Discovering 'Biomatrix sclerofoam'

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Viscous and stable biomatrix sclerofoam seems to be a safe and effective modality to provide vein closure in great saphenous veins, according the conclusions of a presentation by Dr Johann Chris Ragg (Founder & head Of Angioclinic Vein Centers, Berlin, Germany).

Dr Ragg began by explaining that in comparison to thermo-occlusion or surgery, several studies have shown that foam sclerotherapy is inferior concerning primary and long-term results (Rasmussen LH et al. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Br J Surg. 2011;98(8):1079-87 and Van den Bos R et al. Endovenous therapies of lower extremity varicosities: a meta-analysis. J Vasc Surg. 2009;49:230–39). He explained that there are several reasons for this including that sclerofoams are very light (usually 80% gas) so they tend to float on blood and with increasing vein diameter, therefore rather than displacing blood the foam floats on it, leaving certain 'zones' untreated. In addition, sclerofoams have a low viscosity and stability - foams will collapse within 60-240 seconds and thus rapidly loose contact to the vein wall. However, he also noted that overdosage can lead to thrombosis and embolism as the sclerosant and released transmitters (like endothelin-1) appear quickly in the circulation possibly provoking systemic side effects (Frullini A et al. High production of endothelin after foam sclerotherapy: a new pathogenetic hypothesis for neurological and visual disturbances after sclerotherapy. Phlebology. 2011;26(5):203-8).

When first reports began circulating in 2008 on the deactivation of sclerosants by blood proteins, Dr Ragg and colleagues started to evaluate the interactions between heat-denatured whole blood or red blood cell-reduced fractions and liquid sclerosants. In their Zurich laboratory, they developed mixing mechanisms to prepare viscous and stable foams with an in-vitro half life of >60 min (Figure 1), yet rapidly disintegrating when arriving in streaming blood and without particles. The novel foam type - contained 20% denatured autologous blood, 40% liquid and 40% gas – and was called "biomatrix sclerofoam".

The first evaluation took place in 2015 treating the great saphenous veins. However, in order to exclude the risk of foam migration via the junction, the application was combined with a short proximal thermo-occlusion, comparing segments distal to the junction to cases with total thermo-occlusion treatment.

In total, 120 patients (78 female) with great saphenous vein insufficiency (diameters 6-24mm) who were eligible for thermo-occlusion and sclerotherapy were included in the study. Patients were randomised to two diameter-equivalent group, receiving different treatments:

- Group A (n=60) first underwent junction segment closure by endovenous laser (810nm, ball tip; or 1470nm, slim/radial fibre, PhleboCath guide catheter 2.3 mm Ø) in coaxial perivenous anesthesia with randomised varying segment lengths of 3-20cm. The biomatrix sclerofoam (using 1% Aethoxysklerol, foam volumes; 4-10ml) was applied via the guide catheter after proven proximal closure (flushing with 5ml of "foamed saline") during catheter withdrawal under continuous ultrasound monitoring, treating segments of 28–35cm in length.
- Group B (n=60) received endovenous laser for the whole insufficient vein length (38-55cm). Post-interventional examinations with standardised ultrasound were performed after two weeks and after two, six and 12 months by independent, blinded investigators.

The outcomes revealed that vein occlusion along the entire length intended to treat was obtained in all cases (120/120, visit week two) with both modalities in the first attempt. There were no adverse events, in particular no thoracic or cerebral symptoms in cases receiving sclerofoam. Cases of group A required 38-77% less treatment time than those in group B, depending on the segment length.

Interestingly, the investigators failed to discriminate modality-related intraluminal patterns of echogenicity or a borderline separating the modalities, except a few cases (n=7) where high-energy 810nm laser left typical wall bruise. Vein diameter regression was similar (+/- 12%) for laser and biomatrix sclerofoam

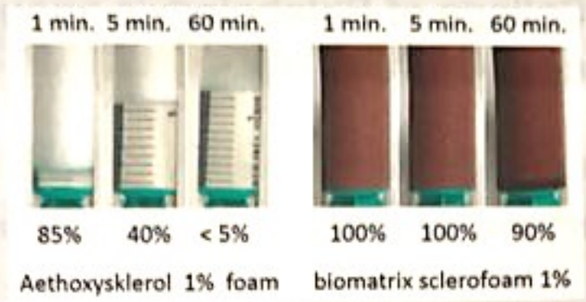

Figure 1: Stability of different foams in vitro

and both groups showed similar mild post-interventional symptoms along the treated vein segments with no detectable difference related to the methods. In group B, veins with diameters >8 mm (n=11) did not show any postinterventional symptoms.

During one-year follow-up, the laser-treated junction segments showed reperfusion in 2/60 cases (group A, 3.33%) compared 1/60 (group B, 1.6%). Failures were not related to a particular wavelength or laser tip geometry. The thigh-to-knee segments showed partial reperfusion in 5/60 cases after biomatrix sclerofoam (8.33%, sources: junction n=2, side branches n=3) and in 6/60 cases after endovenous laser (10%, sources: junction n=1, perforator veins n=3, side branches n=2).

The first clinical application of a biomatrix sclerofoam presented in this report was "surprisingly successful", said Dr Ragg, as the effect on the target vein, according to closure rates, diameter reduction and echogenicity patterns was similar to laser-induced occlusion (Figure. 2). He added that this outcome was very different from earlier experience when his colleagues compared common Aethoxysklerol sclerofoam to endovenous laser - in 2006 in a setting equivalent to this study – that showed less lumen reduction and much higher rates of failure or relapse in foam-treated segments (32% after one year), so the strategy was abandoned (Figure 3).

"To replace thermo-occlusion by a foam-based modality is not just motivated by the redundancy of tumescent anesthesia but also by the option to selectively include perforator veins and relevant side branches," he explained.

He said that his team is currently developing a temporary occluding device integrated within a guide-wire and vein lumen reduction by peri-venous injection of hyaluronan, which could potentially provide a totally symptom-free regression phase even in very large saphenous diameters

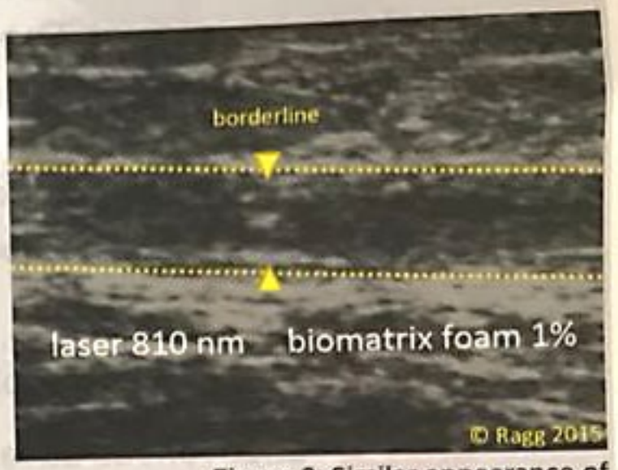

Figure 2: Similar appearance of vein occlusions by 810 nm laser and biomatrix sclerofoam

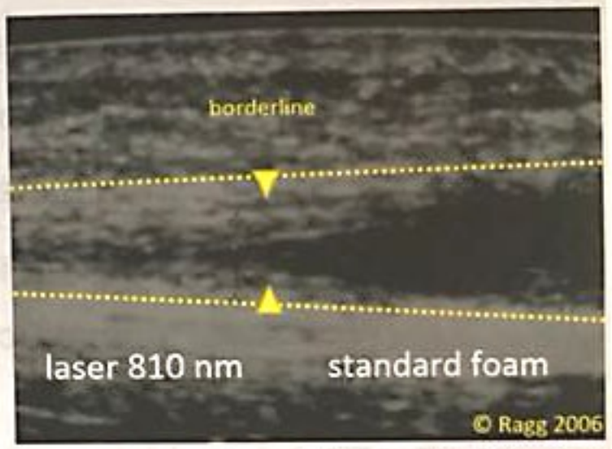

Figure 3: Inferiority of standard Aethoxysklerol foam compared to 810 nm laser: Less diameter reduction, lower echogenicity indicating soft thrombus (study 2006)

(>15mm diameter), competing with vein gluing.

Dr Ragg added that future applications of the novel biomatrix foam (after availability of commercial catheter-attached foam generators) will include saphenous veins of all diameters, large recurrent varicosities, abdominal varices, varicoceles and maybe even low-flow vascular malformations, skipping expensive coils.

"According to these first results, viscous and stable biomatrix sclerofoam seems to be a safe and effective modality to provide vein closure," Dr Ragg concluded. "The primary and one-year results are similar to endovenous laser, apart from the excluded junction segment. Future studies will include biomatrix sclerofoam application in the saphenous junction (stand-alone), with temporary or permanent blocking devices and hyaluronan vein compression, and comparison to common foam sclerosants."