LETTER TO THE EDITOR

Re. "Comments to: Histological and Immunofluorescent Analysis of the Large Tributary of the Great Saphenous Vein Treated With a 1920 nm Endovenous Laser: Preliminary Findings"

I would like to thank Justyna Wilczko and her colleagues for their interest and comments on our work.[1,2]

With regard to the comment about vein diameter, this is of only secondary importance to the thickness of the vein wall. Ever since I proposed the idea that successful ablation needed transmural vein wall cell death in 2004,[3] and suggested that leaving a "living vein wall skeleton" of media and adventitia would allow recanalisation,[4] we have been looking at how the processes of thermal ablation and chemical ablation affect the vein wall.[2,5]

In a series of three papers, we have shown that by modelling thermal spread from an endovenous thermal ablation device in porcine liver,[6] confirming the findings in an *ex vivo* vein can then lead to 100% ablation in the clinical setting at one year.[7,8]

Thus, the diameter of a vein alone is only useful if it relates to the thickness of the vein wall at treatment. To put it simply, if you are going to cook a chicken, measuring the size of the internal cavity is a lot less useful than knowing the mass of meat being cooked.

With regard to the comment about the tumescence, this was included in our discussion. Just before treatment we had put tumescence solution onto the vein, which included adrenaline. Unfortunately, this was omitted from the Methods section in the final draft. However, even *in vivo*, not all veins constrict concentrically, with some giving a "smile sign" on ultrasound before treatment.[9] As subsequent publications on this model will show, it still gives very useful information when used with radial fibres and radiofrequency devices. With regard to the comparison between 1920 mm and 1470 nm lasers, although the comment may appear speculative in the light of the data presented in this study, it is based upon great experience of using 1470 nm endovenous laser in this model. Further papers in this series will elucidate this further.

We thank the authors of the letter for pointing out our lack of clarity in the conclusion, as written in the body of the text. Our conclusion in the abstract is somewhat clearer and owing to word count constraints we failed to make sure this was as clear in the paper. As thermal damage increases, the cells are not damaged at very low energies, and then as the energy increases they first undergo delayed cell death (apoptosis) and then, at even higher energies, undergo coagulative necrosis.

Thus, the progression of effect with endovenous thermal ablation is an undamaged vein wall at low energies, apoptotic markers in the endothelium and inner media as the energy increases and then as the energy increases further, coagulative necrosis (with no expression of apoptotic markers) in the innermost layers with apoptotic markers showing further out. If the energy is sufficient, the coagulative necrosis would be transmural and no apoptotic markers would be seen at all.

The importance of this observation is that histology of the vein wall, which only shows the coagulative necrosis and thermal damage to surrounding proteins and other structural elements, fails to show apoptotic markers and hence underestimates the damage profile from the thermal ablation.

Finally, this study did not set out to answer whether one should use 1920 nm or 1470 nm lasers, but merely to see if we could find any evidence that the 1920 nm laser had any advantages at a biological level over the 1470 nm laser. We have not found any difference between the effects on the vein wall with the two wavelengths.

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DOI of original article: https://doi.org/10.1016/j.ejvssr.2018.09.004.

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Mark S. Whiteley
Whiteley Clinics, 1 Stirling House, Stirling Road, Guildford, GU2 7RF, United Kingdom
Email-address: mark.whiteley@whiteleyclinics.co.uk

https://doi.org/10.1016/j.ejvssr.2018.10.005
DOI of original article: https://doi.org/10.1016/j.ejvssr.2018.09.004