

Current State of Endovenous Ablation

A look at the current clinical and commercial state of this continuously growing field.

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Endovenous therapy has revolutionized the way physicians treat patients with chronic venous disease. For those practitioners who had been treating varicose veins with traditional surgical techniques, the benefits of endovenous thermal ablation are obvious. However, in this era of evidence-based medicine, comfort with a particular form of therapy is reinforced when supported with level 1 evidence in the form of many high-quality randomized trials that demonstrate the benefit of therapy. To this end, the endovenous literature is relatively immature. Endovenous therapy has been strongly influenced by industry marketing. Direct marketing to physicians and patients has made an impact on the treatment of superficial venous disease. The purposes of this article are to help navigate the reader through the world of endovenous ablation in its current state and to explore the truths and possible misconceptions in existing scientific publications and industry marketing.

Much of the endovenous discussion revolves around the analysis of saphenous vein closure. The majority of published literature has reported “percent recanalization” as the absolute number of recanalized veins divided by the absolute number of veins at risk for recanalization. Percent recanalization is not statistically linked to mean follow-up or recanalization at a specific point in time. This less-than-rigorous statistic has been quoted extensively in the endovenous literature, and physicians must consider this in the context of patient care. Reporting vein closure using the Kaplan-Meier method is more appropriate. In the arterial literature, this approach has a long and successful history. With this method, we can link vein closure to mean follow-up, a measure of

the strength of the series and time after the procedure. This method also allows determination of primary, primary-assisted, and secondary vein closure. This approach has been recently endorsed by the recommended reporting standards for endovenous ablation for the treatment of venous insufficiency in a joint statement of the American Venous Forum and the Society of Interventional Radiology.¹

Eliminating an incompetent great saphenous vein (GSV) reduces venous hypertension, relieves patient symptoms, and prevents or slows the disease progression. However, GSV ablation alone is usually not sufficient for elimination of all existing varicose veins.² Complete care of the patient with varicose veins requires adjunctive therapy; the two most common procedures are phlebectomy and ultrasound-guided sclerotherapy (UGS). Phlebectomy allows simple removal of bulging varicose veins on the skin surface



Figure 1. First-generation ClosureFast 1-cm treatment length.

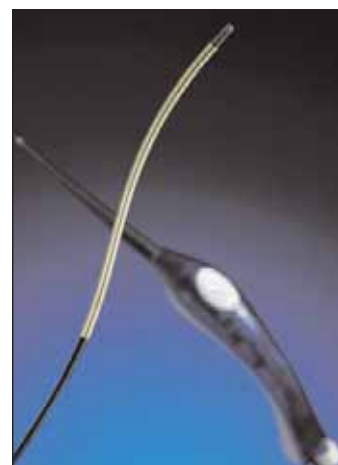


Figure 2. ClosureFast 7-cm treatment length.

and is frequently performed at the time of the saphenous procedure. UGS, on the other hand, has three primary uses: (1) treatment of veins below the skin not easily removed with phlebectomy, (2) treatment of tortuous veins not easily traversed with endoluminal guidewires (eg, neovascularization, perforating veins), and (3) for rescue of recanalized segments after thermal ablation. It is now common practice to treat recanalized segments with UGS; therefore, when investigators present their results to the scientific community, their data should be in the Kaplan-Meier format inclusive of primary, primary-assisted, and secondary closures of the saphenous vein.

To date, only one retrospective clinical study has compared radiofrequency (RF) ablation to endovenous laser ablation (EVL) of saphenous veins using both percent recanalization and Kaplan-Meier analysis.³ A comparison was made between the EVL (n=819) and the RF (n=128) cases. The patient populations were similar in age; gender; clinical, etiological, anatomical, and pathophysiological (CEAP) classification; and comorbidities. All cases were performed endoluminally, using ultrasound guidance and local anesthesia in the office surgical suite. Successful treatment was defined by the absence of flow in the treated vein segment by duplex ultrasound imaging. Recanalization was defined as the presence of flow in a vein segment >5 cm in length. Ultrasound follow-up was performed at 2 days, 1 month, 6 months, 12 months, and then annually. The mean follow-up times for RF and EVL subjects were 198 days (range, 1 to 1036) and 160 days (range, 1 to 890), respectively. Cessation of retrograde flow in the target vein was observed in all patients at the completion of the procedure. Recanalization was observed in 21 veins. When recanalization was present in the GSV, it usually occurred proximal to the posterior thigh circumflex vein; in the small saphenous vein, recanalization occurred proximal to May's perforator. Ninety percent (19 of 21) of the recanalizations occurred within the first 12 months after treatment. In this series, the primary closure rate by Kaplan-Meier analysis was 85% for RF (percent recanalization=5.5%) and 92% for EVL (percent recanalization=1.7%) at 500 days. The study demonstrated a statistically significant difference in favor of EVL over the first-generation RF device (Figure 1).

The first-generation RF device was slowly losing market share because it was less effective and more cumbersome to use than the more nimble endovenous laser products. In May of 2007, VNUS Medical Technologies, Inc. (San Jose, CA) launched their second-generation radiofrequency ablation product called ClosureFast (Figure 2) at the annual International Vein Congress (IVC) in Miami. ClosureFast has shortened the catheter pullback time from 20 minutes to about 3 minutes with little postoperative discomfort. No data are yet available as to whether primary closure rates



Figure 3. Bare laser fiber.

with ClosureFast will improve on the 85% primary closure rate from its first-generation counterpart. However, recent preliminary data from Europe using ClosureFast demonstrate successful saphenous ablation in all cases at 6 months.

With laser ablation, postoperative discomfort and bruising are seen routinely. The laser may act by causing boiling blood to injure, and possibly perforate, the vein wall. Others contend that the mechanism of action necessitates fiber contact with the vein wall. At this time, the theories on mechanism of action are inconclusive, and more basic science data are needed. Lasers designed for ablation of the vein wall can be classified into hemoglobin-specific laser wavelengths (HSLW) and water-specific laser wavelengths (WSLWs) based on theoretical mechanisms of action promulgated by industry, and, further, medical industry continues to make a concerted effort to link outcomes to wavelength. The three HSLWs currently available, in order of increasing hemoglobin affinity, are 810 nm, 940 nm, and 980 nm. Two WSLWs (1320 nm, 1319 nm) are available for use at this time. Although two studies have demonstrated some benefits of higher wavelengths referable to less postoperative discomfort, there has been no conclusive scientific evidence available to support the use of one laser wavelength over another.^{4,5}

The competition among endovenous laser companies entered the legal arena in 2004 when Diomed, Inc. (Andover, MA) filed legal action in the United States Federal District Court for the District of Massachusetts against AngioDynamics, Inc. (Queensbury, NY) and Vascular Solutions, Inc. (Minneapolis, MN), seeking injunctive relief and damages for infringement of Diomed's pioneering "777" patent. In the Order, the judge held that to violate the Diomed patent, a competing method must deliberately put the tip of the laser fiber in physical contact with the wall of the vein, must drain blood from the vein, must compress the vein, and must maintain vein wall con-

tact as the laser energy is delivered. On March 28, 2007, the jury found AngioDynamics and Vascular Solutions liable for both inducing infringement and contributory infringement of Diomed's patent and awarded Diomed a total of \$14.7 million in damages. AngioDynamics and Vascular Solutions responded with release of "covered fibers," which are designed not to allow physical contact of the laser fiber tip to the vein wall. Clinical data referable to primary closure rates of saphenous veins using covered fibers are not available. However, the investor community has had an interesting reaction to these publicly traded laser companies, as stock prices for all the aforementioned companies fluctuate continuously.

From the vantage point of an interested vascular surgeon who has used all of the endovenous lasers on the market, they have one common thread: they all effectively close refluxing saphenous veins. If the laser fiber is positioned properly at the saphenofemoral junction and 60 to 80 J/cm of energy is delivered intraluminally to the vein, the vein will close regardless of wavelength. From a practical perspective, questions regarding whether wavelengths target water or hemoglobin, or whether fibers touch the vein wall, are perhaps more of a concern in academic and legal forums than in clinical practices. Further, among laser devices, there is no conclusive evidence whether one device causes less pain and bruising postoperatively. Of note, all published data have been with the use of bare laser fibers (Figure 3), and data are not available using the newer covered laser fibers for saphenous ablation.

The course of RF ablation of the saphenous vein has been no less fascinating. In July 2005, VNUS filed a lawsuit against Diomed in the US District Court for the Northern District of California alleging infringement of four of its US patents. Diomed filed responses denying the allegations of infringement, and counterclaiming against VNUS for a declaration that none of the patents are infringed, that they are all invalid, and that two of the VNUS patents are unenforceable for inequitable conduct. In October 2005, VNUS served an amended complaint adding AngioDynamics and Vascular Solutions as defendants. The trial is expected to commence in October 2007. There are no published studies that clearly show a difference between a patient's post-procedure discomfort when treated with RF or EVL. There is one prospective, randomized multicenter trial near completion, which should help clarify this. However, anecdotally, all investigators who have used both RF and EVL devices agree that RF ablation causes less postoperative bruising and discomfort than EVL. The investor community has already rewarded the publicly traded VNUS with stock prices climbing since the ClosureFast debut.

In the area of chemical ablation (sclerotherapy), there has been much debate regarding efficacy; most often, discus-

sions include foam versus liquid and the correct sclerosing agent concentration for various techniques.^{6,7} In November 2004, the FDA granted approval to Bioniche Life Sciences Inc. (Belleville, Ontario, Canada, distributed by AngioDynamics) to manufacture sodium tetradecyl sulfate (STS) in 1% and 3% strengths. A recent study found FDA-approved STS to be more effective than STS acquired from compounding pharmacies.⁸ There is no evidence that a commercialized foamed sclerosant will garner FDA approval in the near future due to concerns of paradoxical embolization of foamed particles to the arterial circulation; therefore, using foam remains off-label. Some work is underway with endovenous catheters to optimize the delivery of liquid sclerosants to the vein wall.

The prevalence of venous disease in the US has been widely quoted to be on the order of 40 million persons. As for public awareness of the available new treatment modalities, we are only beginning to scratch the surface. There are enough patients out there for all interventionists interested in this field to participate and thrive. Although protecting intellectual property is clearly necessary in the realm of patent law, on balance, most would agree that competition is a good thing. It acts as a force to push people to excel and create new ideas. It also keeps product prices lower for the consumer. As the interested medical community eagerly awaits the outcome of VNUS versus Diomed, AngioDynamics, and Vascular Solutions, three things are certain: (1) endovenous techniques are proving superior to traditional surgery, (2) endovenous technology continues to evolve, and (3) some vendors of endovenous technology are in tenuous positions at the time of this publication. ■

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