

## Research Article

# Histopathological findings of the human great saphenous vein treated with endoluminal radio frequency ablation

Harinder Singh Bedi<sup>1\*</sup>, Nalini Calton<sup>2</sup>, Kanwardeep Singh Kwatra<sup>2</sup>, Vivek Tewarson<sup>1</sup>

<sup>1</sup>Department of Cardiovascular Endovascular and Thoracic Surgery, Christian Medical College & Hospital, Ludhiana, Punjab, India

<sup>2</sup>Department of Pathology, Christian Medical College & Hospital, Ludhiana, Punjab, India

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### \*Correspondence:

Dr. Harinder Singh Bedi,

E-mail: drhsbedicmc@gmail.com

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## ABSTRACT

**Background:** There is not much data on the histopathologic effect of Radio Frequency Ablation (RFA) on the human vein. In order to better understand the exact mechanism and sites of action of the device we studied in detail the histological changes in the vessel wall of the Great Saphenous Vein (GSV) after it was subjected to RFA.

**Methods:** We studied the effect of RFA on 5 pieces of the human GSV from 5 different patients. The harvested vein was subjected to radiofrequency ablation and then studied in detail by histopathology.

**Results:** On gross inspection immediately during the radiofrequency application, the vein shrunk lengthwise and in diameter with marked narrowing of the lumen and charring. On histopathology the vein showed a photo-disruption in the form of total loss of endothelium. There was a sub-endothelial hematoma with small haemorrhages in the muscle coat and thermal coagulation of smooth muscle. The thermal effect was pan-mural and extending up to the adventitia.

**Conclusion:** Our findings have implications for a better understanding of the mechanism of the action of radiofrequency on the venous system and for further improvements in technique and hardware to improve efficacy and reduce the side effects during endovenous therapy for varicose veins.

**Keywords:** Great saphenous vein, Radio frequency ablation, Endovenous therapy, Varicose veins

## INTRODUCTION

The surgical treatment of varicose veins has undergone many modifications from the open stripping technique to minimally invasive procedures.<sup>1</sup> One of the accepted modalities of therapy today is radio frequency ablation (RFA) with an endovenous technique.<sup>1</sup> The VNUS closure fast radiofrequency system (Coveidien, San Jose, CA, USA) comprising a generator and a bipolar catheter was developed as a minimally invasive technique using radiofrequency to generate heat which causes coagulation of the vessel wall and hence ablation. Despite widespread use of this device (the RFA technique was approved by the FDA in 1999<sup>1</sup>) very little is published regarding the detailed histopathological effects of radiofrequency on

the human vein. In order to better understand the exact mechanism and sites of action of the device we studied in detail the histological changes in the vessel wall of a Great Saphenous Vein (GSV) after it was subjected to radiofrequency ablation.

## METHODS

The study was done on five pieces of human saphenous vein. Three were 15-17 cm long segments of great saphenous vein (GSV) which were harvested in three patients undergoing coronary artery bypass grafting (CABG). The vein was not used as after sternotomy the aorta was found to be calcified and so the right internal mammary artery was harvested instead of the GSV (to

avoid clamping the aorta). Such a vein is usually discarded. The study was done within one hour of removal of the vein and storage of the vein in body temperature (37°C) blood-isotonic saline solution. The vein was flushed with body temperature normal saline before being subjected to the RFA. The rest (two) were 8-9 cm pieces of varicose GSV removed in one piece by phlebectomy from the medial aspect of the calf in two different patients. These segments were also flushed with body temperature normal saline. A 2 cm piece of vein was removed from one end of all the 5 veins and subjected to histopathology to serve as control.

The 5 veins were now subjected to RFA. The RFA procedure used was the same in all segments. The radio frequency catheter of the closure fast system of VNUS medical technologies was inserted into the lumen of the vein, covered with warm packs (body temperature) and the sequence of radiofrequency delivery initiated. One delivery of radiofrequency was given at one site as per the machine fixed specifications (temperature at 120°C for 3-5 seconds, allowed to cool to 50°C, then the probe was pulled by 7 cm and the procedure repeated i.e. same as done in vivo). The whole procedure was photo-documented. The RFA treated specimen was then transferred to 10% buffered formalin and subjected to histopathological examination. After routine paraffin tissue processing, 5 µ thick sections were cut and stained with hematoxylin and eosin, orcein elastic and Masson's trichrome stain.

## RESULTS

On gross inspection - macroscopically - immediately during the radiofrequency application, the vein shrunk lengthwise and in diameter with marked narrowing of the lumen. There was visible charring but no perforation (Figure 1). The heat did not apparently go beyond the vein as the packs just outside the vein did not show any charring. The vein was histologically examined at different levels under magnification and showed vein wall injury. The vessel showed a photo-disruption in the form of total loss of endothelium. There was a sub-endothelial hematoma with small hemorrhages in the muscle coat (Figure 2). The smooth muscles showed thermal coagulation effect in the form of waxy homogenized eosinophilic cytoplasm and hyperchromatic condensed nuclei (Figure 3).

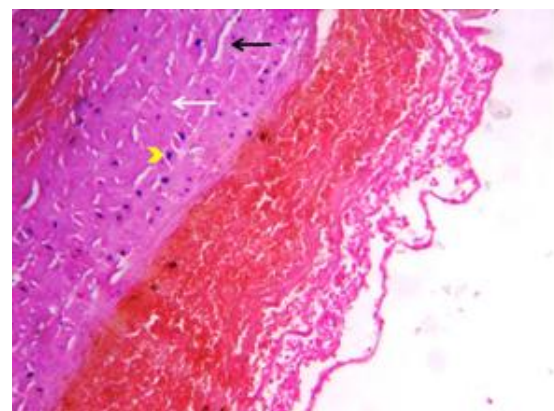
The thermal effect was pan-mural and extending up to the adventitia. Small cleft like spaces also appeared in the media. Masson's trichrome showed altered staining, probably due to alteration of tissue porosity induced by the heat. In some areas there was a total disruption of all layers of the vein wall after RFA. There was no difference in the damage seen in the five separate segments of vein (3 - a normal GSV, and 2 - a varicose GSV removed by phlebectomy). None of the changes of thermal damage were seen in any of the 2 cm pieces of vein removed before the RFA.



**Figure 1: The macroscopic appearance of the great saphenous vein (GSV) showing areas of charring (C) after RFA. RF = radio frequency catheter.**



**Figure 2: Hematoxylin & eosin 200X, showing sub-endothelial hematoma (black arrow), and hemorrhage in the media (white star).**



**Figure 3: Hematoxylin & eosin 400X, shows clefts in media (black arrow), coagulated smooth muscle cytoplasm (white arrow) and condensed nuclei (yellow arrowhead).**

## DISCUSSION

The principal finding of this study was that the VNUS technique produces extensive thermal injury to the entire thickness of vessel wall. This subsequently leads to sclerosis and occlusion of the vessel. Experimental studies in animal models with endovenous radiofrequency have demonstrated similar thermal coagulation effect.<sup>2</sup> There is only one study of the effect of heat on the human vein. This was with the use of the diode laser.<sup>3</sup> This study relied on indirect assessment in the form of D Dimer assays and histopathology was done in only one vein and that too a vein which was removed (after laser therapy) by stripping - which added its own variable of trauma. A study comparing endovenous laser with radiofrequency in goat jugular vein have shown a higher incidence of perforation with the former, especially in the region close to the fiber tip.<sup>4</sup> Schmedt et al. studied the effect on cow vein by laser and RFA and found large variations in thermal damage after laser as opposed to RFA.

We believe our study is the first studying the detailed histopathological effect of RFA on the human vein. The VNUS technique is very extensive - it affects the entire thickness of the wall unlike sclerotherapy which acts only on the intima. The demonstration of the denaturation of the media is proof of the penetration of the heat into the vessel wall and can be confirmed by the evidence of decrease in the lumen of the vessel as seen on ultrasound Doppler. The heat energy triggers the process of sclerosing the vessel wall. The VNUS technique of endothelial ablation for varicose veins is a safe and easy method for treatment of varicose veins. It provides uniform and smooth all-over ablation of the entire vessel wall with minimal collateral damage.

Our findings can help us: (a) to get a better understanding of the endovascular effect of RFA on the vein, (b) to identify histologically the areas of thermal damage to the vein (c) to use this information for possible

improvements and to further fine tune the radio frequency techniques and hardware - e.g. dose, duration, what material to use on the tip etc., (d) to guide us in ways to avoid trauma to adjoining tissue and to adjacent nerves (lengthwise shrinkage of the vein could pull on the nerve besides causing thermal injury), (e) to correlate the histopathological changes to the pain produced and efficacy and recurrence rate, (f) to repeat a similar study with other modalities of ablations e.g. laser, steam etc. and (g) it could be a gold standard to judge other techniques against.

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