

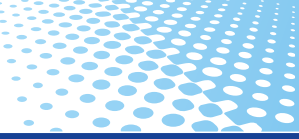
THE FUTURE

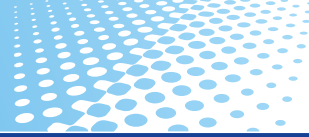
ENDOVENOUS LASER TREATMENT OF VARICOSE VEINS



Executive Summary
for Professionals

2012





ELVeS Radial™, the future of EVLA

**More Effective
Safer & Gentler
Less Pain & More Patient Referrals
More Versatile & User Friendly**

Objectives of this Summary

The objective of this Executive Summary is to provide information with solid clinical references based on international publications to help professionals decide on the best alternatives for endovascular treatment of varicose veins. For further information and specific training please contact your local representative.

Contents

1. The EVLA technology: Introduction, History & Concept
2. ELVeS Radial™ fiber: the future of EVLA
3. Why should you chose it
4. Training & Marketing for the patient
5. Product specifications

1. EVLA: The technology

Introduction

The laser is one of the greatest inventions of the 20th century, one that has revolutionized the way we live. 2010 was a milestone year on laser technology. The 50th anniversary of the demonstration of the first working laser which was first presented in 1960 based on Einstein's theories of electromagnetic radiation.

Since then, tens of thousands of patents involving lasers have been granted on a worldwide scale. Today lasers are used in an infinity of everyday products from DVD players to surgical devices and a whole range of medical procedures and sophisticated diagnostic tools. With an extensive list of Nobel Prizes that have involved lasers and a vast number of research centers working on this subject, the prospects for further advance and improvements in quality of life are in fact a present day reality. Every year over four million eye operations involving laser therapy performed in the USA alone and millions of other surgeries are done in a worldwide basis resulting in patients with more gentle and less invasive procedures in every area of medicine.

General Links & References

<http://www.photonics.com/Article.aspx?AID=42279>
<http://www.greatachievements.org/?id=3706>
<http://www.scilog.eu/en/blog/lindaunobel/2010-06-21/50-years-of-lasers>
<http://news.bbc.co.uk/1/hi/health/86886931.stm>
<http://www.laserfest.org/lasers/history/timeline.cfm>

More than a decade of EVLA

Generally, the beginning of EVLA is quoted to the Spanish doctor Bonè Salat (1999)^[1], however there are earlier publications by Puglisi (1986) and Magi (1990)^[2,3] using the same endovascular approach for the treatment of venous reflux.

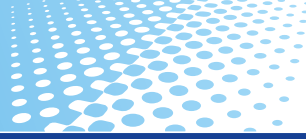
Since its approval by the FDA in 2001, EVLA became the most performed treatment for varicose veins in the USA and now accounts for more than 70% of all procedures.^[4]

- [1] C Bone Salat. Tratamiento endoluminal de varices con laser de diode: studio preliminary. Rev Paurol Vasc. 1999; 5:35-46.
- [2] B Puglisi, A Tacconi, F San Filippo. L'application du Laser Nd:YAG dans le traitement du syndrome variqueux. In Davy A, Stemmer R eds, Phlebologie 89, John Libbey Eurotext Ltd 1989; 839-42.
- [3] G Magi. Aportación de la fleboscopia al diagnóstico y al tratamiento de la insuficiencia venosa del los miembros inferiores. In Brizzio E y Leibashoff G eds, Flebologia estetica. Producciones especiales Ed 1990; cap 1:20-1.
- [4] J Mauriello. Endovenous Laser Ablation of Varicose Veins: Where are we going? Presented at IUA World Congress 2010-Buenos Aires (Argentina).

The EVLA concept

The advances on fiber optics and ultrasound ingaging with color Doppler, facilitated the development of minimally invasive techniques using laser radiation. Lasers and EVLA work by ablating the endothelium of the vein wall, which is mediated by direct and indirect effects of the laser. Direct heating effects occur by direct absorption of photon energy (radiation) by the vein wall and indirectly by convection from steam bubbles and conduction from heated blood. The steam produced by the blood's absorption of laser energy, however, is a small fraction of the energy necessary to damage the vein wall and not thought to be the primary mechanism of injury. Various laser wavelengths have been used for ablation including the 810nm, 940nm, 980nm, 1064nm, 1320nm and 1470nm. The primary target chromophore of the 810 and 940nm lasers is haemoglobin, while the higher wavelength lasers primarily target water. In this case, some of the radiation is absorbed by the water in blood and some by the the water contained in the vein wall generating thermal damage limiting as well the scattered energy leaving the vein and limiting side effects^[5] and pain.

- [5] KM Zhilin, VP Minaev and AL Sokolov. Effect of laser radiation absorption in water and blood on the optimal wavelength for endovenous obliteration of varicose veins. Quantum Electron. 39 781; 2009.



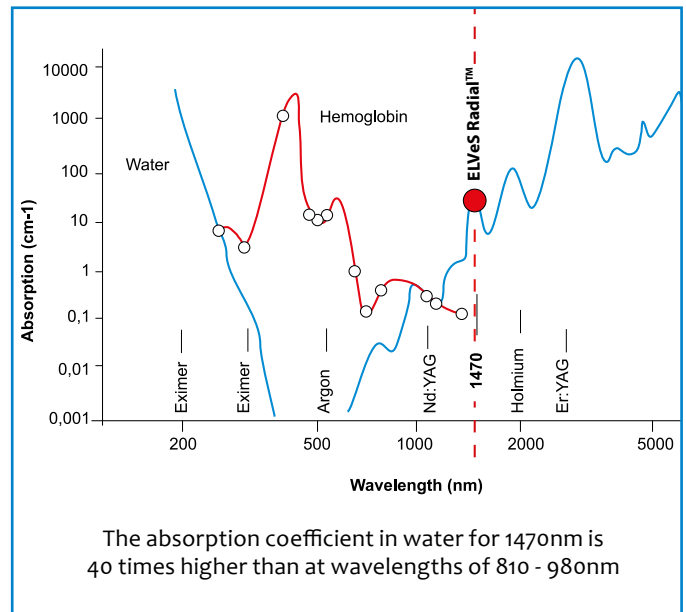
2. ELVeS Radial™ fiber: the future of EVLA

ELVeS Radial™ Laser



Biolitec® pioneered the use of higher wavelength lasers like 1470nm in order to perfect EVLA treatments by primarily targeting water and generating thermal damage directed to the vein wall. This wavelength of 1470nm shows a 40 times higher absorption

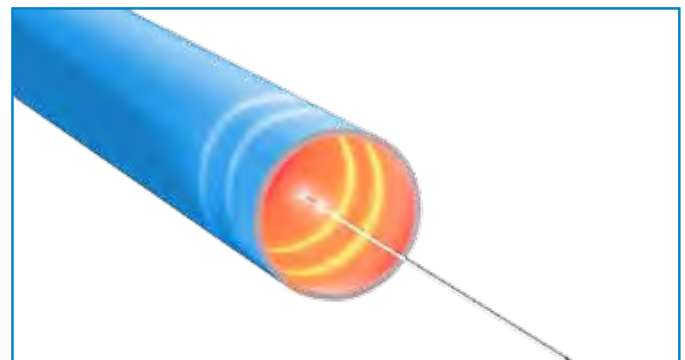
in water compared to 980nm which means less power and energy (LEED) is required to achieve vein closure while limiting as well the scattered energy reducing side effects and pain. Furthermore, 1470nm radiations is less absorbed by hemoglobin which leads to lower carbonization compared to 810nm lasers or RF systems.



Radial® Fiber

Sometimes the simplest solution is the one that takes longer. Like inventing the wheel. The ELVeS Radial™ fiber applies energy more evenly around the 360 degrees of the vein wall to gently but accurately ensure homogeneous photo-thermal destruction of the vein wall.

Avoiding perforation and minimizing complications and side effects by combining optical state of the art technology with the most effective laser system.



3. Why ELVeS Radial™

More Effective

A recent Meta-analysis that reviewed **119 studies** with an average follow-up of 32.2 months compared Surgery, Ultrasound Guided Foam Sclerotherapy (UGFS), Radio-frequency (RF) and EVLA.

After 3 years, Endovenous laser therapy was significantly more effective compared with stripping, foam therapy, and radio-frequency ablation.^[6]



No doubt that Endovenous Laser Ablation will lead the thermal techniques in elimination of saphenous reflux. Can treatment outcomes be improved?

In medicine nothing can be 100% effective and we are already at a very high rate of success with saphenous ablation.

John Mauriello MD, FACPh, (USA).

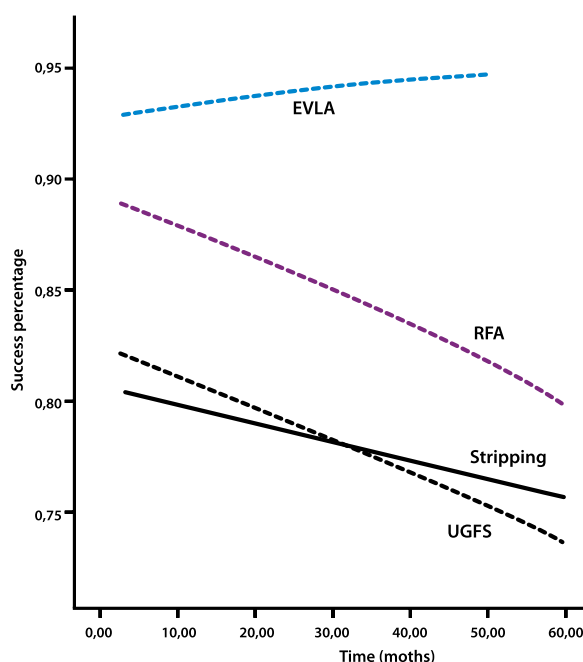
Type of intervention	3 months		1 year		3 year		5 year	
	Success rate (%)	95% CI	Success rate (%)	95% CI	Success rate (%)	95% CI	Success rate (%)	95% CI
Surgery	80.4	72.3-86.5	79.7	71.8-85.8	77.8	70.0-84.0	75.7	67.9-82.1
UGFS	82.1	72.5-88.9	80.9	71.8-87.6	77.4	68.7-84.3	73.5	62.8-82.1
RFA	88.8	83.6-92.5	87.7	83.1-91.2	84.2	75.2-90.4	79.9	59.5-91.5
EVLA	92.9	90.2-94.8	93.3	91.1-95.0	94.5	87.2-97.7	95.4	79.7-99.1

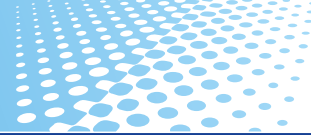
The same conclusion was reported on a new Randomized Controlled trial comparing RF and EVLA, showing that EVLA may provide a more secure closure over the long-term than RF.^[7]

[6] Renate van den Bos, MD, Lidia Arends, PhD, Michael Kockaert, MD, Martino Neumann, MD, PhD, and Tamar Nijsten, MD, PhD. Endovenous therapies of lower extremity varicosities: A meta-analysis - JOURNAL OF VASCULAR SURGERY - Volume 49, Number 1.

[7] Steven S Gale, MD, Jennifer N Lee, RN, M Eileen Walsh, PhD, Dennis L Wojnarowski, BA, Anthony J Comerota, MD.

A randomized, controlled trial of endovenous thermal ablation using the 810nm wavelength laser and the ClosurePLUS radio-frequency ablation methods for superficial venous insufficiency of the great saphenous vein - JOURNAL OF VASCULAR SURGERY, Vol 52, Issue 3, Pages 645-650 (September 2010)





Safer: Less Complications

Both EVLA and RF are well accepted methods for treating venous reflux and in general as safe as surgery to say the least. However, EVLA have proved over the last 10 years to be significantly safer in terms of risk of deep vein thrombosis (DVT) or pulmonary embolism (PE).^[8]

A significant number of reports of **DVT** and quite a few **PE's** related to **RF treatments** has been reported at FDA's website, including some fatal cases.^[9]

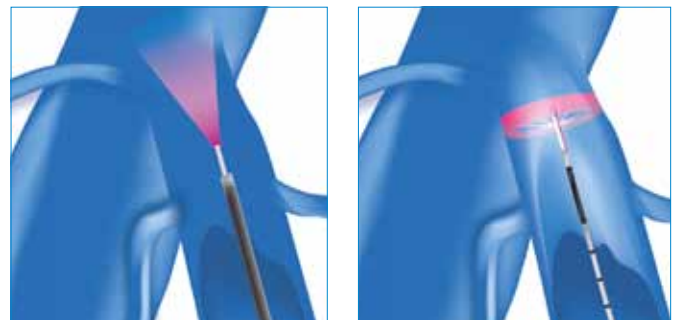
Other potential complications with higher incidence with RF treatments include, but are not limited to the following:

- **vessel perforation:** due to the mechanism of action of RF (electricity in a water rich medium);
- **paresthesia:** the risk of nerve damage is higher with treatment at or below the calf (SSV);^[10]
- **skin burn:** treatment of veins located very close to the skin surface may result in a skin burn.



The 1470nm endovenous laser combined with Radial fiber appears to be the most promising device for endovenous procedures^[12]

Thomas Schwarz MD, Germany



[f] Histology after Radial: circular thermal destruction vacuolization & delamination

The ELVeS Radial™ fiber applies energy more accurately and ensures homogenous photo-thermal destruction of the vein wall, allowing safe closure of the vessel by avoiding perforation and collateral damage to surrounding tissues, minimizing the risk of nerve damage and other side-effects.

ELVeS Radial™ (1470nm laser) proved to be safe and highly effective. The lower energy level needed using the Radial fiber significantly minimized adverse effects compared with the frontal emission fibers.^[11]

[8] A Hingorani, E Ascher, N Markevich, R Scutzer, S Kallakuri, A Hou, S Nahata, W Yorkovich, T Jacob. Deep venous thrombosis after radiofrequency ablation of greater saphenous vein: a word of caution. JOURNAL OF VASCULAR SURGERY. Vol 40, Issue3, Pages 500-4

[9] <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.cfm>

[10] <http://www.nice.org.uk/nicemedia/pdf/ip/132overview.pdf>

[11] Sroka R, Weick K, Da Conta A, Scheibe S, Srika I, Winter S, et al Investigations on the acute effects of circumferential laser light energy application for endovenous laser treatment. Edizioni Minerva Medica, 2009.

Gentle: Less Side Effects

Other potential side effects of EVLA and RF treatment include temporary bruising, swelling and numbness of the treated area and allergic reactions to anesthesia.

Laser devices and fiber optics evolved in the last few years in a way to improve the inherent „Selective Photo-thermolysis Principle“ of laser interaction with tissues. Today, we can achieve a precise targeting of a structure or tissue using a specific wavelength of light with the intention of absorbing light into that targeted area alone. Using the Radial fiber the laser energy is directed into the target area reducing energy requirements which leads to less adverse side effects, and less patient discomfort at a comparable success rate.^[12]

This kind of performance has been the case for many years in other areas of laser medicine and it is now the case for EVLA as well.

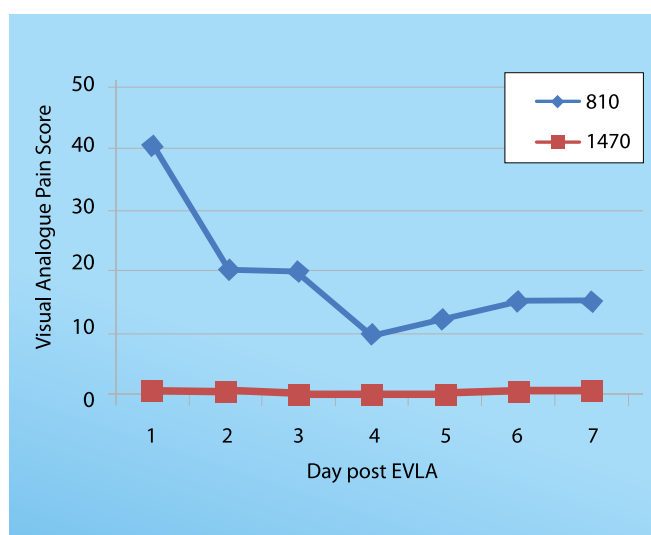
The ELVeS Radial™ procedure minimizes any post-operative inflammatory pain and bruising, due to a 40 times or greater absorption coefficient in water compared to lasers targeting hemoglobin (810nm 940nm) avoiding also vein perforation and nerve damage.

[12] Thomas Schwarz, MD, Eva von Hodenberg, MD, Christian Furtwängler, BS, Aljoscha Rastan, MD, Thomas Zeller, MD, and Franz-Josef Neumann, MD. Endovenous laser ablation of varicose veins with the 1470nm diode laser. JOURNAL OF VASCULAR SURGERY; 2010.

Less Pain

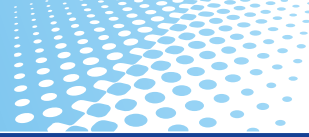
Although safe and with rare complications, EVLA used to be associated with more patients experiencing post-procedure pain and bruising. However, in the last few years, some studies comparing wavelengths report less bruising and a lower requirement for analgesia in those

treated with longer wavelength lasers. A prospective study using either 810 or 1470nm diode lasers, confirms that that longer wavelength lasers are associated with less post-procedural with no complications and 100% of successfully occluded veins.^[13] A randomised clinical trial comparing EVLA using 980 laser with bare tip fiber and 1470 with Radial fiber for the treatment of the GSV, resulted in less postoperative pain and better VCSS (venous clinical severity scores) scores on the Radial group than those treated with a 980 nm laser and a bare-tip fibre.^[14]



[13] A Ikponmwosa, R Darwood, M Gough, M Gaunt. Post-procedure pain, safety and efficacy following great saphenous (GSV) endovenous laser ablation (EVLA) using a 1470nm diode laser. Won prize at UK Venous Forum 2009.

[14] S Daganci, U Demirkilic. Comparison of 980nm Laser and Bare-tip Fibre with 1470nm Laser and Radial Fibre in the Treatment of Great Saphenous Vein Varicosities: A Prospective Randomised Clinical Trial. Presented at the XXIII Annual Meeting 3-6 September, 2009, European Society for Vascular Surgery, Oslo, Norway. Published: Eur J Vasc Endovasc Surg (2010) xx, 1 e 6.



Less Anesthesia

RF requires large amounts of tumescent anaesthesia (a pump is recommended) not only to protect other tissues from thermal damage but also to improve its mechanism of action and of course for the patient to cope with pain. Using ELVeS Radial™ procedures can be performed with only local not requiring tumescent anaesthesia and some centres prefer to use a Femora Nerve sensory block or mild sedation according to patient preference.

This shortens the procedure time, allows for bilateral's to be performed in one intervention and reduce the post-procedure pain and bruising (most of which is caused by the tumescent multiple injections). More importantly, the use of tumescent makes the US live follow up during procedure more difficult which in change is very easy using other means of pain control during treatment.

More versatile

RF uses more rigid catheters and is not as versatile compared to EVLA devices. There is a significant number of patients in whom it is not possible to use RF.

A multi-center study with 6 years follow up Most EVLA systems can deal effectively with over 95% of truncular reflux, including the most tortuous of veins (including Small Saphenous Veins (SSV), Giacomini veins and short angled branches, which are often found behind the knee).

A multi-center study analyzed EVLA results over 3 years for treatment of SSV with concomitant treatment of the incompetent tributaries showing that it seems to be a very good alternative to traditional surgery.



Short and intermediate term results of EVLA of the SSV with the 1470nm diode laser and Radial fibre appears to be highly safe and effective in the eliminatio vein reflux.

T King MD Venous Research Foundation, Illinois -USA

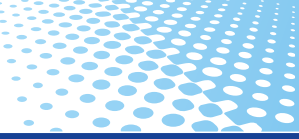


We use ELVeS Radial™ and perform procedures without tumescent anaesthesia and our favourite protocol is the use of the quick Sensory Femoral Nerve Block. This gives a better US image enabling real time visualization of the vein closure which improves results as we can respond according to the individual anatomy. Patients report none or little discomfort and less post procedure pain and side effects.

JHG Ferreira MD,
Phlebology Unit at Sao Lucas Hospital, Pontiac
Catholic University (PUCRS) -Brazil

„Early and mid-term results are excellent, with a very few complications and re-canalization“.^[14] Another great application of EVLA is the treatment of chronic venous insufficiency (CVI) with leg ulcers, always a common and challenging problem.

A multi-center study with 6 year follow-up reported healing of most leg ulcers with primary CVI and reduction of recurrence within the first three years after treatment using EVLA.^[15] More recently, another novel application of **1470nm** lasers as a source of photobiostimulation showed beneficial effect on **wound healing** by reducing inflammation, improving vascular activity and accelerating tissue growth and repair.



Results showed 75% of all the ulcers included in the study completely healed with ulcer related pain significantly relieved after the first or second laser session, especially in arterial ulcers. No side effects were reported and the treatment was well tolerated by the patients.^[16]



The diode laser 1470nm seems to be an effective, non-invasive, simple, painless and pain-relieving treatment with no reported side effects for the ulcer wound healing.

H Elias MD, Athens - Greece

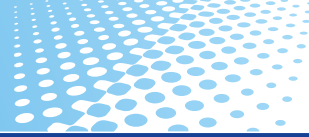
Treat More Veins with ELVeS Radial™: with fibers ranging from 200 micron to the revolutionary Radial and the new Radial Slim you can access from reticular veins and perforators to the larger GSV's for a minimally invasive approach with effectiveness and less side effects.

More complicated anatomies like SSV and recurrences from stripping can also be handled effortlessly with Radial Slim. To complete the range of applicators, a selection of spot handpieces allow for wound healing and telangiectasia with significant effectiveness in a non invasive manner.

^[14] D Kontothanassis, MD, R Di Mitri, MD, S Ferrari Ruffino, MD, E Zambrini, MD, G Camporese, MD, JL Gerard, MD, and N Labropoulos, PhD, DIC, RVT. Endovenous laser treatment of the small saphenous vein. JOURNAL OF VASCULAR SURGERY -Volume 49, Number 4, April 2009.

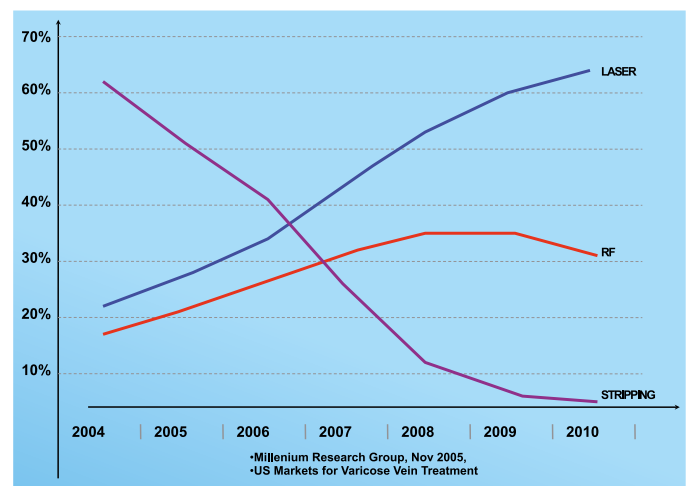
^[15] Magi, GB Agus, P Antonelli, V Nardoiani, O Sereni, PM Bavera. EVLA of saphenous and perforators reflux in 457 patients with venous leg ulcers - 6 year follow-up. Presented at IUA World Congress 2010, Buenos Aires (Argentina).

^[16] H Elias Effectiveness of the EVLA 1470nm diode laser for leg ulcers ablation. Presented at IUA World Congress 2010 - Buenos Aires (Argentina).



More user friendly

- **Easier Access:** ELVeS introduction sets are much smaller than RF. Markings allow for precise and simple control during the procedure.
- **Atraumatic:** the Radial fiber is designed with a round tip for optimal navigation along the fragile vessels (no sharp tips like other bare fibers).
- **Highly Visible by US:** the Radial fiber improves US visualisation both in longitudinal and transversal modes.
- **Extra safety:** laser aiming beam provides extra safety for the patient and physician as it shows that fiber tip is on the target vein and not in the deep system.
- **Faster:** with all the above and less anesthesia requirements, procedure time is significantly reduced. Time is money.
- **Lower cost of consumables:** compared to RF the cost per procedure is up to 40% lower.
- **Preferred by Patients:** Laser technology is perceived as - what it really is, a more modern and gentler energy to interact with human tissues.



Against?

- **No fixed protocol:** Some RF systems claim to have a magic formula to treat ALL veins in ALL patients by just pressing a button. EVLA systems allow the surgeon to select the right parameter for EACH patient according to the different treatment possibilities: more effectivity and versatility.
- **Laser regulations:** The difficulties of setting up a laser service due to laser safety regulations are often quoted. However, most treatment rooms require no modification to make them laser compliant, other than the placement of warning notices on the doors and laser companies provide the necessary training to users.
- **Laser safety:** Although the majority of the treatments are intraluminal, laser safety eyewear is still advised during the time of laser operation and most styles can be worn over prescription glasses if required adding little hassle to the procedure.



*Maybe the future is now.
Endovascular treatments are today
the most preferred
treatment alternative by patients
looking for long lasting results
with less side effects*

G Agus MD
Milan -Italy

Why ELVeS Radial™

Safer: Less complications

Less Anesthesia: possible with local/no-TLA

More versatile: treat more veins

Less Pain

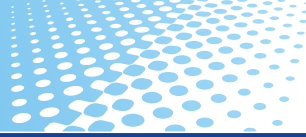
More Effective

Gentle: Less side effects

More User Friendly



Preferred by Patients



4. Training & Marketing for the patient

Education/R&D

Training and Updating



Website

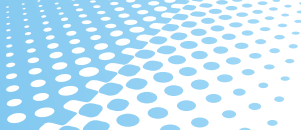
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Notes

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