Interview

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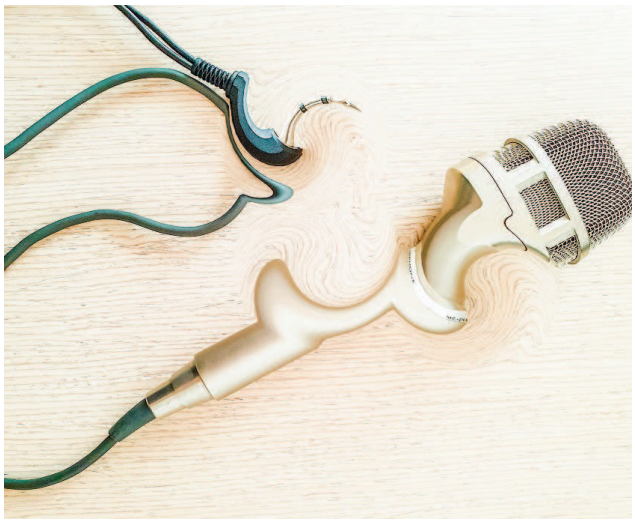
In this section, the JTAVR Editorial Team interviews an international protagonist in biomedical scientific research, to deepen unusual aspects among the current most discussed topics.



A new promise in conservative surgery

Interview with Dr Paolo Casoni

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A new protagonist appears in the phlebology scene: HIFU (High Intensity Focused Ultrasound). It is a new non-invasive thermo-ablative method to treat superficial venous reflux: an ultrasound imaging guides a focused ultrasound energy. The technology was started since 2019 (A Obermayer conceived it and M Whitely applied it widely in phlebology), but it slowed down by Covid diffusion. Nowadays, it is better established, Paolo Casoni being probably one of the most universally recognized experts in the field. The interview aims to highlight some aspect of the HIFU experience, touching some non-cleared or even debatable details. A recent article (Casoni P, et al. Phlebology 2024) stimulated a series of clinical and anecdotal questions that we asked Dr Paolo CASONI, protagonist of a therapeutic experience that allows a true "no touch" treatment on varicose veins, the maximum desire of doctors and patients. In addition, in contrast with current thinking, a conservative strategy is proposed, based on a pathophysiological conception, which is however questionable and still undemonstrated.

Question - What brought you closer to this technique: the novelty, the strategic potential, the tactical treatment solution?

Reply - Yes to all three questions, but in particular I saw the opportunity in ultrasound to be able to focus the energy on points of origin of the reflux. It has always been the dream of the conservative Phlebologist. Even HIFU was created as an alternative to thermal endovascular procedures, regarding this purpose it was not very competitive, especially with the first versions of SONOVEIN®. In fact, the ultrasound emission times were too long, i.e. to hit 2 mm of vein transversally and 3 mm longitudinally it took 4 or 8s per pulse with 30-60s of pause between one and the other. Today it takes 0.5s per pulse for at least 10s of pause.

Initially, SONOVEIN 1® took three hours to treat a 30cm GSV. Then we moved on to SONOVEIN S®, with better imaging, and with HD everything has changed. With SONOVEIN HD® for a GSV of 30 cm the time has gone to an hour and a half, target selection has become faster,

there is an additional echo connector for mapping and the spots are 0.5-1s.

For us who develop a different treatment concept[1], we are at 30 minutes for one limb and an hour maximum on two limbs.

Q - What organizational problems did you have to face?

R - To tell the truth, not many, we were followed by the company: during the installation phase of the machine, in the first 30 cases the consultants were always present, then even subsequently they always assisted us remotely, being the device a complex machine full of technical details.

We were truly pioneers in this and now they bring us visiting doctors from other countries (Lisbon, Abu Dhabi...). Although there are standard protocols for a complete ablation, we now need to better understand how to standardize our protocol to achieve a personalized therapeutic goal.

We are now at 364 cases treated.

1. ***Logistics problems***
The machine is very heavy and rather bulky, however once placed it does not cause problems, thus it is better to put it in one place and leave it fixed.
2. ***Legal Issues (authorization to apply an experimental therapy)***
No legal issue. CE approved for Europe, therefore only informed consent is necessary, furthermore for a purely private centre the documentation in the process of any dispute is simple.
3. ***Practical Problems (manual dexterity, breakages, repairs, accidents)***
It is an operator-dependent, robotic procedure, so practice is needed; then a specific anatomical and haemodynamic phlebological culture is essential; there are breakages as in all machines, however out of over 350 treatments we only had to stop once due to a fault that could not be repaired remotely; in another 3 cases , linked to simple problems, the technician intervened in real time remotely.
4. ***Specific disposable materials?***
Yes, we use a single patient device (the EPack , cooling and degassing system), consisting of a system of tubes connected to a cooling bag (passing through a refrigerator, which is the actual bulk of the machine) to keep the temperature low on the probe that emits the US. (Fig 1)

Q - Has your approach to treating venous disease changed?

R - We have been oriented towards the conservation of the saphenous heritage for many years (not CHIVA, but ASVAL); generally, we look for an interruption of the GSV above the knee, or below the perforator of DODD; with HIFU we have seen that if you have the patience to wait, varicose veins heal on their own in a high percentage of cases, being this a particular reason for interest in the method, which ultimately proved to be successful.

Q - How do you compare with previous surgical solutions?

R - If you want to replace an ablative method of any type (surgery, EVLT, RF), HIFU is penalized for execution times, at least in this phase. In USA for FDA approval they are doing a comparison study with the best current ablative thermal technique; we believe that the real step forward is precisely the conservative and non-invasive attitude, with the possibility of "welding" some reflux points or even just narrowing them! This was the real surprise. We are absolutely conservative.

Q - How did the "learning" phase take place? Was it complicated? Which difficulties did you encounter?

R - We used about twenty cases, but, I repeat, the company followed us and above all the machine evolved rapidly.

Q - When you propose HIFU, how do you explain the method to the patient? What proposal do you offer given that the result, as you write in your work, is not immediately predictable?

R - That it takes time, just tell the truth in simple words

Q - Most patients require treatment of varicose tributaries, performed in conjunction with HIFU closure/tightening. Is the effect of sclerotherapy accentuated by treatment on the venous axis, or vice versa, is axial treatment improved by sclerotherapy?

R - Absolutely yes. We have tested each approach depending on the patient and the case: Sclerotherapy simultaneous, deferred or no treatment.

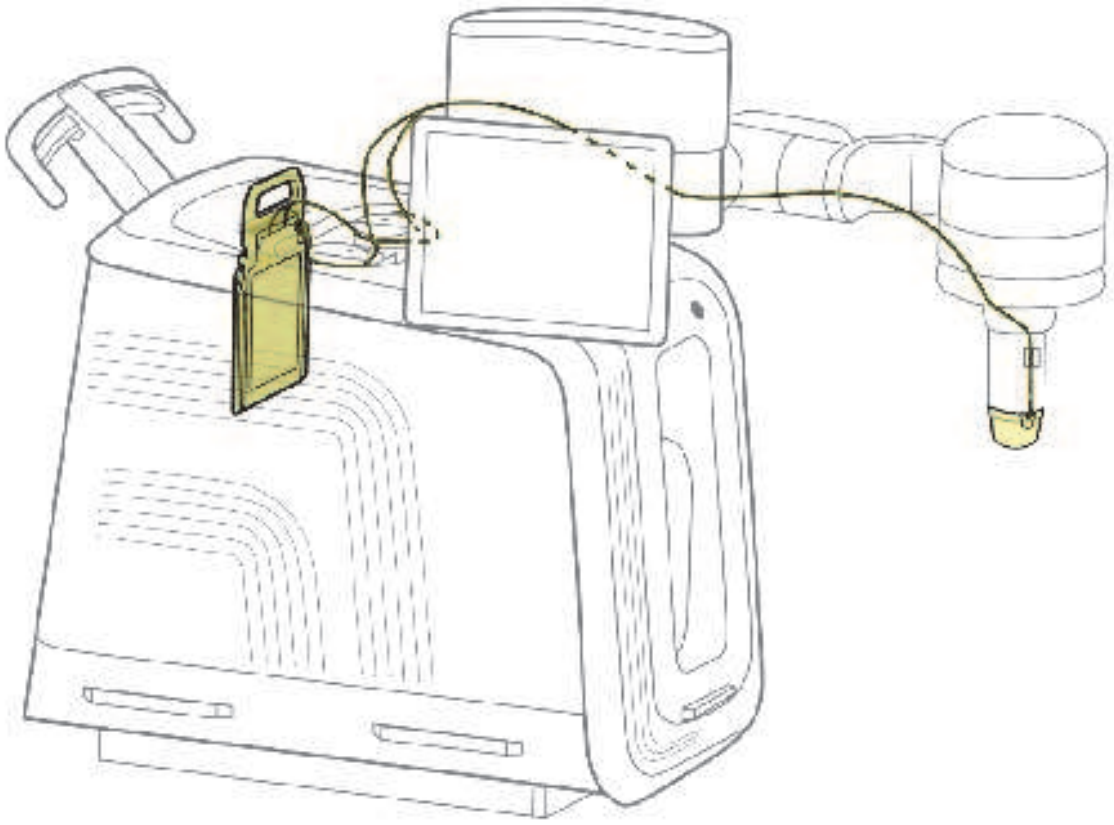

Fig 1 - The EPack (cooling and degassing system) consists of a cooler, two pumps, a disposable set of tubing and a pouch. Components: 1 Balloon - The main function of the balloon is to contain the fluid. 2 Tubes - Standard medical grade tubes, flow-in and flow-out. 3 Stopcocks - Standard medical grade tubes, flow-in and flow-out. 4 Pouch - Contains 500 ml of degassed fluid. It has four holes to fix it to the pouch holder.

In general today we prefer deferred therapy because we will be faced with varicose veins reduced in pressure and volumetric load by over 50/70%, thus reducing the concentration of sclerosing drug; in a few but significant cases, nothing was done! The venous circulation took years to develop varicose veins, so it takes months to improve once the main reflux is removed. In cases where we prefer simultaneous treatment (only in cases with large varicose veins) we use a low concentration (never more than 0.25% of polidocanol with Varixio®) which avoids any complications and, as we have seen, helps the positive evolution of the treatment.

Q - The segmental closure of a section of the saphenous vein, an effect of the treatment, corresponds to a "liquid" sclerosis. Is the possible "narrowing" effect of the saphenous vein also similar to recanalized sclerosis, or is there a difference?

R - The difference is histological. In a still limited series of cases, HIFU creates hyaline fibrosis with intact endothelium (exothermic technique); this leads to a successful "hourglass" effect from a haemodynamic point of view obtaining a narrowing: you leave a small passage instead of a large one and the reflux is reduced. The GSV, having two muscular walls, reduces in diameter on its own. A double treatment in two points, below the junction and above the knee or mid-thigh, in important GSVs, is proving to be excellent

When an occlusive effect is obtained, the vessel never reopens, at least for up to 2 years, because it is a rigid sleeve, but in reality, it has never closed; if you want to close it completely you have to add a little bit of sclerosing foam. We have seen that GSVs opened without reflux gave way to a previously innocent N3 upstream, to create a passage (hence the second treatment below the junction).

Q - When you state that HIFU "preserves the integrity of the vein wall exposed to blood flow, resulting in a 'true' restoration of the vein", you are not sending a contradictory message, since elsewhere you also state

that fibrosis is created ("denaturation characterized by a loss of microfibrillar structure and hyalinization of collagen, as well as perivascular fat necrosis and limited muscle necrosis")?

R - Exactly, but we are at such an early stage that I think an ongoing conceptual evolution is acceptable. The message is not contradictory, on the contrary it is very clear: if I intervene in a specific point of the GSV to achieve a narrowing, the proximal part of the GSV becomes continent in almost all patients. In cases of closure, the interruption of the shunt restores continence. If you create a new hourglass where there was none, less blood passes per unit of time. In reality we are still far from understanding why continence is determined and this will be a territory to be explored.

We must be very careful about the number of tributaries of the GSV near the point of action of HIFU, because in some cases we have seen a recovery as an "escape" of the reflux, precisely in those tributaries, equipped with valves, which however give in to the variation of volume/pressure, so much so that if there is a continent tributary near the site being treated, it must also be included in the same treatment. Leaving time for the spontaneous remodelling of the venous drainage is another fundamental key. But we are very much at the beginning and there is an evolution in the interpretation so that ongoing variations are the rule.

Q - From a strategic point of view, you willingly cite CHIVA and ASVAL as conservative methods, judging HIFU as such. However, these methods tend to preserve the saphenous axis, unlike HIFU. In particular, ASVAL and CHIVA II (first phase) act on the tributaries. Can a certain analogy be found? HIFU as a third way of conservation?

R - The action on the saphenous axis, in our work, is given by the fact that it is the first experience, therefore you have to deal with the saphenous vein; but we have cases of tributaries, perforators, Anterior Accessory Saphenous veins, Short Saphenous veins. A research on histology that will be published soon will be crucial to understand more.

Q - At what distance from the junction is it possible to perform the treatment? Is it possible to close the junction flush with the common femoral vein and what is the minimum length of a treated saphenous segment?

R - No, You can't get flush to the junction also because You don't need it(read randomized study over 8 years: Casoni P, et al. J Vasc Surg. 2013)[2].

You are 3/4 cm below as with any other thermal method.

At the beginning they told us to treat the entire GSV but I opposed it, explaining that I agreed to enter this game only because I believed and believe in a "curative" and not demolitive possibility. Extrapolating the concept of ligation, initially we acted on 3 cm , now we are more generous and we base ourselves on 6 cm (there are 20 slices of 3 mm) because you have a better chance of reducing the power of the reflux especially on large GVS diameters.

Q - Shrinkage can be programmed both qualitatively and quantitatively. Does this stabilize ?

R - Yes in theory, we are practically working on it, sometimes it seems like we have found the key, other times not, so there is an INDIVIDUAL RESPONSE which must be considered as a variable that is not understandable at the moment, but it will be possible over time with the intervention of AI, which will be included in the next SONOVEIN®, whose name is still not known; thus in succession: SONOVEIN 1®, SONOVEIN S®, SONOVEIN HD® (the current one), maybe SONOVEIN AI®? NEXT?

Q - How can we explain, from an anatomopathological point of view, the acquisition of continence after a narrowing of the saphenous axis? Are the valves preserved despite sclerosis? Were they observed on ultrasound? Couldn't the disappearance of reflux be due to the interruption of re-entry via sclerotherapy with a RET-type mechanism?

R - Good question and not an easy one to answer. Certainly, the haemodynamic model of shunt interruption is the answer, as in all cases in which the re-entry perforator is connected to the varix.

But we must answer why a massively incontinent saphenous axis, with an incompetent Terminal Valve, with a trunk even of 8/10 mm with significant varicose veins in the leg, shows a recovery of continence once treated in one or two points obtaining an hourglass effect: we have many similar cases. We have seen that when the reflux is very long, two "hourglass effect" points are necessary, just one is not enough. The reason is yet to be discovered, but what is seen is a spontaneous reduction in the diameter of the entire saphenous vein, even if only one or two points are treated.

Q - A thought about costs comes naturally. Of course, in the implementation phase of the method the argument is out of place, however the need for advanced technologies will always require a greater economic effort for a result that is not so different from sclerotherapy. Besides private individuals, what is the opinion of insurance companies?

R - The topic is quickly covered: nothing can compete with the costs of sclerotherapy, although our initial results are more long-lasting, as also observed by other operators. However, it is not the only method to which we must relate. "Competitiveness" must be compared with LASER, RF, MOCA, with glue and with surgery.

The costs of the device are "single patient" (only for now, because as there is no contact with blood it can also be used for multiple patients, maximum 3). Now for therapeutic protocol reasons each device is linked to the patient, and the machine records every data, but in the future it may be different. In any case, calculating that the cost of the device is the only expense (no nurse, no operating room, no consumables), the overall cost is aligned with that of all the other methods, indeed lower, even if only slightly. While in the future when we would treat 3 patients with one device, the costs will be significantly reduced. But we are talking about the future.

In Italy, insurance companies cover the cost of HIFU: the FASDAC (Healthcare Fund for Commercial Company Managers) has included HIFU among the therapeutic methods for varicose veins; the FASI (Supplementary Health Care Fund) currently reimburses HIFU, but only for diseases other than varicose veins and only in the course of oncological pathology.

Q - Have you observed cases of "non- responders" on which you have used other methods?

R - Certainly there are non-responders and we haven't understood why. In practice however, with a second treatment (about fifteen cases) or a third (only in 2 cases) the result is easily achieved. The wall becomes thick and rigid, so it is probably better prepared to accept the next ultrasonic treatment.

Q - Given the premises of the study, which are very positive, do you think we are on the threshold of a new phase in the treatment of varicose veins?

R - Absolutely. The problem is fundamentally cultural and industrial, let me explain better:

1. ***Cultural** because we need to change our way of thinking compared to the phlebology of the 80s; today we must think in terms of saving the venous heritage, of having patience and letting time help nature, if it's put in a position to restore itself; it goes without saying that such a non-aggressive and "curative" system will find the space to make its way on its own.*
2. ***Industrial** because if companies do not invest in this "particular" sector in making new machines that are increasingly performing, smaller and equally effective, then the system could die. It is not an easy marriage (science, culture and industry), but it's very stimulating.*

Note of the Editor (S Ricci)

The interview, conducted with the aim of clarifying the news related to an emerging technology, answered many of our questions. However, it also added new questions, not so much about the technique, but about the strategy, based on still non-validated concepts (hourglass effect, continence after narrowing, double narrowing, occlusion with persistence of the lumen).

Very honestly, Dr Casoni admits that he is facing a new experience which has yet to reveal its pathophysiological aspects. In the end it's the results that count, and those look very promising!

References

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