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Non-animal experiments

Many scientific journals deal with animal experiments, but just a few of them face the hard problem of animal replacing or sacrifice/suffer reducing or minimizing, together with the related ethical and legal topics.

Since the 1st issue, the Journal of Theoretical and Applied Vascular Research (JTAVR) hosted papers devoted to the methodology for non-animal experiments. JTAVR is open to the discussion about the controversies inside the community of biomedical researchers, i.e. between people who use animals as an unavoidable experimental tool and others which on the contrary point to different research methods.

However, a-priori positions pro or contra total animal replacement in biomedical research do not correspond at all to reality, because the solution is anchored to the ground, it is context dependent and is hidden behind a detailed study of the experiments, aimed to provide a reliable response.

An answer which must not be black or white and must consider instead any involved methodological detail. In addition, there is the strong hope that many actions which were never done will be successful instead in the next future. For instance, consider the unexpected new frontier which in the last years turned up in the field of the organ-on-a-chip technology.

Maybe, not so far in the future, this contra opposition will be seen just as a nonsense.

History and Philosophy of Science

Working

Basic Sciences, Biology and Medicine

The Journal of Theoretical and Applied Vascular Research (JTAVR) aims at gathering contributes to vascular research, coming from biology, medicine, surgery and basic sciences like physics, fluid dynamics and bioengineering as well as biochemistry and genetics.

A special attention is given to the cultural aspects behind medical daily work, like experimental designs, models, epistemology, philosophy and history.

This inter-disciplinary approach uses a wider eye/chakra, placing side by side topics which generally could never go together in medical journals, with the hope that it will succeed in producing new interesting fruits in research.

Editor

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The Journal of Theoretical and Applied Vascular Research (JTAVR) publishes scientific papers on vascular diseases, biological research, history and philosophy of science.



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Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347:284-7.

Books and Monographs

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Homepage/Web site

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Small misunderstandings among us animals

Review of the book by Lisa Vozza & Giorgio Vallortigara

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When I was in Scotland for my PhD course, my supervisor told me once that what was interesting in comparative ecology and ethology was not the differences among different species, but the similarities. Similarities were more interesting, because they would potentially shed some light on significant evolutionary mechanisms. He was obviously right but differences, although perhaps more expected and less challenging, can be source of great interest and fascination too. One of my main interests is the behavior of non-human primates. Most of the times, when I am interviewed, the classical question "how similar are monkeys to us?" comes up sooner or later. It seems that we have this urge to understand other animals in terms of similarities/differences with us, humans, the supreme meter of zoological comparison (some could say: "and what other paradigm could we use?"). Are they intelligent like us? Do they feel like us? Do they suffer like us?

Obviously, the answers to these questions, even if some of us would consider them just inappropriate, are related to the knowledge we have of the other species with which we share (and sometime destroy) the planet we live in. And what we know about the other animals? Do we understand why they are doing what they are doing? Therefore, the question of similarity versus difference between us and the other animals is an old one. However, it still maintains all of its fascination and relevance, because it sits at very heart of what we understand as evolutionary process in Darwinian terms. And it is not all. It also concerns the way we see animals, the way we describe them and the way we interact with them.

The issues of what distinguish us from other animals, but more what we really know about them, are central points, among others, of this little and agile book written by Lisa Vozza and Giorgio Vallortigara¹. The two authors are well known, both in their respective professional environment, being Vozza the Scientific Officer of the Italian Association for Research on Cancer, and Vallortigara a well-known and very respected neuroscientist. Furthermore, they are both authors of popular books which explain in simple and clear terms scientific topics to the general public. The present book is no exception. The continuum between the humans and the other animals is illustrated with a series of little delicious scenarios, which range from the ability to count of chimpanzees to the incredible spatial memory of the scrub jays.

To discuss how we relate to the other animals one of the starting points is anthropomorphism, the tendency to provide animals with feelings and motivations typical of us humans (it is a tendency that dogs' owners, like me, sometimes find incredibly difficult to resist, I must admit...). The authors, although they warn us against the comfort anthropomorphism offers us in making us believe that we do understand other animals' motivations, do not completely deny its possible value. As matter of fact, anthropomorphism suggests interpretations of animal behavior that can be verified with controlled experiments. In my personal experience, to attribute human emotions and feelings to non-human animals can be a way to identify real problems related to the welfare of animals close to us. This



is particularly true for dedicated and empathic technicians working with captive animals in research laboratories.

But the one of the main points of the authors is also to give the lie to some of the beliefs we have about other animals. The cover of the book already offers a good example. The sweet koala tenderly embracing the trunk of a tree appear to us like a fluffy and irresistible lazy animal; not really: the temperature of its environment is very high, Koalas cannot sweat, so they needs to embrace a tree which helps them to cool down.

The book is organized in a series of brief and readerfriendly chapters, each one dedicated to a particular theme, mainly related to animal behavior, and for each topic there is a list of suggested readings. Through the ten chapters, a series of false beliefs about animals are revealed and clarified, with the help of researchers who have approached a particular ethological question. There is also no shame in saying that certain aspects of other animals' lives are just still mysterious to us. Do we really have a way to describe what intelligence is for a species different from ours, for example? I do agree with what Vallortigara and Vozza say in this respect: all of the animals are intelligent, and their intelligence is strictly related to the ecological and social environment in which they have evolved and developed. The same goes for other characteristics, such as vision and other physical and cognitive skills. In this argument we can find the idea that evolution is not directional, does not have an aim to go from less complex to more complex, that complexity is of relative importance in term of evolution and that, surely, we humans are not on the top of an hypothetical evolutionary pyramid.

What about conscience? This is really a slippery topic. I am very tempted to agree with a quotation the two authors use to discuss the nature of conscience: "It is something us humans invented to feel important". The literature about conscience in non-human species is as vast as heterogeneous, and it reflects the fact that it is nearly impossible to measure in a scientific and objective way something that is very personal and subjective. We have difficulties in talking about conscience among ourselves, who can directly express what we feel? Can we imagine asking a bat? I agree with the authors' claim that the moral relevance of a particular animal has very little to do with its cognitive abilities. This leads me to say that the respect for the other animals must not depend on their "intelligence" (whatever that means...), and looking for similarities with humans is not the way to attribute a particular moral status to a particular animal.

The last chapter is dedicated to an issue very close to my heart, that is, the use of animals in biomedical and toxicological experiments. The authors' approach to the issue in a very sensitive way, especially in the case of Vallortigara's experience. To scream against or in favor of animal experiments does not help to understand the complexity of this practice and, surely, does not help the animals that are still used in research laboratories. The authors are very honest in claiming that they simply don't know if it is right or wrong to use animals for research, and suggest finding an acceptable shade of grey. I agree and have no reason to doubt the truthfulness of the argument "I would prefer doing it another way", and I also agree with the affirmation that the evolution of the norms protecting the animals used in research laboratories has to do with the pressure exercised by animal lovers. I think that the author's approach set an example to be followed. There is a need for the scientific community to speak out about their research using animal models. What are their motivations? How do they solve the ethical problems related to animal experimentation? Openness of this kind can really improve the discussion about animal experiments, discussion which suffers in a chronic way of poor theoretical argumentation from both sides.

Lisa Vozza Giorgio Vallortigara Piccoli equivoci tra noi animali

Siamo sicuri di capirci con le altre specie?



Small misunderstandings among us animals, by Lisa Vozza & Giorgio Vallortigara.



Another point I am personally fascinated with is the different treatment we reserve to the same animal, depending on the context. I always thought that, in a way or another, we "create" the animals we deal with: we do not really understand the other animals, we have a vague idea of what they think and what they feel. Therefore, it is very appropriate the choice to illustrate, towards the end of the book, five different scenarios with the ferrets as protagonists. In one case, for example, a ferret is welcome in a house, adopted as a pet, given a name. In another case, the ferret has found a place to stay in the space between the last floor and the roof of a house: the owners will use any possible way (traps, poisons...) to get rid of the animal, with little concern for its welfare. Something completely different happens in a research laboratory, where the ferret is used as a model to better understand how to prevent and cure an infectious disease. In this case the animals are eliminated at the end of the study (although not always), but before reaching that point, they are treated with the most possible respect for their well-being, following the indications of European and local norms and animal experimentation. Completely different situations, but the species is exactly the same. It suggests that our relationship with other species is very ambiguous indeed.

This book can easily be an interesting and stimulating companion, to be read all at once in few hours, or to be enjoyed reading a chapter here and there, as each one of them can stand on its own, and little summaries of the main points are provided. At the very end we can find two very useful sections: "13 false beliefs on animals", and "Probably you did not know...". Here the study of animal behaviour does not want to spoil the bond we think we can create with the other animals, finding aseptic scientific explanations of their behaviours, Instead it is just the opposite: a more objective approach, looking for mechanisms, applying the Occam's razor (consider first the simpler explanations for a particular behavioural phenomenon), can help us to discover real wonders of the other species' variability and ethological richness. Re-think the false beliefs with the help of a bit of science does not have to a defeat for the love and respect we have for the other animals.

The message I get from this reader-friendly book, is that both differences and similarities are relevant for the consideration we must have of the other species. Similarities can make us smile and feel closer to the other species, especially when we can detect similarities in emotions. However, differences are a source of surprise and admiration for something different from us, and the respect for differences is the name of the game.

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The role of ejection fraction in varicose vein disease

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Abstract The article addresses the significance of the parameter ejection fraction for evaluating therapeutic outcomes in varicose vein disease. Whereas in cardiology the ejection fraction is an excellent indicator of cardiac insufficiency, its validity for evaluating results after treatment of varicose veins is limited. This is because of the quite different situation in the heart and in varicose vein disease. Whereas the enlarged end-diastolic volume of the left ventricle is the consequence of decreased heart contractility, the amount of venous volume contained in varicose veins and the contractility of the calf musculature are not interrelated. Consequently, reduction of venous volume occurring after treatment of varicose veins fakes improved calf muscle performance; therefore, ejection fraction is an unsuitable parameter for evaluating results after varicose vein treatment.

Keywords ejection fraction; varicose veins; venous volume; saphenous reflux; venous hemodynamics.

The parameter ejection fraction provided by air plethysmography has been used for evaluation of calf pump performance resulting from the treatment of varicose veins¹; it was borrowed from cardiology. In cardiology, it is the fraction between the ejected volume and the end-diastolic volume of the left ventricle; the normal value ranges from 55% to 70%. Heart insufficiency is characterized both by the dilatation of the left ventricle inducing enlarged end-diastolic volume and the simultaneous reduction of the ejected volume; both phenomena contribute to the diminution of the ejection fraction. It follows that the parameter ejection fraction in cardiology is a sensitive indicator of cardiac insufficiency.

Unfortunately, the situation in varicose vein disease is quite different. The parameter ejection fraction in varicose

veins disease is calculated from the ejected volume and the venous volume, both obtained by air plethysmography: EF = EV/VV. Although the calf musculature operates similarly to the left ventricle - it is able to increase the systolic pressure in deep lower leg veins by 53-128 mm Hg (mean 75 mm Hg) over the level of the hydrostatic pressure² - several conditions differ considerably. In varicose vein disease the contractile force of the calf musculature is not depressed; in many cases it may be even strengthened. The other discrepancy concerns the venous volume contained in varicose veins; its amount and the contractility of the calf musculature are not interrelated. This is the most pregnant contrast to the condition in the left ventricle. Because the ejection fraction in varicose vein disease depends on the amount of venous volume in varicose veins, reduction of this venous volume, which is even the goal of the therapeutic treatment, improves artificially the value of ejection fraction and fakes improved calf pump performance. Therefore, comparison of ejection fraction before and after treatment yields misleading information. In addition, the situation is yet more confusing because the ejected volume might be likewise influenced. Strong saphenous reflux impacts on the size of all veins participating in the so called "Trendelenburg's private circulation": not only the incompetent saphenous system but also calf perforators and the concerned segments of the deep veins enlarge distinctly. Enlarged deep lower leg veins contain more blood. As the contractility of the calf muscles in varicose vein disease isn't usually diminished, it can be deduced that the calf muscle pump is able to produce increased ejected volume in the presence of increased preload. After elimination of saphenous reflux the size of the afflicted venous segments inclusive of deep lower leg veins diminishes significantly in the course of



follow-up ³⁻⁶; the consequence might be diminished ejected volume, which would diminish the post-treatment ejection fraction. Nonetheless, a large discrepancy remains between the markedly reduced venous volume in the treated varicose veins and the possibly slightly reduced ejected volume; consequently, the post-treatment value of the ejection fraction falsely indicates improved calf pump performance. It follows that the parameter ejection fraction is unsuitable for evaluating the results after treatment of varicose veins.

The ejection fraction in varicose vein disease might be useful in situations where the venous volume remains unaffected, e.g. when comparing the effectivity of provocations tests in the same patient⁷.

Conclusion

Whereas ejection fraction is a sensitive indicator of cardiac insufficiency, in varicose vein disease this parameter yields fallacious information about improved calf pump performance after varicose vein treatment. This is because the venous volume contained in varicose veins bears no relationship to the calf muscle contractility. Therefore, ejection fraction is an unsuitable parameter for comparing results after varicose vein treatment. It may be reasonably used only in cases where the venous volume remains unchanged.

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Flush closure of the sapheno-femoral junction with LASER

LASER CROSSECTOMY

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Abstract

AIM

During laser ablation, the terminal segment and tributaries of that part of the GSV are left patent. So the saphenofemoral junction (SFJ), near the epigastric vein is spared. This technique resulted in a 13.8 % early recurrency rate for our patients. Could the results improve if the terminal part of the GSV and tributaries were closed with laser?

PATIENTS

In a retrospective study all patients who underwent endovenous laser obliteration of the GSV more than 1 year previously were investigated clinically and with ultrasound. 83 patients were checked between 1 and 2 years (median interval 14 months) after a modified technique laser ablation.

METHODS

The bare tip of the laser fibre was held nearer than recommended which means 1 cm from the femoral vein. A 980 nm laser equipment was employed and the median Linear Endovenous Energy Density (LEED) was 179 J/cm. 5 ml/cm cooled (3-5 °C) tumescent local anaesthetic was used.

RESULTS

Introduction

Most vascular surgeons and phlebologists agree that the treatment of the sapheno-femoral junction (SFJ) is One accessory anterior recurrent varicosity in connection to the SFJ (1.2%) was observed. Further US findings are: in 33 limbs (39.7%) flush closure of the SFJ without any patent tributaries were in 11 (13.2%) flush occlusion with direct opening of a tributary into the junction or femoral vein. In 39 limbs (47.0%) there was a short (median length 7 mm) saphenous stump. There were no thromboembolic or any other serious complications.

CONCLUSIONS

The flush closure and short saphenous stump of GSV both gave better early recurrency results than the long saphenous stump technique. There was no sign of recanalisation of the GSV and only 1 accessory anterior varicosity. There was no sign of neovascularisation during our follow-up period. This means our early postoperative results are better with this technique than with the formerly used GSV terminal part and epigastric vein saving method. There is not a higher risk of complications if the junction is occluded flush with the femoral vein. Limitations of this study are the short follow-up period and few cases.

Keywords Varicose veins, laser ablation, recurrency, SFJ, tributaries

important in the prevention of early and late recurrencies of great saphenous vein (GSV) varicosity^{1, 2, 3}. Following the surgical operation (crossectomy and stripping), untreated tributaries and new ones (neovascularisation) around the



junction are the main sources of recurrent varicosity^{4, 5, 6}. During laser ablation, the junction part (usually 2 cm) of the GSV and tributaries are left patent^{7, 8}. Colleagues converting from classic to laser surgery often ask whether these patent tributaries around the junction could cause recurrent varicosity. A metaanalysis of laser surgery results really showed a high recurrency rate from these side branches^{9, 10}.

We subdivided our experience into two subsequent periods, according to the adopted method to treat the SFJ. In the first year (1 April 2007- 1 April 2008) varicose vein laser surgery was performed according to descriptions, leaving a 2 cm long distance between the femoral vein and the tip of the laser fibre. This technique resulted in a 13.8 % early recurrency rate. Recurrency patterns were recanalisations and accessory anterior vein dilatations. In this study we were studying the following problem: what happens if the GSV is occluded flush with the femoral vein and side branches are also closed with laser?

Patients

In the second period between 1 April 2008 and 31 December 2010, 102 laser ablations were performed with a different technique on varicose GSVs which were suitable for our study called the flush closure technique. Of these 102 legs, 83(81.4%) came back at the 1-year follow-up, thus they could be examined after more than 1 year, (the longest 21 months following their surgery, median interval 14 months).

The pre-procedural diameter ranged between 4 and 23 mm (median 8 mm) 3 cm below the junction.



Figure 1 - Closure of SFJ is flush with the femoral vein. One year after laser surgery.

Aneurysmatic GSVs were also included. According to CEAP classification, all the patients belonged to the C2 - C6 clinical classes.

Methods

A 980 nm Biolitec laser equipment on 13 Watt and 600 μ m bare fibre was used. The tip of the laser fibre was placed 1 cm from the SFJ. Mean LEED was higher than usual, 179 J/cm. The fibre was pulled manually. Around the GSV, from the canulation puncture site to the SFJ, cooled (3-5 °C) 0.1 % Lidocain and Adrenaline tumescent local anaesthetic was employed (5 ml/cm). General anaesthesia (Propofol) without intubation was also used in all cases. For removal of side branches and interruption of perforator veins along the limb, a saw-knife, Varady's hook and sclerotherapy were used^{11, 12}.

Following surgery, patients were observed for 3 hours and afterwards discharged. Chemical thrombosis prophylaxis was not used. Excentric compression with bandages was applied for two weeks, day and night, and a stocking during the day for a further two weeks. In other regards, we followed the described method^{8, 13, 14}.

Follow-up was planned at 1, 7 and 14 days and 1, 3, 6 and 12 months and every subsequent 6 months and the operated legs were examined clinically and with US (GE Vingmed, System Five). Clinically residual and new varicose veins along the limb, and in the groin region, were additionally examined with an ultrasound examination focused on the patency of deep veins, SFJ patency, tributaries, the distance of the occlusion from the the femoral vein and the occlusion of the treated part of the GSV.



Figure 2 - Rate of recurrency in both groups, 1 year results. Distance of fibre tip from the femoral vein.



Results

One accessory anterior varicosity recurrency (1.2 %) was observed. Further US examination results of the SFJ were ranked into three categories:

Ultrasound patterns in SFJ

- (a) *flush occlusion* of GSV with the femoral vein (EHIT 1) with the closure of tributaries 33 limbs, 39.8%) (Fig. 1). In 3 of these cases the thrombus protruded into the femoral vein (EHIT 2). This protrusion dissolved spontaneously within 3 months without complications.
- (b) *flush occlusion with opening of a patent tributary* into the junction or directly into the femoral vein without a saphenous stump (11 limbs, 13.3 %).
- (c) occlusion with 1-26 mm long *saphenous stump* (median length 7 mm) and 1-3 patent side branches (39 limbs, 47.0 %). In this category, the patent part of the saphenous vein typically extended from the femoral vein to one or more tributaries. In 3 cases the patent part was even longer.

Further findings:

- 1) We did not find any dilated or varicose side branches or reticular veins around the groin or along the limb.
- 2) The SFJ *tributaries* did not become dilated, elongated or tortuous.
- 3) No signs of *neovascularisation* were observed at all.
- 4) Treated GSV *stems* were occluded as long as laser irradiation was performed, there was no recanalisation.
- 5) There were no serious *complications* e.g. deep venous thrombosis or pulmonary embolism.

Elimination of reflux and *closure* of the GSV were successful just after the intervention and also at the last check-up in every case (98.8%) (Fig. 2).

There were no serious complications (deep venous thrombosis, pulmonary embolism, septic complications, etc.), only temporary ecchymosis in every case, pigmentation in 3 limbs, ankle swelling in 2 cases which disappeared following one additional month of bandaging. There was temporary hypoaesthesia combined with hyperaesthesia in 6 cases (7.2 %), on the distal part of the thigh where the laser was used. Later, in other cases 2 pulmonary embolisms were found, so LMWH prophylaxis was introduced in every subsequent case.

Discussion

At first sight, varicose veins laser ablation is just a method that replaces the stripping part of the classic surgical modality, which is why some colleagues proposed separate surgical interruption of the SFJ^{15, 16, 17}. However, laser closure of the saphenous stem is one of its effects, because laser surgery has an effect on the SFJ as well⁸, 13, 18, 19. In many cases the anatomical results of the laser intervention at the SFJ resembles the Trendelenburg operation (distal ligation), which has been criticised for many decades. In some cases laser operation gives results which are similar to crossectomy. It seems that laser ablation combined with surgical crossectomy did not improve the results^{20, 21, 22}. Our study focuses mainly on the question of what happens if the anatomical results of laser ablation are similar to crossectomy. Are the clinical results better or worse?

What could be the topical technique for *flush* occlusions? We think there are two factors, one being the higher delivered energy. The other is, that the fibre tip position is nearer to the femoral vein: at 1 cm^{8, 13}, *Theivacumar et al.* also found that it can cause flush occlusion²³.

Why does the closure stops at the junction? The bare tip laser fibre delivers the laser beam mainly in front, although the effect of the laser within the blood is limited 14 . On the other hand, the reason that the occlusion stops at the junction of the GSV, is because the *diameter* of the femoral vein is bigger than that of the GSV. The femoral vein is wider and would require much more energy to cause any occlusion there. A further reason could be the higher speed *flow* in the femoral vein than in the saphenous $vein^{24, 25}$. The tumescent solution also has some mechanical effect, because it compresses the saphenous vein, so it does not let out too much heated blood and bubbles, or slows their movement towards the femoral vein. There is a further mechanism which safeguards the femoral vein: the tip of the laser fibre is held 1 cm away, and around the terminal segment there is cold tumescent solution which cools down the heated blood and steam bubbles before entering the femoral vein. Also, the direct contact of the tip of the fibre only comes up to this segment of the GSV^{26} .

We should also mention the special case in which the *thrombus protrudes* into the femoral vein (EHIT 2).



This was our finding in 3 cases in which the protrusion disappeared spontaneously without any complications, as described by others as well^{13, 21, 27}.

The mechanism and *pattern of recurrency* after classic surgery differs from the processes following laser ablation¹⁰. It is well known that, after classic surgery, open side branches and neovascularisation are responsible for recurrency in many cases^{4, 5, 6}. In spite of this, with laser ablation, *recanalisation and dilatation of the accessory anterior vein* are the reasons for recurrency^{28, 29, 30}. The reason for recanalisation could be that less treatment energy was employed^{18, 31}. It is thought that these tributaries

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participate in the drainage of venous blood in the abdominal wall^{26, 32}. We and colleagues with similar results²³ did not find any dilatation in the vein of that region. During our follow-up period there were no signs of neovascularisation. According to other experience, the good results at one year continue to last^{8, 33, 34}.

Conclusions

Flush closure and short stump gave better early results than the formerly recommended technique. There is not a higher risk of complications if the junction is occluded flush with the femoral vein.

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REVIEW

Nerve Injury in venous procedures: Malpractice, characteristics, and strategies to avoid it

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Abstract Nerve damage is the most important reason for malpractice claims after venous procedures. The incidence of nerve damage varies according to the technique and 4% to 23% present symptoms of nerve damage after varicose vein operations. The knowledge about nerve physiology and anatomy, proper preoperative ultrasound planning, clear communication, safe operation protocols, and good clinical records are pivotal to avoid such complications. Even so, there is no guarantee that a lesion will not occur. Nerve damage can happen with the best surgeons. The purpose of this paper is to review nerve physiology and its anatomy in relation to saphenous veins, to relate the incidence of nerve injury to each surgical technique and to outline strategies to prevent and treat this complication.

Keywords Peripheral nerve injuries, Malpractice, Varicose veins, Echo anatomy, Doppler ultrasound

Introduction

Chronic venous insufficiency (CVI) is a complex disease of high prevalence. A third of the population may present the disease and interventions to treat varicose veins are among the most common in the world according to the Edinburgh Study¹.

Despite the benefits of surgical treatment for varicose veins (VV), malpractice lawsuits are becoming common in most regions of the world. Data shows that VV surgery is the most common procedure involved in claims for adverse events in vascular surgery, in both Sweden (34%) and UK $(48\%)^2$.

Campbell *et al*³ showed that nerve damage is the most common reason for malpractice claims after venous procedures, accounting for 31% of the claims. Additionally, the prevalence of nerve damage after VV operation is not low. Literature reports show that 4% to 23% of patients remain with a sensory loss after the procedure, depending on the testing method and study⁴.

Sam *et al*⁴ showed that nearly all treatment methods are accountable for nerve damage. Phlebectomies, stripping, radiofrequency and endolaser cause nerve damage and studies vary greatly concerning the incidence of this complication (from 0% to 33%)⁴.

Although knowledge about nerve anatomy is pivotal to avoid such complications, even the best surgeons can cause nerve damage. Since variation in nerve anatomic patterns are very common, high resolution ultrasonography is an important tool to visualize the nerve and to plan surgical treatment⁵.

The aim of this review is to review nerve physiology and its anatomy in relation to saphenous veins, discuss the importance of nerve damage in VV surgery, to evaluate the incidence of these lesions in each surgical therapeutic option and discuss strategies to prevent and treat nerve injuries.





Fig 1 - Sciatic, peroneal (common fibular) and tibial nerves - cutaneous innervation.

Pathophysiology

In 1943 Seddon⁶ divided nerve injuries into three categories - neuropraxia, axonotmesis, and neurotmesis.

Neuropraxia is the mildest form and presents as focal demyelination without damage to nerve continuity and without distal degeneration. It may occur after compression, traction or burning of the nerve. Usually, the complete recovery time varies from 1 week to 6 months⁷.

Axonotmesis is the damage to the axons with demyelination preserving connective tissue (perineurium and epineurium). Distal axon and myelin degeneration cause complete denervation but the supportive tissues allow total but slow recovery.

Neurotmesis is the most severe form of injury, it is a full anatomical and physiological transection of the nerve. In this case, there is no recovery without surgical intervention.

Venous operations cause injury mainly to the saphenous nerve, sural nerve, peroneal nerve and femoral

nerve (groin reoperations mainly). The anatomy of these nerves will be briefly described.

Surgical and Ultrasonographic Anatomy

Complications and inconvenience of VV treatments may be explained by the anatomy of the lower limb veins and nerves which will be depicted in the following sections.

Variant anatomic patterns are very common. High-resolution ultrasonography permits visualization of peripheral nerves⁵ and a better understanding of this important matter. The tibial nerve, the common peroneal nerve and its branches, the sciatic nerve, the division of its two branches, the sural nerve and its primary branches, the saphenous nerve, the femoral nerve and the posterior cutaneous nerve of the thigh can be visualized by US^5 .

Ultrasonography (USG) is an excellent costeffective imaging for visualization of peripheral nerves. In cross-section, nerves usually appear as a round formation, hyperechogenic, often containing small round hypoechogenic areas. When veins are dilated, the nerve may have a slightly compressed cross-section appearing a rhomboid shape⁸.





Fig 2 - Thigh nerves - cutaneous innervation.

Sciatic, peroneal (common fibular) and tibial nerves (Fig 1)

The sciatic nerve is usually formed by branches of the sacral plexus and exits the pelvis at the sciatic foramen. It runs posterior in the thigh, where it branches in peroneal (common fibular nerve) and tibial nerve. At the popliteal fossae, there are reports of damage during thermal $ablation^9$.

The peroneal (common fibular) nerve starts when the sciatic nerve branches and travels to the anterior and lateral compartments on the leg. It may be damaged both in the popliteal fossae and in varicose vein dissection in the anterior leg^{9-11} .

The tibial nerve is a branch of the sciatic nerve and it runs deep to the posterior compartment of the leg. The tibial nerve is not usually damaged in varicose vein surgery. A US study of the veins of the popliteal fossa in patients with SSV insufficiency revealed that 88% of the time the tibial nerve ran along the medial edge of the SSV and 4% it coursed horizontally behind the SSV or wrapped by the SSV. In a cadaver study, at the saphenopopliteal region, the average shortest distance between the SSV and the tibial nerve was 4.4 mm; in 20% of studied patients, the distance was less than 1 mm⁹.

Thigh Nerves

Nerves of the thigh (Fig 2) are at risk during VV surgery. Intermediate and medial femoral-cutaneous nerves (IFCN and MFCN)



originate from the femoral nerve below the inguinal ligament; some branches supply the skin as low as the front of the knee, some innervates the anterior medial thigh and some, its medial aspect. The distribution of cutaneous nerves in the thigh is important in the analysis of nerve injuries following VV surgery: in the groin and upper thigh, the ilioinguinal nerve is at risk during the initial groin dissection; in the central and distal sections of the thigh, the branches of the MFCN and IFCN are at risk¹².

Saphenous Nerve (SN)

The terminal and the longest sensory branch of the femoral nerve is the saphenous nerve¹³ (Fig 3). In the thigh, within the femoral triangle and adductor canal, the SN lay in a deeper plane in comparison to GSV and remained separated from the vein by a considerable amount of fat, fascia, and sartorius muscle14. In the thigh, it courses subfascial and follows the superficial femoral artery¹³. Beyond the adductor canal, the SN passed between sartorius and gracilis muscles and became subcutaneous¹⁴. At the medial aspect of the knee and along with the upper third of the leg, SN and GSV remained separated by connective tissue sleeves of varying thickness ranging 0.5-2.5 cm depending on the thickness of the adipose layer. Along the middle third and lower third of leg, the SN and GSV lay in close contact, sometimes inseparably adhered to each-other. The point from where SN and GSV had an intimately related course ranged between 26 and 35 cm from the tip of the medial malleolus. A study recommends avoiding lower 2/3rd of the leg while harvesting saphenous venous graft to avoid damage to SN and subsequent neuropathy¹⁴.

The SN also has a large number of small branches that run in an anterolateral or posterolateral direction in the middle of the lower leg. These are the medial and lateral crural cutaneous branches¹⁵. Another important anatomical relation is its neurovascular axis. The SN is accompanied until it pierces the deep fascia by the saphenous branch of the descending genicular vessels, which connected to perforators of the posterior tibial vessels¹⁶.

Sural Nerve (SuN)

Two nerve branches (tibial and peroneal) join at a variable level in the leg to form the SuN (Fig 4).

The tibial branch (medial sural cutaneous nerve, MSCN) emerges from the tibial nerve and runs parallel to the SSV in the connective tissue of the groove of the two heads of gastrocnemius, ventrally and outside the SSV compartment.

The peroneal component of the SuN (lateral sural cutaneous nerve, LSCN), arises from the common peroneal nerve (the lateral division of the sciatic nerve), descends laterally in the popliteal fossa along the border of the biceps femoris muscle, towards the peroneal head.

The tibial branch joined the peroneal branch in the middle third of the calf forming the final SuN. The SuN usually enters the SSV compartment at this level, but the exact anatomy is very variable. It lies close to the SSV. Behind the lateral malleolus, it turns anteriorly along the lateral border of the foot5.

The SSV runs behind the lateral malleolus and ascends through the middle of the calf17, to the lower portion of the popliteal fossa, where it usually reaches the popliteal vein17. It lies in its own fascial compartment all along its course. In the midcalf, the superficial fascial parts get much thicker upon the gastrocnemius muscle. The SSV runs between the main crural fascia and a membranous layer of the superficial fascia and this is the basis for applying tumescent anesthesia¹⁸.

In the popliteal fossa, SSV is in close relation with the tibial nerve and the common fibular nerve. SSV lies between the medial and lateral heads of the gastrocnemius muscle, medial and close to the tibial nerve that is the medial branch of the sciatic nerve¹⁷.

Studies of the lower limb demonstrate that whereas the GSV is intimately associated with the saphenous nerve17 the SSV courses closely with the sural nerve. In a US study, the sural nerve was found to be within 5 mm of the SSV in 90% of cases⁹.

About the anatomy of the vein of Giacomini and surrounding neural structures, there are no detailed studies⁹.

Symptoms of superficial nerve injury

Injuries to the saphenous nerve are uniformly manifested as sensory deficits (decreased sensation, paresthesias, and dysesthesias, in decreasing order of frequency) in the anteromedial aspect of the calf to the level of the ankle. There are no motor deficits associated with saphenous nerve injury¹⁹.

The sural nerve supplies the skin of the lower half of the posterior surface of the leg, the lateral part of the dorsum of the foot, and the lateral side of the little toe. Sural neuropathy is presented with symptoms of pain, paresthesia, or numbress in the distribution of the sural $nerve^4$.

The lesion of sciatic and peroneal nerves causes motor impairment and there are reports of drop foot after varicose vein surgery^{9,10}. The peroneal (common fibular) nerve has several reports of damage in venous procedures9– 11, which can result in loss of foot eversion, pain and paresthesia over the majority of the dorsum of the foot and the anterolateral aspect of the lower leg. Fortunately, the damage to these nerves is rare, but it can lead to severe motor sequelae^{9,10}.

Tibial nerve lesion results in loss of plantar flexion, loss of flexion of toes and weakened inversion.

Peculiarities of available techniques concerning nerve injury

Sclerotherapy

Sclerotherapy is a common procedure and the incidence of nerve damage is very low. Cavezzi *et al*²⁰ reviewed the complications of sclerotherapy and found a 0.2% incidence of nerve injury.

Nerve damage has been described in patients undergoing sclerotherapy both in the initial procedure and in the drainage of post sclerosis hematoma21. The authors considered the most probable causes of these damages to be direct transection of the nerve by a needle and perivenous inflammation. Another possible pathophysiology of the injury is inadvertently injecting a sclerosing agent in the nerve or nerve vasculature. All the cases of nerve damage after sclerotherapy had uneventful procedures described by the doctor performing the procedure.

Vein ligation and stripping (L& S)

The stripping procedure consists of vein removal using mechanical traction of the vein. Avulsion can damage surrounding nerves and cause paresthesia or even chronic aesthetic symptoms.

After saphenous vein stripping, saphenous nerve injury is reported at rates from 27%22 to $40\%^{23,19}$ based on subjective patient reports, but with neurologic testing, the rate is found to be much higher $(58\%)^{23}$. Even mini phlebectomy can make a patient suffer from a sensory deficit²⁴.

Stripping below the knee increases the incidence of paraesthesia, due to the saphenous vein proximity to the nerves distally. This is due to the fact that the saphenous vein proximates the nerves progressing distally. Despite the risk of recurrence, the incidence of nerve injury decreases from 23%-40% to 5%, when selective preservation of the saphenous vein is performed. The technique of invaginated stripping can reduce the incidence of nerve injury to $1.5\%^{24}$.



Comparative trials for the treatment of SSV are lacking as of today and literature remains heterogeneous regarding techniques and treatment protocols. A systematic review and meta-analysis from 2015 demonstrated paresthesia in 19.6% of patients after SSV incompetence surgery²⁵. Saphenous invagination, in theory, would be damage-free but the practical use of this technique shows no significant advantages to other techniques²⁶.

Concerning saphenous stripping, studies showed no differences between the upwards or downwards technique. We consider that partial stripping has anatomical advantages concerning nerve damage, but data suggesting real advantage is not based on large nor multiple studies and further evaluation is needed to corroborate possible advantages²⁷⁻³¹.



Fig 3 - Saphenous nerve - cutaneous innervation.

Thermal Methods

Radiofrequency (RFA)

Radiofrequency ablation (RFA) of the saphenous veins causes the burning of the vein to produce vein closure and the expected results. But thermal damage to superficial nerves is a known complication in this technique. It is believed that the mechanism of neural injury is incurred through thermal effects radiating from the ablated venous segment into the surrounding structures⁹.

With longer monitoring, a prospective study published in 2011 compared the results of different methods of RFA. Six patients (13.9%) reported saphenous nerve paresthesia on the 10th postoperative day; after three months, paresthesia disappeared in all but 2 patients from RFA group³².



Fig 4 - Sural nerve - cutaneous innervation.

Comparing with saphenous stripping, RFA presents a lower risk of nerve damage in the vast majority of studies³³. But the incidence of paresthesia rates was higher after RFA (26%) compared to high ligation and stripping in a Korean retrospective review³⁴.

Shahid *et al* reported a case of multifocal neural injury to the distal sciatic, tibial and peroneal nerves resulting in significant morbidity after RFA of the SSV in a 42-year-old woman, who had complete neurolysis of the sural, tibial, peroneal, and distal sciatic nerve after surgery⁹.

Endovenous Laser Ablation (EVLA)

EVLA, similar to RFA, causes the burning of the saphenous vein to achieve clinical results. Nerve and skin can be collaterally injured by



The wavelengths provide power from 10 to 15 watts and lead to 20–140 J/cm linear endovenous energy density (LEED) in the vein lumen. This amount of energy density is sufficient for vein wall heating and the formation of fibrosis³⁵.

A prospective nonrandomized single-center cohort study using a 1470 nm wavelength laser with bare-tip fiber reported 3.9% paresthesia³⁶. Similar to these statistics, but with different design studies, Gifford *et al.* described paraesthesia after treating the whole GSV with EVLA/RFA in 4%³⁷ and Dermody *et al*³³ showed that EVLA had a 3.8% incidence of paresthesia.

In each one of these articles, no data is available to evaluate long term symptoms. With longer follow-up, a 2011 publication using EVLA of GSV with a 1470 nm diode radial fiber laser showed that local paresthesia occurred in four patients (8%) at 30 days with average paresthesia area of 47 cm2. After six months, paresthesia disappeared in one patient. In the other patients (6%), the paresthesia area reduced to 24 cm²³⁸.

EVLA of the SSV seems to be a safe modality with excellent short-term results but temporary paresthesia of $6\%^{39}$. Boersma *et al.* evaluated 28 studies of laser treatment on 2950 limbs and found postoperative paresthesia in 4.8 % (EVLA) of the cases²⁵.

Transient paresthesia was seen even in EVLA of insufficient perforating veins and despite careful administration of tumescent anesthesia; in two patients of 124 total according to Boersma *et at*⁴⁰ and two patients in a total of 13 treated in Dumantepe's publication⁴¹.

Cryosurgery

Cryosurgery for varicose veins was introduced in 1978 and first clinically applied in 1982. It works by the passage of nitrogen oxide (N2O) through a very small nozzle under very high pressure, which decompresses and lowers the temperature of the probe to -85° C in only a few seconds. During freezing, an ice ball forms at the tip of the probe, adhering the vein to the tip. Removal of the vein is obtained by withdrawing the probe in the direction of the entrance. A retrospective noncomparative study with a total of 84 patients (131 limbs) with varicose veins with GSV incompetence was treated with cryosurgery over a 2 year period showed cutaneous nerve damage - defined as numbness and paresthesia - in 3 limbs (2.3%)⁴².

High Intensity Focused Ultrasound (HIFU)

More recently the use of high intensity focused ultrasound (HIFU) has been proposed to treat venous insufficiency. HIFU heats the vein at a temperature about 95-90°C. Obermayer treated varicose veins and reported 4 legs out of 50 with dysesthesias suggesting damage to nerves.

No deep vein thrombosis, pulmonary embolism or arterial damage was reported in the initial cases⁴³. The focused ultrasound has been shown to damage arterial structures neighboring the treated vessel and the initial clinical data demonstrate that nerves are probably affected in the treated region⁴⁴.

Preventing nerve damage

Techniques

Sclerotherapy procedures and low volume of the sclerosant are possible ways to prevent complications.

When performing an EVLT a radial fiber is preferable to bare tip fiber, as the latter causes more nerve damages as shown in a comparative study³⁵.

The lower is the energy level used the less nerve damage will occur, as Rathod has shown that a higher linear endovenous energy density increased significantly the incidence of paresthesia⁴⁵. Although, the decrease of energy should not jeopardize the long-term occlusion of the vein.

Another important factor is the infiltration with perivenous tumescent anesthesia, as it helps to dissipate the heat generated by $EVLA/RFA^{46}$.

Regarding the site of endovenous access, studies comparing puncture sites are small and do not allow us to make important conclusions. A small study showed less nerve damage in SSV after midcalf puncture as compared to distal puncture⁴⁷. Another small study did not find significant differences between mid-calf access and distal access to treat the GSV⁴⁸

Local Anesthesia Methods

The incidence of nerve damage is decreased when the technique is more conservative and less aggressive, using only local anesthesia to the skin. Conservative surgery such as CHIVA (*Conservatrice Hémodynamique de l'Insuffisance Veineuse en Ambulatoire* / ambulatory conservative hemodynamic treatment venous insufficiency)⁴⁹, Muller Phlebectomy and ASVAL (ablation under local anesthesia)⁵⁰ added a new perspective for eliminating reflux, sparing the main saphenous trunks with fewer nerve injuries. Also, the patient warns the doctor if a nerve is touched and it makes it hard to cause injury⁵¹.

The CHIVA technique has a near-zero incidence of nerve damage with significantly less damage than stripping in randomized clinical trials^{49,52}. The ASVAL technique also has a low incidence of nerve damage, supposedly for the same reasons considered before⁵⁰.

Recurrence

Recurrences might be a problem with the partial stripping strategy. Jones *et al*³⁰ showed that recurrence was greater in patients stripped to the knee level (43%) as compared to patients with complete stripping (25%). But the most common cause of recurrence was the neovascularisation rather than the saphenous remnant.

Obviously, treating recurrence of the GSV has higher complications rates due to scar and fibrosis.

Van Groenendael *et al.* showed a large occurrence of temporary paraesthesia in 13% of these patients⁵³. Recently, these cases have been treated by foam sclerotherapy with good results⁵⁴. However further studies are welcome to clear this indication since thrombophlebitis and recurrence are common problems with foam sclerotherapy.

Anatomy and ultrasound

The knowledge about nerve anatomy is pivotal to avoid such complications but it is not a guarantee that lesions will not occur, as pointed out by Sam *et al*, nerve damage can happen with the best



surgeons⁴. Figures 5 and 6 address the "risky points", where nerves and veins are close and most lesions occur.

Finally, ultrasound is increasingly becoming essential for the vascular surgeon for surgical planning. Nerve anatomy of the lower limb is extremely variable.

A publication found a relationship in anatomical variation between SN and GSV; in 54 cases, the nerve was posterior to the vein and anterior in 32 cases¹⁵. Ricci *et al* identified contact points between NSu and SPV ("risk points") in 39 of 40 members (97%) studied⁵. The use of ultrasound, especially performed by the surgical team, identifies points of possible injury ("risk points" - Fig 5 and 6) and avoid nerve damage during VV surgery.

Possible treatments after nerve injury

Nerve injury pattern is well documented on clinical examination, electromyogram, magnetic resonance imaging and surgical pathology⁹. The vast majority of nerves damaged in varicose vein operations are only sensitive and do not require treatment.

Transient changes in nerve transmission observed weeks after surgery can be due to the temporary neuropraxia caused by edema, hematoma, inflammatory processes, or simply by the mechanical irritation during operation⁵⁵.

After an injury to nerves is detected, it is recommended to wait 4 to 6 weeks for the appearance of clinical signs of motor recovery indicating neuropraxia.

If motor recovery does not occur within this period, exploratory surgery of the nerve should then be performed. Intraoperative findings will determine the technique to be used (neurolysis, neurorrhaphy, or nerve grafting)¹⁰.

Peroneal nerve damage, femoral and sciatic may cause great disability and the possibility of nerve reconstruction should be considered in patients not responding to clinical therapy⁵⁶.

Malpractice Claims after varicose vein surgery

Campbell *et al*³ showed that nerve damage is the most common reason for malpractice claims after venous procedures, accounting for 31% of the claims. A review concerning nerve damage after varicose veins operation found that between 4% and 23% of patients remain with sensory loss after the procedure, depending on the testing method and study⁴.

The same review showed that nearly all treatment methods cause nerve damages. Phlebectomies, stripping, radiofrequency and endolaser present nerve damages and studies vary greatly concerning incidence of this complication (from 0% to 33%)⁴.

Nerve lesions were the cause of malpractice claims in 62 out of 200 claims⁵⁷. A review of 200 consecutive lawsuits on venous operations found that the lesion was on the saphenous nerve in 8 patients, the sural nerve in 15 patients, the peroneal nerve in 18 patients and cutaneous nerve in 21 cases.

Claims due to improper communication and inadequate medical record keeping are also frequent58. Although it seems obvious, good anatomical knowledge, proper preoperative planning, clear communication, safe operation protocols and good clinical records are important to prevent claims. The preoperative duplex scan should be performed by the surgical team or at least well communicated to the surgeon, and it is pivotal⁵⁸.



Fig 5 - "Risk points". 1) Ilioinguinal nerve at risk during initial groin dissection. 2) Femoral-cutaneous nerves at risk when anterior accessory saphenous vein or veins in the anterior region of the thigh are committed. 3) Relationship between the great saphenous vein and nerve. 4) Lateral cutaneous nerve (common fibular nerve) can be damaged in varicose vein dissection in the lateral compartment of the leg. 5) Superficial fibular nerve can be damaged during dissection in local varices.

Claims due to nerve injury are frequently settled after accepting liability. This is due to the fact that this



complication may cause permanent disability even when instantly repaired⁵⁹.

A study about litigation claims after vascular surgery showed that nerve damage is responsible for nearly a third of the successful malpractice claims in the courts after venous operations. This British study showed a 61% success rate of malpractice claims in varicose veins operations⁶⁰. The mean compensation for damage was $100.000 \in$ and some cases received higher sums.

No matter how simple a procedure may appear, all operations carry risks for the patient. Therefore, knowledge about adverse events is essential for providing patients with accurate advice and information regarding the potential risks and benefits of treatment options².

Endovenous techniques will still be affected by claims of recurrence, unsatisfactory outcome/poor cosmetic result, pigmentation, and scarring. Patients' expectations will be higher with endovenous techniques, which are being marketed as less invasive than surgery. Patients undergoing varicose vein treatment/surgery must be made aware of these risks and this discussion needs to be clearly recorded in the patient's records and/or consent form, along with the receipt of a supporting patient information "sheet"⁴⁶. There are no current articles on litigation in modern techniques for treating varicose veins.

The patient's choice now seems to be a clinical priority and most practitioners agree that at least one alternative to conventional surgery should be available. Not all patients may be suitable for all modalities, and selection criteria differ according to Doppler ultrasound and clinical findings and chosen method¹⁷. We should not forget that elastic stockings and venoactive drugs are possible alternatives for most varicose vein procedures and patients should be aware of this possibility⁶¹.

Conclusion

Chronic venous insufficiency is a high prevalence disease and nerve damage is the most common reason for malpractice claims after venous procedures. Nerve damage during varicose vein procedures should always be kept in mind; even good surgeons can cause nerve damage.

Anatomical knowledge, team experience and respecting the characteristics of every procedure are pivotal for minimizing the risk of nerve damage.

Some techniques may present more nerve damage than others⁴ and both the choice of the type of procedure and strategies to prevent such lesion with every technique are advisable. For example, partial stripping/ablation instead of total saphenous stripping may reduce its incidence⁴.



Fig 6 - "Risk points". 1) Sciatic nerve and sciatic varices are related. 2) Tibial nerve is not usually damaged during varicose vein surgery but can suffer thermal lesion. 4, 5 e 6) relationship between the medial and lateral sural cutaneous nerve, sural nerve and the small saphenous veins.

The type of anesthesia is also an important factor because if the patient is responsive and the nerve is not blocked, the patient can tell the surgeon if the nerve is touched. The use of ultrasound before the procedure by the surgeon himself, with localization of nerves and "risky points", could reduce the incidence of nerve lesions. High-resolution US permits visualization of peripheral nerves prior to the intervention⁵.

In order to minimize nerve damage, the authors usually perform same-day preoperative ultrasound and operation under local anesthesia in all patients. The ultrasound considers vein reflux and anatomy and nerves related to these veins. We prefer saphenous sparing procedures that further minimize nerve damage. All patients are offered elastic stocking as an alternative treatment and full informed consent is signed by all patients (in which the nerve damage possibility is disclosed).

If damage happens, identification should be prompt and treatment fast in order to obtain good results, mainly in cases involving motor disability.



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DICOM format: definition and practical use in vascular medicine

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Abstract The imaging is essential in vascular medicine for diagnosis and treatment. New imaging techniques since the advent of the spiral CT scan, invented by Hounsfield and Mac Cormack in 1972, brought us a revolution in whole medicine. This has been possible thanks to the development of new standards for imaging, particularly DICOM format. The aim of this paper is to explain what is DICOM and how we use it in vascular medicine. DICOM (Digital Imaging and Communications in Medicine standards) is an universal worldwide format used for medical imaging for all vascular investigation techniques: sonography, CT (computed tomography) and MRI (magnetic resonance imaging). This format allows 3D reconstruction of the patient's anatomy and gives access to quantification of all anatomical structures of the body, in particular of the vessels. It is achieved with dedicated software called DICOM browsers. These new tools of



Fig. 1 - A: Hounsfield Unit scale B: Segment encompassing certain remarkable anatomical stuctures

tridimensional (3D) modeling of the vessels bring us more accurate data of vascular anatomy. They make us enter in an era of new endoscopic and surgical techniques fully based on the image data, and so open the way for simulation, training and augmented reality.

Keywords DICOM, imaging, 3D modeling, 3D reconstruction, vessels-anatomy

Outline

What is DICOM file? What is DICOM used for? What is the content of a DICOM file? Imaging and reconstruction modalities with DICOM Practical use in medicine Methodology for 3d printing of the vessels Examples of the DICOM use

Introduction

The DICOM¹ is a standard of medical image and is universally used by radiologists and practitioners for the diagnostic in radiology all over the world.

Furthermore, the reconstruction of rendered volumes from DICOM bioimages has proven to be a great tool for the analysis and virtual reproduction of human anatomy. Knowing the procedure and the scope of the different tools is mandatory to lead to an accurate diagnosis, improve the surgery thanks to simulation and augmented reality techniques.



The DICOM header

AccessionNumber AcquisitionDate AcquisitionNumber AcquisitionTime BitsAllocated BitsStored BodyPartExamined CodeMeaning CodeMeaning CodeMeaning CodeValue CodeValue CodeValue Columns ContentDate ContentTime ConvolutionKernel DataCollectionDiameter DateofLastCalibration DeviceSerialNumber DistanceSourcetoDetector **DistanceSourcetoPatient** Exposure ExposureTime FileMetaInformationVersion FilterType FocalSpots FrameofReferenceUID Gantry/DetectorTilt GeneratorPower HighBit ImageComments ImageOrientationPatient

ImagePositionPatient ImageType ImplementationClassUID ImplementationVersionName InstanceNumber InstitutionAddress InstitutionName KVP LargestImagePixelValue Manufacturer ManufacturersModelName MediaStorageSOPClassUID MediaStorageSOPInstanceUID MetaElementGroupLength Modality OperatorsName PatientID PatientPosition PatientsAge PatientsBirthDate **PatientsName** PatientsSex PatientsWeight PerformedProcedureStepDescription PerformedProcedureStepID PerformedProcedureStepStartDate PerformedProcedureStepStartTime PerformingPhysiciansName PhotometricInterpretation PixelData PixelRepresentation PixelSpacing PositionReferenceIndicator ProcedureCodeSequence ProtocolName ReconstructionDiameter ReferencedImageSequence ReferencedPerformed ProcedureStepSequence ReferencedSOPClassUID ReferencedSOPClassUID ReferencedSOPClassUID ReferencedSOPClassUID ReferencedSOPInstanceUID ReferencedSOPInstanceUID ReferencedSOPInstanceUID ReferencedSOPInstanceUID ReferencedStudySequence ReferringPhysiciansName RequestAttributesSequence

RequestedProcedureCodeSequence RequestedProcedureDescription RequestedProcedureID RequestingService RescaleIntercept RescaleSlope RotationDirection Rows SamplesperPixel ScheduledProcedureStepDescription ScheduledProcedureStepID ScheduledProtocolCodeSequence SeriesDate SeriesDescription SeriesInstanceUID SeriesNumber SeriesTime SliceLocation SliceThickness SmallestImagePixelValue SoftwareVersions **SOPClassUID** SOPInstanceUID SourceImageSequence SpecificCharacterSet StationName StorageMediaFile-setUID StudyDate StudyDescription StudyID StudyInstanceUID StudyTime TableHeight TimeofLastCalibration

 Table I - Contents of a DICOM file header

The practical use of DICOM could be very important also for telemedicine. In addition, DICOM is used also to store functional data, like blood velocity signals and spectral analysis. In this paper we will just focus on the imaging data.

TransferSyntaxUID

WindowCenterWidthExplanation

WindowCenter

WindowWidth

X-rayTubeCurrent



I- What is a DICOM file?

The DICOM¹ Image file is a tagged image file; the file contains both an image (most of the time) and a collection of data about the image. The data in a DICOM image file is stored as a sequence of individual elements. Each element contains one item of information about the image or the image itself. DICOM elements are binary, so DICOM files cannot be viewed with a text editor.

Although each method has its own physical principles and specific equipment, all biomedical data are stored in a common format: the DICOM file.

For the digitization* of bioimages and prevent the subsequent conflicts of compatibility between files of different origin, in 1993 the American College of Radiology (ACR) in conjunction with the National Electrical Manufacturers Association of the United States (NEMA) developed and implemented the Digital Imaging and Communications in Medicine standards¹ (DICOM).

These are a series of detailed specifications that describe the suitable formats and exchange of medical images mode. The core information of a DICOM file is the bioimage (.dcm) and contains inseparable data on the patient and the study performed since it has IOD (Information Object Definition) containing all the informations of the patient.

In this way it is possible to transfer and reproduce images beyond the manufacturer (Siemens Healthcare®, Philips®, GE Healthcare®, etc.), and even via the web (HL7 v3), for the convenience of its various users.

*Digitize: Convert or encode into digit (numbers), data or information such as an image or a document.

Principle of CT scan

It is necessary to understand what are the voxels, the Hounsfield Units and the Threshold tool.

Definition of a voxel

Just as the pixel represents the smallest element that make up a flat (2D) image, the voxel is a small cube with a side of 100 microns that make up the acquisition volume of the patient.

Hounsfield Units (HU)

It is the unit assigned to each voxel that makes up a biomedical digital image and expresses the coefficient of linear attenuation corresponding to the anatomical structure subjected to X radiation. For practical application, these units are subject to a scale called the Hounsfield Scale, which is a quantitative scale that discriminates the radiodensity of human tissues. (fig 1) Thus, water corresponds to 0 HU; liver under normal conditions, an attenuation of approximately 60 HU, while lung tissue -500 HU and compact bone about 1000 HU.

This tool also allows to determine the colors (RGB) and the degree of opacity of each structure.

Threshold tool

The thresholding is the simplest way to achieve a segmentation of the image. It consists in the selection within the volume of voxels included between a minimum and a maximum HU value. The voxels outside these values are not displayed.

DICOM standard references

The DICOM Standard1 with its official documents can be downloaded or read online as web pages.

DICOM Browser - https://DICOM.innolitics.com/ -This link is a useful website for browsing the various DICOM information objects.

What is DICOM used for?

DICOM is used in virtually all health structures² worldwide. It ensures the interoperability of systems used to: Produce, Store, Display, Send, Query Process, Retrieve, print medical images and derived structured documents, as well as to manage the related workflow.

Who needs DICOM?

Radiologists and physicians get better access to images and reports when DICOM is in place. This allows them to make a faster diagnosis, potentially from anywhere in the world.

Patients can obtain faster and more effective care when DICOM is used to send their information through the healthcare enterprise.

Hospitals, clinics, imaging centers and specialists can make conformance to specific features of DICOM part of their purchasing requirements to ensure these tools work together across vendors to produce, manage and distribute images.

Manufacturers of imaging equipment (CT, MR, Ultrasound ...), **P**icture **A**rchiving and **C**ommunication **S**ystem (PACS), and peripheral equipment (workstations, 3D printers, CD importers) conform to DICOM to ensures compatibility of their equipment at every medical imaging facility.



3D viewers

free website

MAC	YES	https://horosproject.org/
	NO	https://www.osirix-viewer.com
Mac/pc	NO	https://www.slicer.org
PC	YES	http://www.microDICOM.com/downloads.html
PC	NO	https://www.radiantviewer.com/
PC	NO	clinical.netforum.healthcare.philips.com/global/Explore/
		Clinical-News/MRI/Philips-DICOM-Viewer-download-
		version-R30-SP3
PC	YES	https://www.santesoft.com/win/sante-DICOM-viewer-
		pro/download.html
PC	NO	http://www.theobjects.com/orsvisual/index.html
Mac	NO	http://ric.uthscsa.edu/mango/mango.html
PC	NO	https://www.orpalis.com/labs/DICOM-viewer
		• •
PC	YES	http://www.onis-viewer.com/ProductInfo.aspx?id=19
PC	NO	https://www.millensys.com/forms/
		download_miviewer.php
PC	NO	http://ginkgo-cadx.com/en/
PC	NO	http://www.bme.teiath.gr/medisp/
		downloadMEDISPDICOMViewer.htm
PC	YES	https://sourceforge.net/projects/dcm4che/
PC	NO	https://www.kuhp.kyoto-u.ac.jp/~diag_rad/intro/tech/
		DICOM_tools.html
PC	YES	https://www.robomedical.com
PC	YES	https://sourceforge.net/projects/opendicomviewer/
PC	YES	http://www.e-DICOM.com/
	MAC Mac/pc PC PC PC PC Mac PC PC PC PC PC PC PC PC PC PC	MACYESMac/pcNOPCNOPCYESPCYESPCNOPCNOPCNOPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYESPCYES

Table II - Main DICOM viewers

3D printing					
Software	function	input format	action	output format	
HOROS®	DICOM viewer	DICOM	Extracting a 3D mesh gross segmentation	obj	
MESHMIXER®	3D modeling	obj	Refinement of segmentation Cleaning – mesh repair	obj/mix	
CURA®	for 3D print	obj	Parameters for 3D printing	gcode	

Table III - the 3 steps to build 3D printable mesh models from angio-CT





Fig. 2 - Maximum intensity projection technique (MIP)



Fig. 3 - Multiplanar reconstruction technique (MPR) correspondence of the 3 planes sagittal (top left) axial (bottom left) and coronal (right)



Fig. 4 - 3D direct volume rendering of the thorax (VRT)

Payers benefit from this faster and more effective process through potentially lowered cost of care.

DICOM's purpose is to meet each of these different requirements.

What is the contents of a DICOM file?

2 parts: header and data

1- the header contains all informations regarding the patient, the exam and the parameters of the following data: tag, data type and length (see table I)

2- image DATA = images under the DICOM format (512 x 512 pixels) commonly coded into on 256 bits that is 256 levels of gray. But DICOM could support higher resolution and color-coded images.

II- IMAGING & RECONSTRUCTION MODALITIES with DICOM

It is possible to use dedicated software named DICOM browser³ (see Table II) to obtain different reconstructions of the DICOM files:

1. Maximum intensity projection (MIP) is a method for 3D data that projects in the visualization plane the voxels with maximum intensity that fall in the way of parallel rays traced from the viewpoint to the plane of projection (fig 2). It connects the high intensity dots of the blood vessels in three dimensions, providing an angiogram that can be viewed from any direction.

2. Multiplanar reformation or reconstruction (MPR) involves the process of converting data from an imaging modality acquired in a certain plane, usually axial, into another plane (fig 3)

3. 3d reconstruction by volume rendering technique (VRT) It is a type of visualization technique which creates a three dimensional representation of data with voxels, using view-aligned texture mapping and diffuse reflection (Figure 4).

III- Practical use of DICOM imaging in medicine

3d reconstruction for patient assessment IN SURGERY and RADIOLOGY by VRT is a true revolution: More accurate morphological 3D information from new imaging techniques open the way for pre-procedure surgical planning and simulation.

3D printing from angio-CT DICOM⁴⁻⁶ files makes surgery safer for patients by placing real anatomy in the hands of surgeons before they go to theatre. Image-guided is also becoming mandatory to help endoscopic and miniinvasive procedures and lower the risk of complications.



It is commonly used by orthopedic surgeons⁷

It is mostly true for hepatic surgery surgery as demonstrated by Soler and Marescaux 8

It has also multiple applications in neurosurgery, in particular treatment of craniostenosis⁹, in plastic and reconstructive surgery¹⁰. In the vascular field, we commonly use today 3D models for planning, simulation, and training in vascular surgery¹¹

Laparoscopic Quantitative 3D Endoscopy¹² as well, is used for Image Guided Surgery.

3d dose delivery in radiology $^{13-14}$ and Radiotherapy 15 are essential to improve efficiency and avoid complications

The new dose validation system for Gamma Knife radiosurgery¹⁶ uses a DICOM-RT interface.

Working with DICOM images from CT and MRI scan data will also help Dental¹⁷⁻¹⁹, Medical and Veterinary practitioners²⁰ by producing true to life 3D printed models of patient anatomy to inform procedures and reduce risk.

IV- Methodology for 3d modeling and 3d printing of vascular models

This could be achieved by several companies on the web providing the full service "from DICOM to print":

Medimodel (https://medimodel.com)

Think3D (https://www.think3d.in)

D2P from 3dsystems (<u>https://www.3dsystems.com/</u> DICOM-to-print)

We also propose here a simple way in three steps, using the following available free software:

1- Horos® (working only on Mac computers) is a DICOM® viewer and provides a 3D reconstruction of the venous anatomy. It produces 3D vector models, also called 3D mesh, obtained by a segmentation process. Available at: <u>https://fr.freedownloadmanager.org/Mac-OS/</u> <u>Horos-GRATUIT.html</u> (april 2020)

2- Meshmixer® is then used to clean, simplify and repair the huge 3D mesh file produced by Horos®. Available at: <u>https://meshmixer.updatestar.com/fr</u> (april 2020) - Cura® is finally used to build a "gcode" file. This will tell the 3D printer how to slice and print the 3D anatomical model. Available at: <u>https://</u>cura.updatestar.com/fr (april 2020)



Fig. 5 - Methodology of 3D printing of educational models of venous anatomy. (workshop presented at Charing Cross 2019 and Krakow's 2019 UIP chapter meetings)

V-PRACTICAL EXAMPLES of the DICOM use

1- Educational use of 3D modeling

- CT-venography (CTV) is both a great educational tool to learn venous anatomy and a powerful research tool to improve our understanding of the venous system.

- Building with Horos® 3D animations, rotational models and journeys inside the body.

- Allows a virtual dissection of the human body ; it is a powerful teaching and learning tool for the students in human anatomy: to prepare, but not replace, cadaver dissection. (table of virtual dissection²¹, see figure 6)

- 3D printing of anatomical models is a great tool to study anatomical variations, which are so common in the venous network. Examples of variations of the short saphenous vein termination and the femoral vein variations are shown on figure 7.





Fig. 6 - Virtual dissection table "DIVA3d" using a huge touch screen to teach and learn human anatomy.



Fig. 7 - 3d printed models of a patient from a CTvenography: example of a dilated Giacomini vein (in purple) Left: posterior view middle: lateral view right: posteromedial view 1= Great saphenous vein (in light blue) 2= Giacomini vein (in purple) 3= Popliteal vein (in dark blue) 4= Venous arcades of the semimembranosus muscle (in green) 5= Hunterian perforator vein with GSV (in red) 6= Thigh perforator with the Giacomini vein.

2- Web communities for sharing 3d anatomical models

For sharing 3D anatomical models, several websites are available on the web.

Some of them are totally free, and you can even download several printable 3d models.

- www.embodi3d.com (biomedical 3D printing) with possibility to Automatically convert CT scans into 3D Printable Models for Free with democratiz3D®.

- NIH 3Dmodels.com show a large collection of 3D models of vascular cardiac pathology.

Other web solutions propose to host your models: Sketchfab®. (www.sketchfab.com.)

You have to subscribe to buy or sell your own collection of 3d models. You can include labels of the structures (fig 8) and display the model in Virtual Reality mode.





Fig. 8 - Display of the interactive 3D model of the head & neck with labels using Sketchfab® (available at: <u>https://</u><u>skfb.ly/6QYxZ</u>)

Conclusion

DICOM format is a worldwide format of imaging in medicine, making possible to build realistic 3D models of human anatomy, especially in the field of vascular pathology.

The new tools of 3D modeling constitute a true revolution in educational anatomy and for clinical applications in the case of complex vascular anatomy.

It is also the future of surgery providing an accurate information about the vascular anatomy of each patient. The modern surgery has to be an image-guided surgery for an elective and more limited ablation of organs (segmentectomy) and for less complications.

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Foam Washout Sclerotherapy, a single center experience

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Abstract

Introduction: The author has designed and implemented a modified method of foam sclerotherapy (FS) over some years which he believes lowers the rate of complications of the procedure while maintaining efficacy of the procedure as assessed clinically and by duplex ultrasound. This modified technique is termed Foam Washout Sclerotherapy (FWS) and involves the removal of the injected foam from a point distal to its administration level. This article compares the success rate and the rate of complications between FWS and FS of varicose veins. All procedures have been performed by the author over a period of 4 years. The basic principle of FWS is to inject a certain volume of a detergent-based foamed medication at the proximal part of the targeted vein and removing the injected foam from the same vein via a distally placed IV catheter within 5-10 seconds. The primary end point of the study was limited only to the comparison of the closure rate of treated vein segments (success rate) and complication rates.

Materials and Methods: A retrospective review of FWS and FS cases performed between late 2008 to late 2012 was carried out. The review included only the cases that had regular follow-ups for one year consisting of 823 sclerotherapy treatments (292 in FS group and 531 in FWS group) among 657 patients. Studied veins were great saphenous (GSV), small saphenous (SSV), and anterior accessory saphenous vein (AASV) varicosities. Follow up included a phone call in 24 hours, re-exam and ultrasound studies in 2 months, 6 months, and 12 months. Most patients had additional follow up in 2-3 weeks at which time physical examination & ultrasound study was performed.

Introduction

Foam sclerotherapy (FS), as practiced by the author for more than 2 decades, has consisted of the injection Some patients received sclerotherapy of unsightly spider veins of legs at time of follow-up visits. For better visual understanding of the FWS technique a clip on YouTube.com is available:

https://www.youtube.com/watch?v=Usw9_d2uTvI&t=4s Results: The cohort consisted of 823 incompetent veins in 657 patients. 505 patients were female and 152 were male. Mean age was 48.5 (23 - 76). Each case was followed for 12 months. Overall success rate of sclerotherapy in both the FS and FWS groups was similar at around 90% or above for different groups of veins treated. Overall complication rate was 20.2% in the FS group versus 6% in the FWS group. Discussion: The author presents the results of a retrospective analysis of success and complication rates between the standard method of foam sclerotherapy (FS) of varicose veins, as practiced at his vein clinic, with a modified method named foam washout sclerotherapy (FWS) that he implemented for the first time in late 2008. The author presents that by removing the injected foam from the lumen of targeted varicosity, complication rate is lowered while success rate is identical in both methods.

Conclusion: The author suggests that the modified technique of FWS in the treatment of lower extremity varicose veins is associated with fewer complications compared to FS, is equally as effective as FS and in the future FWS may replace the current FS technique for chemical ablation of some cases of varicose veins of legs.

Keywords Foam Washout Sclerotherapy, Foam Sclerotherapy, Varicose veins, Sclerotherapy Complications, Chemical Vein Ablation

of a small volume (4-7ml in most cases) of a detergentbased sclerosing agent into a targeted incompetent varicose



vein of lower extremity with the goal of complete sclerosis resulting in occlusion. On the average, the success rate of foam sclerotherapy has been reported at around 75.8-87%¹⁻². However, there have been reports of several complications such as deep venous thrombosis (DVT), migraine headaches, vision disturbances, and strokes¹⁻¹¹

The mechanism for Central Nervous System (CNS) symptoms and migraine headaches has been suggested to be related to the release and circulation of vasoactive

mediators (endothelins) from injured endothelial cells associated with foam sclerotherapy 8,9,12 .

The author has pioneered and implemented a new method of foam sclerotherapy attempting to lower the rate of the above complications. This new method, Foam Washout Sclerotherapy (FWS), involves removing most to all of the injected foam from the lumen of the targeted varicosity, and potentially removing the endothelins thought to be responsible for some of the complications. Thus, the current paper searches for a possible lowered risk of DVT as well.



Fig. 1 - Potential for complications in foam sclerotherapy of a superficial varicosity.



Fig. 2 - Foam Washout Sclerotherapy of superficial varicose veins.



Table I - Success Rate					
FS Group	# of cases 292		Sustained closure cases in 12 months		
	GSV	162	149	(91%)	
	SSV	98	87	(89%)	
	AASV	32	30	(94%)	
FWS Group	# of cases 531				
	GSV	178	165	(93%)	
	SSV	308	289	(94%)	
	AASV	45	41	(92%)	

FS (foam sclerotherapy), FWS (foam wash out sclerotherapy) GSV (great saphenous vein), SSV (Small Saphenous vein) AAV (anterior accessory vein of the thigh)

Table II - Complication Rates					
FS Group Total 292	Transient Vision Disturbance	Transient Neurologic Symptoms	Headaches / Migraines	DVT	Superficial venous thrombosis
GSV 162 SSV 98 AASV 32 FWS Group Total 531	6 (3.7%) 3 (3%) 1 (3%)	1 (0.6%) 0 (0%) 0 (0%)	5 (3%) 5 (3%) 1 (3%)	1 (0.6%) <u>a</u> 2 (2.04%) <u>b</u> 0 (0%)	15 (9%) 15 (16%) 4 (13%)
GSV 178 SSV 308 AASV 45	0 (0%) 0 (0%) 0 (0%)	0 (0%) 0 (0%) 0 (0%)	2 (1.1%) 0 (0%) 0 (0%)	0 (0%) 0 (0%) 0 (0%)	12 (7%) 15 (4.9%) 3 (6.6%)

FS (foam sclerotherapy), FWS (foam washout sclerotherapy) GSV (great saphenous vein), SSV (small saphenous vein) AASV (anterior accessory vein of the thigh), SFJ (sapheno femoral junction), gastrocnemius vein (GV). a: GSV DVT, thrombus limited to proximal GSV with 2mm extension into SFJ. b: SSV DVT, thrombus limited to a single GV.

Material and methods

Techniques

Foam sclerotherapy (FS) as practiced by the author: After ultrasound/doppler mapping of reflux sources in all cases of varicose veins, foam sclerotherapy begins by injecting the proximal segment of the incompetent vein at 3-5 cm distal to the source of reflux (junctional reflux or incompetent perforating vein). The patient is placed in the supine position and the leg is elevated 10-20 degrees during the foam injection. Then, while the ultrasound transducer



is monitoring the appearance of foam in the lumen of the targeted vein, the foamed sclerosing agent is injected over 3-5 seconds. Using the ultrasound transducer, as soon as the foam appears at the reflux source, since the injection is done near the incompetent connection to a deep vein, manual compression is applied there for a few seconds until the injection is completed and catheter is withdrawn to prevent the foam from entering the deep vein system. Foam is prepared by mixture of CO2 gas with either sodium tetradecyl sulfate (STS) or Polidocanol using the Tessari method. The author used STS in concentrations 1.5%-3% for varicose veins with a caliber > 7mm. Polidocanol 1% is used for veins up to 7mm in caliber. Liquid to gas ratio is usually at 1:3 or 1:4. The foam is allowed to stay in the system and none of the injected material is withdrawn. After the treatment compression stockings are used for 7-14 days. (Figure 1)

The author's modified technique (Figure 2), named foam washout sclerotherapy (FWS) consists of placement of at least two IV access catheters 20G-19G size, with lengths between 3-5 cm at two levels (approximately 10-12 cm apart) in the targeted varicose vein segment. The tip of the most proximal catheter, which receives the first foam injection, is approximately 3-5 cm distal to the identified incompetent perforating vein or junction. To avoid collapse of the lumen of the targeted varicose vein, the leg is kept at body level (the leg is not elevated). Then the ultrasound probe, in transverse orientation, is placed at the source of reflux over the target varicose vein.

Next, injection of 4-7 ml sclerosing foam (STS 1.5%-3% for large varicose veins and Polidocanol 1% for small varicose veins up to 7mm in diameter) into the proximal IV catheter is started. The injection is made over 3-4 seconds, while applying pressure over the reflux source using the ultrasound probe to prevent the foam from entering the deep vein system. In the middle of the injection an assistant starts applying a very gentle negative aspiration force to the out-port syringe very slowly at the beginning (to avoid collapsing the vein walls over the tip of the IV catheter) and starts to aspirate the foam and continues this gentle action until withdrawal of foam ceases. Next, while proximal to distal direction massage is applied, both catheters are removed and compression stockings are put on the leg, and the patient is ambulated. Following both methods of sclerotherapy, 30-40mmHg Compression stockings are used for a period of 7-14 days (14 days for GSV & SSV reflux cases and 7 days for AASV reflux treatment).

When the incompetent varicosity is longer than 12 centimeters, more than 2 access catheters are placed (A, B, C..) before starting the treatment and the same procedure is repeated in a stepwise fashion starting from the most

proximal segment first (A-B, B-C). This modification is named multi-segment FWS.

The aim of the current preliminary paper is to present the FWS procedure. A thorough statistical analysis of FWS data will be included in future articles covering FWS subject.

Patients Characteristics

Our cohort consisted of 657 patients, 505 of which were female and 166 received treatment on two different varicose veins, making a total of 823 treatments. There were 292 treatments using FS and 531 using FWS. Mean age was 48.5 (23-76).

The high proportion of SSV cases included in the FWS group is due to the choice of the patients and availability of other treatment options for GSV and SSV disease during the latter part of the study period.

Since this was not a prospective study, no attempts were made to allocate cases in equal numbers between different treatments. Therefore, the total number of incompetent vein types which received either type of treatment technique was not planned. Patient preferences were a major factor in choosing the treatment method.

Patients were followed up for 12 months (9 -14): by phone calls in 24 hours and re-exam and ultrasound evaluation in 2 months, 6 months, and 12 months. Most patients had a follow visit at 2-3 weeks as well. At follow up visits some patients received sclerotherapy of unsightly spider veins. None of the varicose veins treated by FS and FWS methods received retreatment during follow up visits.

Treatment success was defined as: Complete occlusion and lack of reflux in treated varicose veins at both 6 and12 months follow up. Any recanalization that demonstrated reflux was not considered a success.

This retrospective study looked only at success rates in the two groups as defined above and compared complication rates in the two groups without attention to any other factor.

For better visual understanding of the FWS technique a clip on YouTube.com is available:

https://www.youtube.com/watch?v=Usw9_d2uTvI&t=4s

Results

In the FS group success rate was 91%, 89%, 94% for GSV, SSV, and AASV respectively. The success rate was 93%, 94%, and 92% for GSV, SSV, and AASV respectively for the FWS group. Overall, the success rates are essentially identical (Table 1).



In the FS group the total combined complication rate for combined complication rate was 20.2%, while the total complication rate in the FWS group was 6% (Table 2).

There were no cases of DVT in FWS cases. In the FS group one patient treated for SFJ/GSV reflux developed extension of great saphenous vein (GSV) thrombus into the saphenous femoral junction (SFJ) region and two cases of gastrocnemius vein thrombosis (classified as DVT in this series) were found.

There was no case of PE in either group. There were differences in other complication rates between the two methods: vision disturbances, headaches, and superficial venous thrombosis were lower in the FWS compared to the FS group. It may be noteworthy to mention that regarding the very few cases of DVT that were observed, all were in the FS group and 2:3 of the cases involved only part of gastrocnemius veins.

Transient neurologic symptoms was in 0.6% of FS group and was not noted in FWS group.

Discussion

FWS has been introduced and implemented by the author in 2008 in a clinical setting, at a time when there were no prior articles covering the FWS technique or its comparison to FS.

A first glance at the complication rate in our FS group may suggest a higher rate of DVT than in some published articles^{3,10}. However, the author points out that no previously published articles have included in their DVT complication rates such things as gastrocnemius vein thrombosis and thrombus extending to the SFJ level without involvement of the femoral vein, as we have done in this paper³.

Superficial venous thrombosis is commonly observed in phlebology practice and we recorded this as a complication. Our series recorded superficial venous thrombosis at 4.9% to 16% depending on which veins were injected. This compares favorably with one previous article recording a rate of phlebitis of 8.2% to 33% 2 .

Our rate of transient headaches after foam sclerotherapy (FS) is similar to published rates4). We regard the overall published rate of major neurological complications is under estimated and more research into actual complication rate is recommended ⁵⁻⁷. Thus, the author's complication rate in the FS group is similar to published articles. Our complication rate with the new method of foam washout

sclerotherapy (FWS) is less than with FS group, while the success rate is similar in both groups.

We consider that the most important factor through which FWS provides safer foam sclerotherapy, appears to be the fact that in the FWS method the application of positive pressure (injection of foam) at the proximal site of injection and negative pressure at the distal foam withdrawal point (out-port) of the same varicose vein provides a desired directional foam flow, which prevents the foam from flowing into unwanted territories such as deep veins through perforating veins^{3,5-7} and adjacent healthy veins. With FWS the treating physician selects exactly the segment to be sclerosed. Furthermore, the absence of any vision disturbance and migraine headaches in FWS suggests that most probably the withdrawing syringe content contains the used foam as well as any immediately released endothelins, which are extracted in place of being allowed to circulate in the patient's circulation^{8,9}.

Since the success rate between FS group and FWS group are identical, it appears that 5-10 seconds of contact of the endothelium with an effective concentration of a detergent based sclerosing foam, as is done in FWS, is sufficient to achieve effective chemical ablation of varicose veins (Table II).

If the FWS technique is performed correctly, since the injected foam is removed instead of being left in the circulation system, the treating physician has more freedom over choice of volume and concentration of the injected foam, as well as the contact time of foam with the endothelium of the targeted segment of varicosity. Thus, the FWS may achieve better results in cases of large caliber varicosities.

Future studies comparing FWS with FS and other treatment modalities may provide additional useful information regarding foam sclerotherapy techniques in clinical practice.

Conclusion

Based on a 4-year single center experience, the author presented the results of a retrospective analysis of success and complication rates of two foam-based chemical ablation methods of treating varicose veins consisting of standard method of foam sclerotherapy (FS), as practiced at his vein clinic, with a modified method named foam washout sclerotherapy (FWS) that he implemented for the first time in late 2008.

The type of incompetent veins that were included in this article were great saphenous vein (GSV) and small



saphenous vein (SSV) and anterior accessory saphenous vein (AASV). The study included chemical ablation of 832 incompetent vein cases among 657 individuals. Treatment success was defined as complete occlusion and lack of reflux in treated varicose veins at both 6 and 12 months follow up visits. Any recanalization that demonstrated reflux was not considered a success.

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After analysis of all data it was shown that the success rate was similar in both groups while the overall complication rate was lower in the FWS group. The author presents that by removing the injected foam from the lumen of targeted varicosity, complication rate is lowered while success rate remains identical in both methods.

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Book Reviews

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Multiple Sclerosis & CCSVI

Missed Key Evidence

BB Lee¹

¹Professor of Surgery and Director, Center for the Lymphedema and Vascular Malformations, George Washington University, Washington DC, USA. submitted: Jan 7, 2019, accepted: Jan 7, 2019, EPub Ahead of Print: Feb 26, 2019, published: Aug 25, 2020 Conflict of interest: none

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Multiple Sclerosis & CCSVI. Missed Key Evidence with self-explanatory illustrations.

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It was quite an exceptional and challenging task but I have never had such unique experience to read about multiple sclerosis (MS) as 'always wanted to know but afraid to ask!'

This is a monumental summary for such mythembedded MS, no one ever clarified sufficiently so far as I know of, I once again confirmed.



Although he wrote this manuscript in an 'essay' style, adding much of his personal opinion/feeling on current status of MS, unfairly governed by the neurologists, with full of despair, his review on the MS from CCSVI point of view is logically impeccable with no doubt.

One of few interesting highlights in his summary is he also shared same hemodynamic interpretation on the reflux versus obstruction in the peripheral venous system.

Indeed, this manuscript gave me an eye-opening opportunity to learn what I do not know about MS - MS has a higher prevalence as coexisting condition with the venous malformation- and further what I should know more about MS, clarifying much of confusion/misunderstanding on 'undeniable' relationships between MS and CCSVI.

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The CTG Compression Therapy

Consensus Conference on Compression Therapy

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Compression Therapy Study Group (CTG). Compression Therapy. Consensus Conference on Compression Therapy.

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- Compression therapy in sports
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- Rules and regulations on elastic stockings
- Biochemistry and compression

The Compression Therapy Group (CTG) released in Sep 2018 a comprehensive report of the 3rd Consensus Conference on Compression Therapy¹ in phlebo-lymphology, with the aim of unifying the evidence based knowledge with the daily clinical practice. The book is organized in several sections, which authoritatively guide the reader into the apparent complexity of compression.

History of compression starts in the prehistorian age, while compression develops in parallel with the knowledge of venous diseases. The historian chapter contains a lot of precious details about forgotten authors of the past as



well as of the modern era and describes alto the birth of compression industries and patents.

Bandages were knows since the ancient age, while the elastic stockings were born just in the middle XIX century. An interesting paragraph tells us the history the textile fibres and how they evolved into the materials used today.

A thorough attention is given to the pathophysiology of compression and to its biophysical properties like elasticity, hysteresis and extensibility. Pressure of bandages is different during muscle contraction (working pressure) or at rest (resting pressure) and applying a bandage it's necessary to take into account its elasticity. The classification follows several national standards, between them the German **RAL-GZ 387** and the English **BS 7505:1995**. Anyway, the practical behaviour of a bandage depends strongly on the application technique, which has its learning curve.

A current issue, which captures today the attention of several manufacturers, is the in vivo measurement of compression of bandages as well as compression stockings. Another actual debate about the advantages of progressive vs. graduated compression stockings is thoroughly treated together with the available evidences.

The Consensus deals also with the use of compression in several pathological conditions. Limiting to vascular surgery, interventions can be classified according to their

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thromboembolic risk (low, score 0; medium, score 1; high, score 2) and to the need of a compression device for thrombosis prevention. For instance, superficial venous surgery has a 0 score, while open aortic surgery a 2 score.

However, in superficial venous surgery compression is used generally to reduce pain and to improve aesthetic results as well as quality of life (QoL).

As regards lymph diseases, compression is not only a mandatory therapeutic resource in clinical practice, but enters in the definition of the complex decongestive therapy (CDT), which uses stockings, bandages and intermittent pneumatic compression (IPC).

Interestingly, preliminary data and hypotheses are presented about the role of biochemical changes after compression in venous and lymphatic diseases. Though the study is just in a preliminary way, these suggestions open to a new promising point of view in research.

In conclusion, the CTG Consensus is a comprehensive report about the role of compression in all its variegate forms, as a successful tool in vascular daily practice.

References

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In case of positive response, send a free copy of the book to the address Fondazione Vasculab ONLUS. Via Francesco Cilea 280. Napoli, 80127, Italy.

If eligible, you could also profit of a reviewing article. Please, ask the redaction at jtavr@vasculab.eu.





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Congress reports

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SCP Post Congress Report

44th Biannual National Congress, Nov 1-3, 2019 Montreal, Qc Canada.

P Raymond-Martimbeau¹



For the past 44 years, the Canadian Society of Phlebology (SCP) has been hosting a congress on chronic venous disease. The last congress took place in Montreal, Qc, Canada, November 1-3, 2019. Leading experts from all the scientific fields in phlebology got together to provide meaningful multi-faceted explorations of complex issues.

Vein care professionals participated in a threeday dynamic event. The first day, the program allowed interactive discussions and debates on curriculum topics of interest and all aspects of ultrasound- guided sclerotherapy. ¹Vice-President, Canadian Society of Phlebology. Director, Dallas Non Invasive Vascular Laboratories. Director, Vein Institude of Texas. submitted: Jan 3, 2020, accepted: Jan 3, 2020, EPub Ahead of Print: Jan 7, 2020, published: Aug 25, 2020 Conflict of interest: none

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Drs. Bentley, Hill, Hamel-Desnos, Wong, Raymond-Martimbeau, Gianesini, Crebassa, Paradis, Zerrouk, Antignani, Cervi, Danylewick, Dupuis, Kieffer, Nadeau, St-Amour and Zummo contributed through case studies and debates to make this day a great educational experience.

The second day, delegates shared their research output and clinical experience whereas advanced issues and novel surgical and non-surgical technologies were covered. In collaboration with the vWin Foundation, an historical Pupil & Tutor session organized by Drs Gianesini, Bentley, Serralde and Raymond-Martimbeau was very successful. Young phlebologists coached by mentors presented common research. Discussants commented on their work. An award was given to the paper: Iliocaval Recanalization for Permanent Filter-Associated Venous Thrombosis from Drs Perez-Lucas and Torres-Martinez.

Drs. Perez Lucas, Rodrigues, Sumaj, Nguyen and Esper were the young finalists for this project. The third day, the high quality of research presentations also contributed to the great success of this event.

We wish to thank the presenters, participants and industry sponsors for their ongoing commitment to education and their support which directly benefit our patients.

The SCP congress takes place twice a year, in the Fall in the East part of Canada and in the Spring in the West part. Each time, a multidisciplinary Canadian and International faculty mingle together, both researchers and clinicians to offer a global vision of phlebology and create knowledge exchange for better patient care.







dr. P. Raymond-Martimbeau

dr. L. Arias Villarroel

dr. S. Gianesini

dr. JA Martinez

dr. A. Orrego



Congress reports

The next congress will be held in Vancouver, BC, Canada on 25-26 April 2020. The highlights will be: pelvic venous disease, interactive case studies, and discussion of original papers. Physicians from different disciplines will be sharing the same vision and educational purpose. We are looking forward to welcoming you to Canada,

Pauline Raymond-Martimbeau, MD, FAVLS, DABVLM Vice-President, Canadian Society of Phlebology Director, Dallas Non Invasive Vascular Laboratories Director, Vein Institude of Texas

National Congress of the Italian Society for Vascular Investigations

SIDV - Rome May 3-5, 2019

L Aluigi¹



The event, arrived to its 36th edition, represents the national appointment that takes place every three years in Rome and brings together eminent national ¹President of Italian Society for Vascular Investigations (SIDV)

submitted: Jul 1, 2019, accepted: Jul 1, 2019, EPub Ahead of Print: Oct 1, 2019, published: Aug 25, 2020 Conflict of interest: none

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and international personalities in the world of Vascular Medicine, Vascular Surgery and research, to address issues of general interest concerning vascular pathology and to discuss, particularly, what's new in vascular diagnostics that technology makes available for increasing accurate clinical-therapeutic pathways.

The scientific committee has established as main topics what is usually done in diagnostic terms during surgical procedures and on what must be done in the control of the same and in the follow up of the performed procedures, both in the arterial and venous field, given the many possibilities, especially in phlebology, to deal with the same pathological condition with different methods.

If it is true that vascular diagnostics is the true company mission, it is also true that only knowledge and competence in vascular medicine can allow the correct application of technological advanced diagnostic methods: the "transversality" of vascular diagnostics cannot therefore ignore the deep clinical knowledge of the treated pathologies as well as the knowledge of the intervention procedures to allow an adequate verification of the results of the therapeutic acts.

After a pre-congress moment traditionally dedicated to training through theoretical and practical courses concerning a "vascular pathway in phlebo-lymphatic pathology" and a "vascular pathway in arterial pathology", the congress has been opened with a session dedicated to technological updating. Other sessions was on "chronic venous disease", "trophic lesions" and "venous thromboembolism" discussing the methodology and diagnostic technique, pointing on the difficulties for a



correct post-procedural or post therapeutical diagnosic evaluation.

The second part of the congress was dedicated to a theme often forgotten but of fundamental importance such as "diagnostics in the operating theater" with particular regard to: *technology at the service of quality control in the operating room of vascular surgery* and the *modern aortic center*. Large space has been devoted to the management of carotid, aortic pathology and arterial pathology of the lower limbs. The high scientific level of the speakers and the presented reports have guaranteed the excellent success of the event with great satisfaction of the faculty and the numerous participants.

Prof. Leonardo Aluigi

President Italian Society for Vascular Investigations (SIDV)



Memorial pages

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Prof Michael Földi (10/01/1920 – 20/10/2018)

S Michelini^{1,2}

¹San Giovanni Battista Hospital, Rome, Italy

²President of the International Society of Lymphology submitted: Feb 25, 2019, accepted: Feb 25, 2019, EPub Ahead of Print: Feb 26, 2019, published: Aug 25, 2020 Conflict of interest: None

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Figure 1 - Prof. Michael Földi.

of Lymphology). In both contexts he constantly brought his contribution of scientific and human wealth with the active and participatory presence in congress discussions, always conducted with refinement, pragmatism and high scientific level.

It is not possible to foresee how many doctors and physiotherapists were trained over time at his School of Formation founded in Interzarten, coming from all over Europe and even from overseas. He chaired also several practical and theoretical courses abroad. I had also the honour to participate to one of them, organized by Prof. Corradino Campisi in Genoa, having the good fortune to listen to him as a teacher, apparence under which he excelled.

His studies were published in all the major international journals of the sector and many of them were particularly innovative and enlightening. Among them I would like to mention his experience on guineapigs, that demonstrated the lymphokinetic effect of alpha-benzopyrones highlighting the marked increase in the frequency and contractile intensity of the thoracic duct following administration of a synthetic coumarin derivative.

Michael Földi has left us.

He did with great dignity, as he had done for a long life dedicated to the relief of the suffering of patients, and to the education of a huge number of health workers who today, in the world, spread his experience and are sad for his death.

I prefer to remember him, on behalf of the many lymphologists who adhere to the International Society of Lymphology (ISL), for his extraordinary interest in research and continuous updating.

Together with his wife Ethel he spent his life dedicating it to the study and treatment of patients with lymphedema, creating in Germany, at Interzarten near Freiburg in the wonderful Black Forest, one of the most famous lymphological Centers in the world, where together with his specialized staff he welcomed patients coming from every continent for their necessary treatments.

Among the founding members of the ISL, in Zurich in July 1966 (also in this forerunner and far-sighted) he joined the new European Lymphology Group just as early in March 1982 (which later became the European Society





Figure 2 - Földi's Textbook of Lymphology.

Michael Földi produced a long series of scientific papers, covering a wide range of topics related to Lymphology. His very rich scientific production culminated in the 2007 edition of the Földi's Textbook of Lymphology, a real treatise on lymphology, with particular attention to all the chapters with the ability to update all the main topics treated, insomuch as it shortly became the main reference text (and still is today) for many doctors, physiotherapists, nurses and experts of the subject.

The book is written in English, with the strong contribution of Ethel, the woman of his life, and together they wanted to transmit all their experience to future generations with a strong scientific imprint message. The whole world International lymphology Community should consider their diagnostic and therapeutic indications as a treasure for the health of patients.

In the text it is contained the essence of the inspiring principles of the activity of the Földi Clinic in the Black

Forest, where thousands of patients from all over the world found a sure point of reference to alleviate their suffering.

I remember him, in particular, in Rome, in the San Giovanni Battista Hospital where I work, on the podium of the Great Hall (during the Congress of the European Society of Lymphology in 2005), in one of the last conferences in which I had the pleasure to meet him (the last one was perhaps the following year at his home, in Hinterzarten), when I had the honor of moderating together with him a scientific session on the medical therapy of lymphoedema. He recalled me his first experiences with benzopyrones and their effect on the contractility of the thoracic duct. He agreed with the arguments I had just presented on the combined use of several benzopyrones, which if associated have a much greater clinical effect than if taken alone. At the end of the session, giving me some written sheets, he told me 'keep Sandro, this is a job for your Journal!' (the European Journal of Lymphology).

He was an "essential" man and, at the same time, highly authoritative.

I do not want to remind you his prestigious positions in all the main national and international scientific societies of the discipline, nor the important scientific and didactic production that he continuously provided for decades. I'd like instead to remind him to you as one of the Fathers of world Lymphology, a great Clinician, a great Man!

In the last years of his life, Ethel told me what wonderful life-partner he had been. He no longer had the strength to participate in the Congresses, due to the physical limitations that his old age imposed on him. Nevertheless, he continued transmitting to those who were close to him all his experience, polished as always. until the end of his days.

We will not miss him as a simple colleague, a simple scholar, a clinician or a teacher. He has left us as the Master of Lymphology.

Thank you Michael: our knowledge today owes so much to You!

Sandro Michelini

President of the International Society of Lymphology

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Dr Evi Kalodiki (10/01/1956 -31/12/2018)

CR Lattimer¹

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Dr Evi Kalodiki, Venous ThromboEmbolism (VTE), May 2013, Napoli (Italy).

Evi shared the birthplace of Aphrodite in Larnaca, Cyprus. However, she differed in that she worked with foam rather than being born out of the foam. From a mother and father of eminent personages in law she studied medicine in Athens and made a name in venous disease through her position at St Mary's Hospital, Paddington, London. She holds the Fellow of the Royal College of Surgeons (2009) as well as an MA in English literature (1984) and a PhD in venous disease (1996) from Imperial College, London. Her academic achievements are well known and can be obtained through a simple search on the Internet. This includes over 100 publications in Pubmed, membership of 21 societies, co-editor of 5 books, scientific secretary of 14 consensus statements, reviewer of 5 academic journals with membership of the editorial committee in 4 others. She achieved recognition through her international presentations and gained 12 prizes. The highlight was the Mauro Bartolo lifetime achievement award in 2016 in recognition of her outstanding scientific contribution in vascular disease and her visiting professor status at Loyola University Chicago.

In research she was the queen of air-plethysmography as the ultimate investigation of venous disease in quantifying reflux, obstruction and venous tone. Her legacy will decide on this simple, non-invasive, practical test for everyone with a venous disorder in an outpatient setting. In culture she supported Ghiorgos Sarandaris, an eminent scholar, for his life and works in the field of poetry.

Evi had impact. In her younger years she was a match for the most beautiful people in the world. She shook hands with the king of Sweden, the Archbishop of Melbourne, the sultan of Malaysia, Kojak and many others. She gave generously to charities and was an executive board member of the Hellenic Society in London for decades. She was responsible, in part, for Greek culture in the UK. Her only true mentors in life with directional influence were Dr Fareed from Loyola University Chicago and PL Antignani. Others had fleeting interests, nothing more.

Evi will be remembered from her unique individual personality, trying on occasions, and her generosity in time and money for friends and complete strangers. She always valued people above possessions and added to life in hope and purpose, with her smiles and pedantic dedication to research. She held an open house in Paddington with endless parties, meetings, reunions and celebrations all year round.

Her body rests in the family tomb (second shelf on the right) in the First cemetery of Athens next to her mother. She leaves behind her husband Christopher Lattimer, sister Maria Karamanoli, cousin Pavlos, special nephew Phaedon and her nieces Veroniki and Eva.

Christopher R Lattimer





VASCULAR NEWS

Vascular News

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Prof. GC Bracale, President Me.F.A.V.S



Me.F.A.V.S

Mediterranean Federation for Advancing Vascular Surgery (Me.F.A.V.S.) aims to promote the cooperation between the principle organizations involved in Vascular Surgery and countries of the Mediterranean basin: in particular Italy, France, Spain, Greece, Portugal, the Balkan area, Lebanon, the Middle East, the United Arab Emirates, Egypt, Morocco, Tunisia and other countries that face the Mediterranean and that wish to adhere to the Network.

Within these areas, and in coherence with this aim, Me.F.A.V.S. promotes knowledge regarding epidemiology, diagnostics, and treatment of vascular diseases in populations of different ethnicities and lifestyle habits, based on a multi-disciplinary approach, for greater scientific and cultural integration between the different shores of the Mediterranean.

For the attainment of the aims indicated above, Me.F.A.V.S. avails itself of a multicenter organization to develop didactic and research projects, exchange of educators and experts on the discipline, multidisciplinary training and multi-centers of specialists and young medical residents, exchange of clinical-assistance experience in open, endovascular and hybrid surgery, and integration of treatment therapies.



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VASCULAB, The Vascular List

Vasculab is a free-access non-profit vascular mailing list on Internet

VASCULAB was born in 1990.

Since August 2015 VASCULAB is the official mailing list of the "Fondazione Vasculab impresa sociale ONLUS".

TOPICS

Vascular Diseases Discussion List, Vascular Ultrasound Diagnosis, Vascular Biomechanics, Chiva Discussion List (Chirurgie Hemodynamique de l'Insuffisance Veineuse en Ambulatoire), Haemodynamic Venous Map (MEV), Minimal MEV, V N e t, the Model of the Venous Circulation, Micro-Circulatory Disorders,



VASCULAB RULES

1) VASCULAB is a restricted Yahoo! Message List, open only to members

2) Active participation to this List is subjected to approvation of the Moderator.

3) Accepted members, mainly people of several professions involved in the management of vascular diseases, must respect generic "Netiquette" rules (Net Etiquette), as also the specific rules and the discussion topics listed in the first message they receive from the List.

4) Topics are many, but they all are scientific ones.

5) Direct consultation with patients is not allowed.

6) Drugs or medical devices promotion is forbidden inside the messages (as also hidden in messages, e.g. mail address of companies and their web sites).

7) Outside of the messages and clearly separated from them, commercial information can be given, though generally subjected to a fee.

If these rules do not comply with you, it's better to unsubscribe. Participating actively to the discussions automatically implies the Vasculab Policy agreement.



The Vasculab Foundation



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