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Concepts in a Multiprong Approach to Photoaging

Z. D. Draelos, MD

**Department of Dermatology, Wake Forest University School of Medicine,
Winston-Salem, North Carolina, and Dermatology Consulting Services, High
Point, North Carolina, USA**

ABSTRACT

Photoaging is a multisystem degenerative process that involves the skin and the skin support systems, including the bone, cartilage, and subcutaneous compartments. These structures provide the architectural support for the dermis, epidermis, and stratum corneum. A multiprong approach to photoaging involves reversing the undesirable changes in each of these structures. Dermatologists should become adept at treating all of the visible manifestations of photoaging.

Key Words: *photoaging, multiprong approach*

The multiprong approach to photoaging involves addressing medical, invasive surgical, minimally invasive surgical, and noninvasive approaches. The medical approach to photoaging is based on the use of pharmaceuticals, nutraceuticals, and cosmeceuticals. The surgical invasive approach is based on cutting away and redraping the facial skin. The minimally invasive surgical approach is predicated on resurfacing, redistributing, and reshaping the skin. Finally, the noninvasive approach is based on muscle relaxation and rebuilding the dermis. Each of these approaches has advantages and disadvantages in terms of risk, scarring, healing time, and final outcome. Each aims to reverse the effects of cutaneous photoaging.

Dermatologic Approach to Facial Rejuvenation

The compartments of the face that require attention include:

- Bony architecture
- Cartilage architecture
- Subcutaneous compartment
- Viable dermis and epidermis
- Nonviable epidermis
- Stratum corneum

Bony Architecture

One of the most important areas for consideration is the bony architecture over which the skin lies. Without a strong framework, the skin hangs formless over the face. Bone demineralization begins earlier than thought, at around age 25 in fair-complected females. It is this bone loss that leads to dulling of the facial features. Unfortunately, published results outlining the risks and benefits of

hormone replacement therapy¹ lead many women to discontinue estrogen supplementation due to concerns about coronary disease; however, bone replacement therapy, such as bisphosphonates, is usually not begun until overt evidence of osteoporosis is present. Furthermore, many fair-complected women are Vitamin D deficient according to the new revised laboratory normal values.² Dermatologists should become proficient at advising patients regarding facial bone health.

Instituting therapy for anticipated or existing osteopenia or osteoporosis is not difficult. Women who are at risk for facial bone loss should probably have a hip or spine Dexascan yearly to chart the success of therapy. Vitamin D therapy should be initiated at 50,000 IU for 2 weeks followed by 800 IU daily as a nutraceutical. Calcium carbonate should be given as a supplement at 1gm daily accompanied by a bisphosphonate administered once weekly. At least 30 minutes of weight-bearing exercise should be undertaken 3 times weekly. Patients should be reminded that swimming and cycling do not constitute weight-bearing exercise.

Cartilage Architecture

The architecture of the cartilage of the face, in addition to the bony architecture, defines the shape of the face. The most important facial structure dependent on cartilage is the nose. The cartilage does not disappear with advancing age, but does change shape. Much of the change occurs during pregnancy due to the relaxins that are secreted at high levels during the final trimester to allow childbirth. I believe these relaxins also cause the tip of the nose to droop, which contributes to a more mature appearance of the female face. At present, there is no research regarding the preservation of the youthful nasal shape during pregnancy. Perhaps the use of hyaluronic acid fillers during pregnancy could preserve the up-turned, youthful female nose.

Subcutaneous Compartment

The subcutaneous compartment undergoes much of the change that contributes to the aged appearance of the face. It is presently unclear why subcutaneous fat from all over the body is removed, including the facial fat, and redeposited intrabdominally. Some researchers who study anti-aging have advocated the notion that these changes are due to lower growth hormone levels and recommended supplementation.³ This recommendation is certainly outside current mainstream medicine. Others point

to the fat redistribution on the body that occurs with menopause.^{4,5} In postmenopausal women fat is typically redistributed to the breast, arms, waist, thighs, and buttock with loss of facial fat.

At present, the best way to replace large amounts of fat that are lost from the face, resulting in prominent nasolabial and melolabial folds, is through autologous fat transfer. The fat is removed from the hips or thighs and moved to the face for insertion on the bone, in the muscle, and below the skin. This dermatologic technique can result in a more youthful appearance without the downtime and scarring of a face-lift. I believe that autologous fat transfer is preferable to a face-lift because it does not change the essence of the individual's face. Many women lose their characteristic appearance after a face-lift because the skin has been stretched and repositioned over the fat-devoid bones creating an angular, gaunt appearance. Although the skin folds have been removed, the youthful curves of the face have not been recreated.

Viable Epidermis and Dermis

The viable epidermis and dermis are the essence of the skin. It is the loss of dermal collagen that leads to wrinkling and the increased appearance of muscular attachments. Irregular melanization leads to lentigines, melasma, and poikiloderma, and prominent telangiectasias lead to erythema. It is in this area that many new developments have occurred. Fillers, deep chemical peeling, and laser resurfacing can replace or encourage regeneration of lost dermal collagen. Botulinum toxin can be used to minimize the appearance of hyperkinetic muscles. Medium depth chemical peeling, cryosurgery, and intense pulsed light can be used to even out pigmentation abnormalities. Light sources, electrocautery, and sclerotherapy can be used for telangiectasias. This is an area of treatment where dermatology has much to offer.

Nonviable Epidermis

Dermatology also excels at treating the nonviable epidermis. It is in this area where desquamatory failure leads to retained corneocytes and poor skin texture. Superficial glycolic and salicylic acid chemical peels and microdermabrasion can enhance desquamation. Actinic keratoses can also contribute to poor skin texture, but are readily treated with 5-fluorouracil, diclofenac (Voltaren[®], Novartis), imiquimod (Aldara[®], 3M), or cryosurgery.

Stratum Corneum

The last area to consider is the stratum corneum. This is really the area of the cosmeceutical. It is the stratum corneum that is impacted by most of the creams for aging skin sold at the cosmetic counter. The most common treatable stratum corneum problem that leads to fine wrinkling is dehydration. In addition, the skin barrier may be in need of repair. A well-constructed moisturizer, e.g., Cetaphil® (Galderma) or CeraVe® (Coria Laboratories), creates an environment for healing in which the corneocytes and intercellular lipids can be restored to their normal brick-and-mortar lamellar organization. The stratum corneum also provides an opportunity to prevent photodamage through the application of sunscreens.

Conclusion

Dermatologists should consider a multiprong approach to photoaging by considering its effect on all of the facial structures, including the bone, fat, dermis, epidermis, nonviable epidermis, and stratum corneum. The best long-lasting solutions for the prevention and treatment of photoaging can be achieved through this multisystem approach.

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Advances in Techniques for Endovenous Ablation of Truncal Veins

G. S. Munavalli, MD, MHS,^{1,2,3} and R. A. Weiss, MD^{1,3}

¹Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

²Division of Dermatology, University of Maryland School of Medicine, Baltimore, Maryland, USA

³Maryland Laser, Skin and Vein Institute, Hunt Valley, Maryland, USA

ABSTRACT

The latest techniques for endovenous occlusion, i.e., radiofrequency ablation catheters or endoluminal laser targeting water are our preferred methods for the treatment of saphenous-related varicose veins. Clinical experience with endovenous techniques in more than 1,000 patients shows a high degree of success with minimal side effects, most of which can be prevented or minimized with use of tumescent anesthesia. Within the next 5 years, these minimally invasive endovenous ablative procedures involving saphenous trunks should have virtually replaced open surgical strippings.

Key Words: endovenous occlusion, saphenous related varicose veins, radiofrequency ablation catheters, endoluminal targeting water

Venous disease affects 40%-55% of the population; common symptoms include leg pain, swelling, and skin changes.^{1,2} It encompasses a wide spectrum of clinical manifestations, from asymptomatic spider veins overlying the ankles, to bulging branches of the greater or great saphenous vein (GSV) extending across the anterior thigh, to leg swelling and chronic ulceration of the lower medial calf. Venous insufficiency, the most common form of venous disease,² occurs when a high-pressure leakage develops between the deep and superficial systems, or within the superficial system itself (e.g., within GSV,

and the lesser or small saphenous vein (LSV), (Figure 1)), followed by sequential failure of the venous valves in the superficial veins. Venous blood escapes from its normal flow path and flows in a retrograde direction down into an already congested leg. Over time, incompetent truncal veins acquire the typical dilated and tortuous appearance of varicosities. Furthermore, insufficiency can lead to chronic morbidity in the form of ulcerative and edematous skin changes in the lower extremities.

Previous methods of treating saphenous vein reflux include vein stripping, ligation and division, echosclerotherapy, and valve replacement. Vein stripping has a failure rate as high as 60%, and has historically required general or spinal anesthesia. Recovery can often take 2-3 weeks. Similar to vein stripping, the reported incidence rate for GSV reflux following high ligation alone is significant, with up to 71% recurrence. Postulated reasons for this include under-recognized anomalous anatomic vascular patterns in the saphenous systems and neo-vascularization.

In 2002, the US FDA approved endovenous laser treatment as a minimally invasive method of ablating incompetent saphenous veins. This in-office procedure uses local anesthesia, thus eliminating the need for general or spinal anesthesia. Unlike the invasive processes of stripping and ligation, obtaining percutaneous access to a vein under local anesthesia and using a form of directed laser energy from the

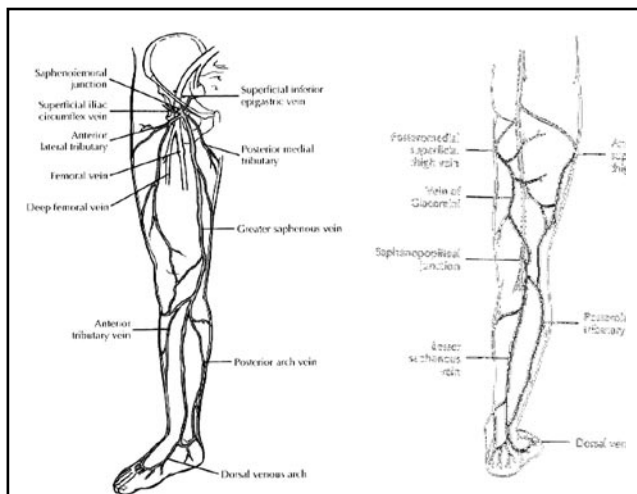


Figure 1: Distributions of the Greater (Great) and Lesser (Small) Saphenous Veins



Figure 2: Clinical improvement 6 weeks after treatment of the LSV with endovenous ablation

inside to shrink and seal the targeted vein allow for quick patient recovery (Figure 2).

Endovenous ablation was first performed by inserting a bipolar radiofrequency (RF) fiber into a targeted varicose or refluxing saphenous vein and heating from within.³ With more than 60,000 procedures performed worldwide since 1999, radiofrequency shrinkage of veins has become a valuable addition to treating large varicose veins resulting from saphenous reflux. Today, systems are also available that utilize various infrared wavelengths to accomplish endoluminal heating and shrinkage of saphenous trunks. This article will focus on two types of endovenous treatment using laser: laser targeting hemoglobin (810nm, 940nm, and 980nm) and laser: laser targeting water (1320nm).

Utilization of Tumescent Anesthesia

Tumescent anesthesia, or the placement of large volumes of dilute anesthesia in a perivascular position under the direction of duplex guidance, serves several purposes:

- It protects perivascular tissues from the thermal effects of intravascular energy by serving as a heat sink.
- It decreases the diameter of the treated vein to allow for better absorption of energy by the target chromophore and thus, secondarily, reduces intravascular blood for nonspecific coagulation.
- It provides a more effective and safer anesthesia for patients.

Using the tumescent technique, sealing the GSV via the endovenous approach is a painless procedure permitting immediate post-treatment ambulation. In our experience, the incidence of deep vein thrombosis (DVT) as measured by Duplex ultrasound 3-14 days after treatment is 0%.

Endoluminal Laser Ablation Targeting Hemoglobin (810nm, 940nm, and 980nm)

Endovenous laser treatment allows delivery of laser energy directly into the blood vessel lumen in order to produce endothelial and vein wall damage with subsequent fibrosis. Various lasers are used (Table 1). The presumed target for lasers with 810nm, 940nm, and 980nm wavelengths is red blood cells. Steam bubbles are generated as blood is boiled within the

Wavelength	Brand Name	Target Chromophore	Mechanism of Action
810nm*	EVLV™ (Diomed) – endovenous laser treatment	Hemoglobin	Heating blood, transmitting to vein wall
940nm	ELT – endovenous laser treatment	Hemoglobin	Heating blood, transmitting to vein wall
980nm	ELVeS™ (biolitec) – Endo Laser Vein System	Hemoglobin	Heating blood, transmitting to vein wall
1320nm	CTEV™ - (CoolTouch) Endovenous Laser	Water	Heating of water in vein wall

Table 1: Currently available endovenous lasers

*Other 810nm devices are presently being sold by Vascular Solutions (Vari-Lase 810nm) and by MedArt® (ILVO™ Intra-luminal Laser Vein Occlusion using MedArt 426).

lumen, resulting in thrombotic vein occlusion. Direct thermal effects on the vein wall are probably not important. The extent of thermal injury to the tissue is dependent on the quantity of blood in the lumen, the rate of pullback, and the amount of tumescent anesthesia placed around the vein.

The 810nm diode laser appears to have good short-term efficacy in the treatment of the incompetent GSV, with 96% occlusion at 9 months, and a <1% incidence of transient paresthesia. More recently, a 2-year follow-up of 499 limbs indicated a recurrence rate of less than 7%. However, 90% of the patients contacted experienced degrees of postoperative ecchymosis and varying degrees of discomfort.⁴ In other series, skin burns have been reported, as have cases of deep venous thrombosis extending into the femoral vein.

Our patients treated with an 810nm diode laser have shown an increase in post-treatment purpura and tenderness. Most of our patients do not return to complete functional normality for 2-7 days as opposed to the 1-day “down-time” with RF closure of the GSV. Recent studies suggest that pulsed 810nm diode laser treatment may be responsible for intermittent vein perforations, and continuous treatment may be safer.⁵

When using a wavelength strongly absorbed by hemoglobin, such as 810nm, there is a significant amount of intraluminal blood heating with transmission of heat to the surrounding tissue through long heating times. Temperatures in animal models have been reported as high as 1200°C.⁵ When we have tried *ex vivo* vein treatment without blood, the 810nm wavelength simply chars a groove along the inside of the vein.

In vivo, varicose veins are not straight segments, but rather saccular and irregular, so that pockets of hemoglobin are frequently encountered which leads to sharp rises in temperature and vein perforations when hemoglobin-absorbing wavelengths such as 810nm are used. Minimizing direct contact with the vein wall for hemoglobin-dependent methods minimizes the charring of the vein wall and probably lowers the postoperative pain levels.

It can sometimes be very difficult to gauge the correct amount of tumescent solution needed to compress the vein and still leave some intraluminal blood (necessary for the mechanism of action). If too much tumescence is used, and hemoglobin is eliminated, there can be charring of the inner wall of the vein, with resulting pain and failure of vein occlusion.



Figure 3: CoolTouch CTEV™ 1320nm laser and automatic pullback device (Courtesy CoolTouch, CoolTouch Corp)

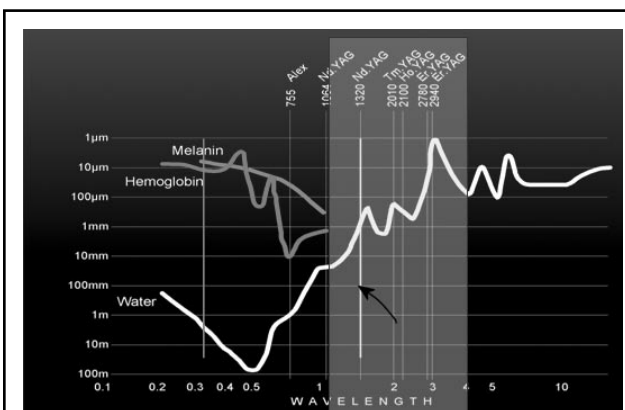


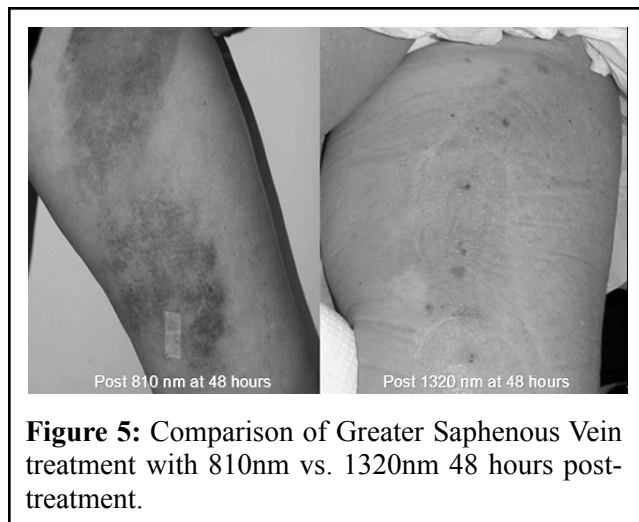
Figure 4: 1320 nm wavelength is selective for water as the chromophore. This allows for targeted heating of the vein wall.

Endoluminal Laser Ablation (1320nm) Targeting Water

In an attempt to circumvent problems associated with hemoglobin-absorbing wavelengths, the 1320nm laser was investigated for endovenous ablation beginning in 2002. US FDA clearance was achieved in September

2004 for treatment of GSV, and in August of 2005 for the obliteration of reflux in the lesser saphenous vein. The 1320 nm CoolTouch CTEV™ (CoolTouch) uses a special conducting laser fiber coupled with an automatic pullback device pre-set to pull back at 1mm/sec (Figure 3). Tissue water is the target, and the presence or absence of red blood cells within the vessels is not relevant to the effectiveness of the procedure. This 1.32 μ wavelength is unique among endovenous ablation lasers in that this wavelength is absorbed only by water and not by hemoglobin (Figure 4).

Our own experience with the 1320nm device reflects a reduction in pain and bruising of 80% as compared



with the 810nm device. Having treated more than 200 greater saphenous veins with the 1320nm laser, we have found the incidence of mild pain is 5%, and our success rate of vein ablation is 95% at 2 years. Goldman⁶ has reported a similar experience, concluding that at 6 months follow-up, a 5-watt, 1320nm intravascular laser with 1mm/sec automatic pullback, delivered through a diffusion-tip fiber, was shown to be safe and effective for treating an incompetent great saphenous vein up to 1.2 cm in diameter (Figure 5).

We believe that there is reduced pain with the 1320nm laser due to reduced vein perforations, less thrombus formation, and more uniform heating. Pain that is experienced after treatment with the 1320nm laser is probably related to heat dissipation into the surrounding tissue, rather than to vein perforations, as the incidence of bruising is extremely low. In our own unpublished studies we have found that emitting 5 watts of 1320nm radiation through a 600 μ fiber moving at 1mm/sec in a 2mm-thick vein wall results in a peak temperature

of the exterior vein wall of 48°C. Unfortunately, in a saphenous vein, for effective sealing and shrinkage, higher energies must sometimes be utilized. (Figure 5). The 1320nm water-targeting device appears to be associated with less pain and bruising than 810nm, 940nm, or 980nm hemoglobin-targeting endovenous devices.

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Update on Drugs

Class	Name/Company	Approval Dates and Comments
<i>Antipsoriatic Agent</i>	Calcipotriene/ Betamethasone Dipropionate <i>Taclonex® Ointment</i> Warner Chilcott/ LEO Pharma	The US FDA approved this topical ointment in January 2006 as a once-daily treatment of psoriasis in adults. Taclonex is sold as Dovobet® or Daivobet® outside the US.
<i>Antibacterial Agent</i>	Retapamulin GlaxoSmithKline	The US FDA began its review process in January 2006 for this investigational antibacterial drug. Retapamulin belongs to a new class of antibiotics being developed as a topical treatment for uncomplicated skin and skin structure infections due to susceptible strains of <i>Staphylococcus aureus</i> and <i>Streptococcus pyogenes</i> .
<i>Wound Care</i>	Antimicrobial Barrier Dressing <i>Acticoat™ Moisture Control with SILCRYST™ Nanocrystals</i> NUCRYST Pharmaceuticals	The EMEA approved this foam dressing in February 2006 for the treatment of wounds with light-to-moderate exudate for up to 7 days. It was approved by the US FDA and TPD Canada in 2005.
<i>Diaper Dermatitis</i>	Miconazole Nitrate 0.25%, Zinc Oxide 15%, White Petroleum 81.35% <i>Vusion® Ointment</i> Barrier Therapeutics	The US FDA approved this ointment in February 2006 for the treatment of diaper dermatitis complicated by candidiasis.

Drug News

<i>Drug Warning</i>	The US FDA sent out a warning in December 2005 advising consumers not to use Miracle II Neutralizer and Miracle II Neutralizer Gel products manufactured by Tedco, Inc. because the products are bacterially contaminated and have not been proven to be safe and effective. These products have not been approved by the FDA. Unapproved uses include the treatment of diaper rash, dermatitis, hives, psoriasis, and skin cancer. Use of these products could pose a risk of serious adverse events such as infections, particularly in children, the elderly, and individuals with weakened immune systems, who are particularly susceptible to illness.
<i>Drug Warning</i>	According to a Canadian study being published in the <i>New England Journal of Medicine</i> *, elderly people who took gatifloxacin (Tequin®, Bristol Myers Squibb) were 17 times more likely to develop serious diabetes than if they took another antibiotic, and were four times more likely to be hospitalized for low blood sugar. Gatifloxacin is a fluoroquinolone antibiotic indicated for the treatment of skin and skin structure infections, pneumonia, urinary tract infections, and certain sexually transmitted diseases. The investigators further reported that this drug does not permanently damage the body's ability to control blood sugar; however, it could be deadly if a person's blood sugar falls too low. Doctors were urged to stop prescribing it. *Park-Wyllie LY, et al. <i>N Engl J Med</i> (2006 Mar 1). Available from URL: http://content.nejm.org/cgi/content/abstract/NEJMca055191v1 .
<i>Systemic Lupus Erythematosus</i>	A study recently published in the <i>New England Journal of Medicine</i> * reported that women with either inactive or stable systemic lupus erythematosus were able to take oral contraceptives without increased risk of flares. Subjects who took triphasic 35µg ethinylestradiol/0.5-1mg norethindrone for twelve 28-day cycles had no statistically significant difference in the occurrence of flares than those taking placebo. Severe flares occurred in about 7% of the women regardless of whether they received oral contraceptives or placebo. *Petri M, et al. <i>N Engl J Med</i> 353(24):2550-8 (2005 Dec 15).

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