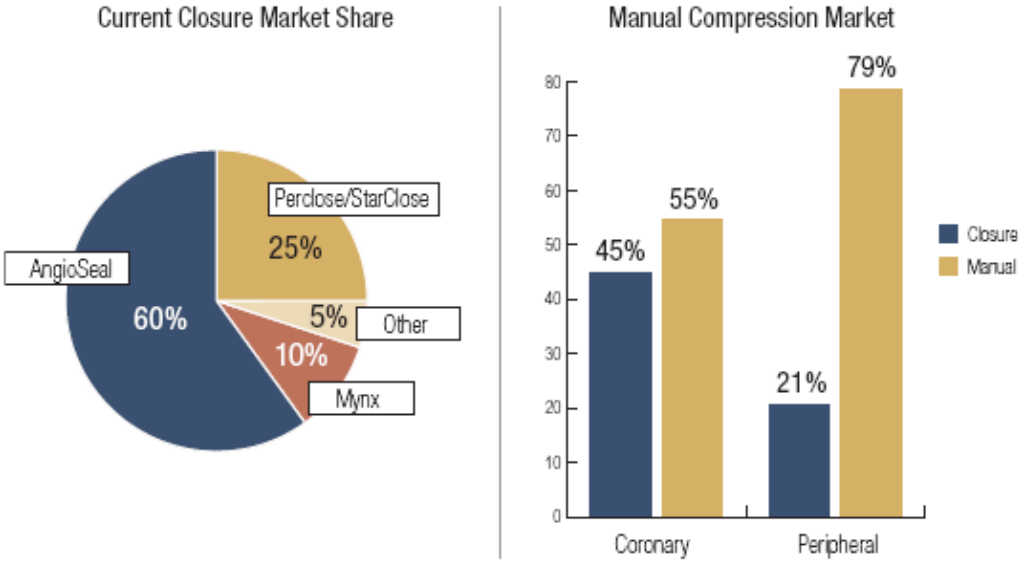
SOURCE: AccessClosure

Despite the size of the market, it remains underserved by existing devices, which currently generate only an estimated $400 million in sales. That reflects the fact that vascular closure devices (VCDs) have only penetrated 40% of the interventional procedure market (combining diagnostic and therapeutic procedures). In the remaining 60% of cases, the punctures are sealed using manual compression. That distinction is even more evident in the growing peripheral vascular space. In coronary procedures, 45 to 50% of cases use VCDs, with the rest relying on manual compression, whereas in peripheral cases, only 20 to 25% use VCDs, leaving the majority of patients to have their punctures sealed manually.

Although companies, both large and small, have attempted to introduce new vascular closure technologies, this space continues to be dominated by the two players that have long been the market leaders: **St. Jude Medical Inc.**, with its *Angio-Seal* device, which has 60% of the US market, and **Abbott Vascular Devices**, a division of **Abbott Laboratories Inc.**, with its *Perclose* and *StarClose* products, which has a 25% market share. (*See Exhibit 2.*)

Exhibit 2

US Vascular Closure Landscape



SOURCE: Industry estimates

Fred Khosravi acknowledges that the current devices on the market are successful in sealing vascular punctures, but he saw significant room for improvement, primarily in terms of creating a device that was more patient-friendly. "The incumbent closure technologies have been around for more than a decade and, while they work, they are associated with significant complications, and from a morbidity standpoint, they are not all that patient-friendly," Khosravi suggests. "They were designed primarily to be physician-friendly in terms of being easy to use and simple to operate, but they can be hard on the patients." Among the complications and patient complaints are bleeding risks, and that the current devices can be painful, and they remain implanted in the puncture site where they can cause sustained discomfort and create vascular obstructions.

The idea behind AccessClosure s device was to come up with a product that, while still easy for the physician to use, was also less painful and easier on the patient. The primary vision for the product, according to Khosravi, was the idea of not leaving a permanent implant in the patient following closure.

The company s first-generation product was called *Matrix* and it was a liquid hydrogel that was injected into the tissue at the site of the vascular puncture to create a sealant. The product was initially used successfully in Europe and then the company launched a US randomized clinical trial, which met all of its end points. The

clinical trial data served as the basis for AccessClosure s PMA application, which the FDA approved in 2005.

Normally, FDA clearance of a PMA device would be cause for celebration at a start-up and the beginning of US commercialization. However, during the course of the US clinical trial, the company had been receiving mixed reviews from physicians on how *Matrix* was performing. In terms of safety, efficacy, and clinical end points, the product was doing well; it was being used to successfully seal vascular punctures without leaving a permanent implant behind and without creating some of the bleeding complications and other risks that sometimes occur with current devices.

However, physicians were also telling the company that they were finding *Matrix* to be difficult to use. "What we were hearing from the doctors was that the process of injecting the liquid and reconstituting the polymer was a little too cumbersome for interventional procedures," Khosravi explains. Apparently, while that approach was fine for surgeons either in the OR or in post-surgical recovery rooms, the process was too complex for the cardiac cath lab with its shorter, simpler procedures and premium on fast procedural turnaround.

That physician feedback left AccessClosure with a dilemma: should the company go ahead and launch its FDA-cleared product and then make any necessary improvements to the next-generation device, which is the approach device companies typically take, or should it adopt a more cautious strategy of waiting to introduce its first product in the US until the company addressed physicians concerns, knowing that would delay the product s launch and forestall the anticipated revenue?

AccessClosure decided to take the more conservative route and delay commercialization pending a redesign of the product to make it easier for interventionalists to use. "I have no doubt that many companies in that position, armed with an approved technology, would have gone ahead and commercialized it, with the idea that they would fix the problem in the next iteration. But our strategy was to try to be the market leader in this space and we decided that, since that was our goal, we would have to come in with a market-leading product right off the bat," Khosravi explains. "We didn t think it would work to enter the market with a product that could get, let s say, 10% market share, and then try to become the market leader based on our next-generation product."

That non-traditional strategic decision raised all kinds of red flags in the industry, causing people to wonder what kinds of problems the company was experiencing that would cause it to not bring *Matrix* to market following FDA clearance. What many in the industry didn t realize--that AccessClosure employees, investors and board members knew--was that the company had a second-generation technology close behind that addressed the ease-of-use issues that were physicians primary concerns.

Serendipity Strikes Again

As with many device innovations, the success of AccessClosure s next-generation product was largely fortuitous. In early 2005, around six months before the FDA approved the company s PMA application, Amar Sawhney conducted an experiment at Confluent unrelated to anything at AccessClosure in which he dried some hydrogel in a lab dish, for no specific purpose, and sent it to Fred Khosravi at AccessClosure just in case they could use it to help develop the *Matrix* technology.

Khosravi took the dried polymer to his senior engineers, Celso Bagaoisan and Suresh Pai, and they rolled it up in the shape of a coronary stent, put it in a delivery system to try it as a vascular sealant, and found that it worked perfectly. By maintaining the hydrogel in a dried state, the company was able to eliminate the additional steps that physicians had been complaining about in using the liquid sealant. The result was a product that maintained *Matrix* s superior clinical performance, while also providing the simplicity and ease of use that clinicians were looking for. Khosravi recalls, "Within a matter of 48 hours, we had completely transformed our technology, and come up with an approach that we believe will revolutionize how closure is done."

Armed with this new approach, AccessClosure made the decision to hold off on introducing *Matrix* after receiving FDA clearance later in 2005. "We knew that we now had a greater technology that we believed was going to capture doctors imagination and enable us to basically leap-frog our competitors and put us in a position to become the market leader," Khosravi explains.

The company accelerated development and came up with a new device called *Mynx*, which resembles a sponge that expands to five times its size when inserted into the puncture site. After the puncture seals, the hydrogel dissolves naturally within 30 days, leaving no permanent implant, and minimizing bleeding complications while being less painful for patients.

Nearly two years later, having completed clinical trials, the product received FDA approval and entered the US market in May 2007. In its first full year of commercialization, AccessClosure generated $32 million in revenue (selling at a price premium compared with its competitors products), and has now been used in more than 250,000 patients in over 700 hospitals nationwide. The company recently has introduced another new product, called the *Mynx M5*, the first VCD designed specifically for closure of 5-French diagnostic cases. This new device is designed to enable the company to further penetrate the large manual compression market for diagnostic cases, which remains largely underserved by current devices.

Turning Failure Into Success

The initial success that the company is experiencing since launching the *Mynx* device feels especially sweet to employees and investors who, Khosravi acknowledges, were feeling quite disappointed by the decision to hold off on introducing the *Matrix* device. "Not being able to commercialize that product felt like a failure for the team that worked so hard on it, and even for some of the physicians who worked with us to get that device through the clinical trial," he notes.

Now, it looks like company management and the board made exactly the right call. Khosravi attributes the success resulting from that tough decision to the fact that management, the product development team, and physicians all were working closely together and communicating with one another on the virtues and problems of the *Matrix* device. "This process was one of the best examples that I ve seen of all the players engineering, clinical, management, and the board collaborating and listening to the customers because ultimately, in interventional cardiology, you need simplicity and ease of use just to get in the door," Khosravi says. "And in the end, it proves the benefits of good collaboration between physicians and entrepreneurs, as opposed to us just going to the doctors and saying that we have a product that met its end points; use it for a while until we come up with a better one."

This kind of decision also cannot be made without getting the buy-in of a company s investors because, in the case of AccessClosure, the company had invested more than $20 million in developing the *Matrix* device and getting it approved. Khosravi credits his investors with having the patience and foresight to agree to forestall the revenue that would have been generated by the *Matrix* in order to wait for the *Mynx* to be developed.

Khosravi believes the *Matrix* could have captured a small part of the market and generated some early revenue for the company. And the decision cost the company about a year and a half until the *Mynx* was ready, during which time management also had to sustain company morale to enable the accelerated development of the new product. "That was probably the hardest part of that decision," he admits, "because the team inside the company felt that they had failed themselves and the investors. Keeping them motivated so that they understood this was just a bump in the road was especially hard because the perception from outside the company was that we had failed even though internally we knew exactly where we were going."