The Functional Characteristics of Normal Venous Perforators as Observed with Duplex Ultrasound

Brigid Geraldine Hill

A Thesis submitted for the degree of Masters of Health Science

University of Otago/ Te Whare Wananga o Otago

Dunedin/ Otepoti

Aotearoa New Zealand

March 2011
Abstract

Varicose veins are an extremely common condition, with significant challenges in regard to the best approach to the management of incompetent venous perforators. In order to better understand the role of the venous perforator in venous disease, we set out to understand how venous perforators function in a normal population.

Venous perforators were examined using duplex ultrasound in twenty healthy volunteers with normal venous function. The diameter, distribution, and communication of all lower limb perforators was assessed. This was followed by a more detailed assessment of the perforators along the tibial and paratibial region of the medial calf. Participants were examined in three different positions to further assess changes in function. The anatomical appearance of the perforator was also investigated, particularly the communications between compartments, as was the ability to detect perforator valves using high-resolution ultrasound.

The effect of venous surgery on perforator distribution and recurrence rates over a three-year time period was also studied based on ultrasound findings. A comparison was made between the normal and diseased population with regard to regional distribution, diameter and communication of the perforators.

Resin casts were made of normal venous systems of the medial calf and the perforator characteristics examined and compared with ultrasound findings.

The study found that the diameter of the medial calf perforator in the gaiter region to be the most significant amongst normal subjects. The medial calf was found to have no obvious
difference in relation to venous blood velocities on distal augmentation in the standing position when compared to a planter flexion / isometric contraction. Neovasculization occurred in surgical ligated venous perforators. Resin casts of perforators more clearly demonstrate the presence of valves and multiple channels.

The perforators between the superficial and deep compartments of the venous system of the lower leg remain difficult to truly understand. The distal medial calf perforators in the normal population had a larger diameter, greater blood flow and higher velocities suggesting that these perforators may exist in a more demanding environment and be more susceptible to failure. They may play a key role in maintaining normal venous function. Incompetence in this region could be of a greater significance in a diseased population.

While some valves were identified on duplex ultrasound, resin casting demonstrated the presence of valves in all perforators of the medial calf. This provided a cautionary message as to the limitations of even the best in diagnostic ultrasound.
Acknowledgements

I would like to take this opportunity to thank a number of people who played an important part in the thesis.

My Supervisors:
Professor A.M. van Rij, without whose constant encouragement, support, critical mind and enthusiasm, this thesis would not be possible. If I gained within my career the same hunger for knowledge and desire to advance the venous cause then I will have only my Professor to thank.

Associate Professor Greg Jones, for his wonderful Histology and Resin casts. These casts have helped to link the whole project together. They have amazed us all in their detail of the venous perforator and intricacies of the venous system.

To Josie Macfarlane who also helped in the immense task of the venous longitudinal study and all those many perforators. She has been a wonderful
support and great encouragement. Josie thanks for all those many interesting
talks on venous perforators.

To my team within the Vascular Laboratory, Ms. Kate Thomas, Mr. Riordan
Dickson, Mrs. Judy Norrish, Mrs. Sarah Watts, Ms. Maria Jenkins, Mr. Matt
Verstegg and Ms. Julia Sinclair for all their support. Thank you all- it’s a
pleasure to both know you and work with you.

Ms. Denice Whiunui for your reading of this thesis and to Megan Drysdale for
Statistics support.

To my dear friend Jenny McCullum, thank you for your kindness, friendship
and support over these past months.

To my husband Ken and daughter Meghan, thank you for everything, no words
would ever be enough to express my gratitude.
# Table of Contents

1 Introduction ......................................................................................................................... 1

1.1 Role of the fascia in perforator function ......................................................................... 8

1.2 Anatomy of the perforator vein wall ................................................................................ 9

1.3 Venous Physiology .......................................................................................................... 10

1.4 The Physiology of the Perforator ................................................................................... 12

1.5 Investigations of the Venous System .............................................................................. 13

1.5.1 Phlebogram .............................................................................................................. 13

1.5.2 Computer Tomography and Magnetic Resonance Imaging .................................... 14

1.5.3 Ambulatory Venous Pressure (AVP) ........................................................................ 14

1.5.4 Non-invasive Plethysmography .............................................................................. 14

1.5.5 Ultrasound ............................................................................................................... 16

2 General Methodologies for Clinical Studies ..................................................................... 22

2.1 Ultrasound Imaging and Quantitative Measurements .................................................. 22

2.2 Ultrasound Examination Protocol for all Study Groups .............................................. 23

2.2.1 Ultrasound Criteria for Venous Assessment ............................................................. 23

2.2.2 Distal Augmentation ............................................................................................... 26

2.2.3 Valsalva Maneuver ............................................................................................... 27

2.2.4 The Research Subjects .......................................................................................... 27

2.2.5 Ethical Approval .................................................................................................... 27

2.2.6 Data Security and Privacy of the Participants ......................................................... 28

3 The Distribution of Venous Perforators in Normal Subjects .......................................... 29

3.1 Methods ......................................................................................................................... 29

3.1.1 Research Subjects ................................................................................................. 29

3.1.2 Results .................................................................................................................... 30

3.1.3 Perforators and their Superficial Communications .................................................. 31
3.1.4  Perforators and Deep Venous Communications ......................................................... 32
3.1.5  Discussion .................................................................................................................. 33

4  A Detailed Examination of the Medial Calf Perforators in Normal Subjects...... 36

4.1  Methods.......................................................................................................................... 36
    4.1.1  Medial Calf Perforator Identification ........................................................................ 36
    4.1.2  Quantification of Venous Perforator Blood Flow .................................................... 37
    4.1.3  Peak Venous Velocity Flow ....................................................................................... 37
    4.1.4  The Participants Examination Position ....................................................................... 38
    4.1.5  Distal Augmentation via a Foot Stimulus ................................................................. 39
    4.1.6  Exercise effect on medial calf perforators ............................................................... 39
    4.1.7  Isometric Planter Flexion Test .................................................................................. 40

4.2  Results ............................................................................................................................ 41
    4.2.1  Perforator Diameters of the Medial Calf ................................................................. 41
    4.2.2  Vertical Zones .......................................................................................................... 43
    4.2.3  Direct Vs Indirect Venous Perforators ..................................................................... 43
    4.2.4  Valves Identification of Perforator valves by duplex ultrasound ............................. 46
    4.2.5  Perforator Peak Systolic Velocity (PSV) ................................................................. 47
    4.2.6  Peak Venous Flow (PVF) ......................................................................................... 48
    4.2.7  Direct Vs Indirect Peak Velocity Flows ................................................................. 49
    4.2.8  Spontaneous Perforator Blood Flow ...................................................................... 50
    4.2.9  Exercise Effect on Spontaneous Flow and Flow Pattern ....................................... 51
    4.2.10 Isometric Planter Flexion Effects .......................................................................... 52
    4.2.11 Spectral Doppler Pattern Type On Distal Augmentation ....................................... 54

4.3  Discussion ....................................................................................................................... 58

5  The Fate of Venous Perforators following Varicose Vein Surgery .................. 61

5.1  Method............................................................................................................................. 61
    5.1.1  Patient assessments................................................................................................. 62
List of Tables

Table 1.1 Normal distribution of venous valve numbers within the superficial and deep venous system of the lower limb. ................................................................. 4

Table 3.1 Regional Perforator Location and Diameter (mm). .................................................. 31

Table 4.1 Medial Calf Perforator Diameter (mm) in Males and Females ................................ 42

Table 4.2 Medial Calf Perforator Diameter (mm) by Zone as seen on Ultrasound. ................ 43

Table 4.3 Medial Calf Perforator Diameters (mm), Direct and Indirect. .............................. 43

Table 4.4 Distribution of the Direct and Indirect Perforators when Split by Zones along the Medial Calf 44

Table 4.5 Ultrasound B-mode Finding of Venous Perforators With and Without Valves. ........ 46

Table 4.6 Diameter (mm) of Perforators with and without Valves ...................................... 46

Table 4.7 Peak Systolic Velocity (cm/s) in Medial Calf Perforators in Different Positions .......... 48

Table 4.8 Peak Systolic Velocity (PSV) cm/s in Medial Calf Perforators in Different Zones .... 48

Table 4.9 Peak Venous Blood Flow (mL/min) through the Perforators following a Distal Augmentation. 49

Table 4.10 Peak Venous Blood Flow (mL/min) in Medial Calf Perforators in Different Zones . 49

Table 4.11 Peak Venous Flow (mL/min) when Comparing Direct and Indirect Perforators. .. 50

Table 4.12 Proportion of Perforators with Spontaneous Flow in the Medial Calf at Rest ........ 50

Table 4.13 Spontaneous Blood Velocity (cm/s) in the Medial Calf Perforators of Normal Limbs Pre Exercise Split by Zone ................................................................. 51

Table 4.14 Spontaneous Blood Flows (cm/s) in the Medial Calf Perforators of Normal Limbs following Exercise Split by Zones .................................................. 51

Table 4.15 Percentage of Spontaneous Flows seen to Perforators following Exercise along the medial calf. 52

Table 4.16 Pre and Post Exercise Spontaneous Perforator Velocities (cm/s) of the medial calf 52

Table 4.17 Comparing PSV (cm/s) on Planter Flexion to a Standing Distal Augmentation. .......... 53

Table 4.18 Spectral Doppler Pattern Types following Distal Augmentation in Different Positions 55

Table 4.19 Spectral Doppler Compared to Diameter (mm) .................................................... 57

Table 4.20 Spectral Doppler Pattern Types Compared to Peak Systolic Velocity (cm/s) ........ 57

Table 5.1 Comparison of Limbs Preoperatively to Limbs with and without Incompetent Perforators Three Years Following Surgery. ........................................... 64

Table 5.2 Comparison of Disease Severity in Limbs with Six or more Incompetent Perforators Preoperatively to Limbs with less than Six Incompetent Perforators. ............. 65
<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3</td>
<td>Comparison of Diameter among Perforator Types preoperatively and at Three Years.</td>
</tr>
<tr>
<td>5.4</td>
<td>The Progression of Incompetent Perforators in 155 Limbs.</td>
</tr>
<tr>
<td>6.1</td>
<td>Average Number of Perforators Per Limb Across Three Groups</td>
</tr>
<tr>
<td>6.2</td>
<td>Total Number of Perforators, their Diameters (mm) as Observed Between Groups</td>
</tr>
<tr>
<td>6.3</td>
<td>Regional Distribution of Normal Perforators Across Three Groups.</td>
</tr>
<tr>
<td>6.4</td>
<td>Normal Perforator Diameters (mm) in Three different Venous Populations and their Season Effects.</td>
</tr>
<tr>
<td>7.1</td>
<td>Ultrasound-derived Perforator Diameters Prior to Surgical Amputation.</td>
</tr>
<tr>
<td>7.2</td>
<td>Perforators and Valves Detected by B-mode Ultrasound Prior to Amputation.</td>
</tr>
<tr>
<td>7.3</td>
<td>Perforators and Valves Detected in Resin Casts Post Maceration.</td>
</tr>
</tbody>
</table>
List of Figures

Figure 1.1 Gross anatomy showing a cross-sectional image of the GSV within the superficial compartment...9
Figure 1.2 Gross anatomy of a venous perforator within the lower limb. ......................................................... 10
Figure 1.3 Calf muscle pump pressure profile observed within deep and superficial veins .............................. 12
Figure 1.4 B-Mode image of a medial calf venous perforator ........................................................................ 18
Figure 1.5 Colour and Spectral Doppler image of a perforating vein ............................................................. 20
Figure 2.1 B-Mode Ultrasonographic Image of a Venous Perforator Crossing the Fascia Plane. ....................... 24
Figure 2.2 Spectral Doppler Ultrasonographic Image demonstrates Venous Flow Direction .......................... 25
Figure 3.1 Regional Distribution and Diameters (mm) of Perforators within a Normal Population of Rt. Lower Limb ........................................................................................................................................ 31
Figure 3.2 The Percentage of Perforator Communication with the Superficial Compartment of the Lower Limb of Normal Subjects. Great Saphenous vein (GSV) Accessory GSV (AGSV); Lateral Superficial Vein (LSV), Short Saphenous Vein (SSV) & Thigh GSV ........................................................................................................................................... 32
Figure 3.3 Percentage and Number of Perforator Communication with the Deep Venous Compartment ......... 33
Figure 4.1 Medial Calf Perforator Diameters (mm) Split by Gender ................................................................. 42
Figure 4.2 Venous Perforator Anatomy - Tissue Cross Section. (a) Indirect perforator (b) Direct Perforator. 45
Figure 4.3 B-Mode Ultrasonographic Image Demonstrates a Venous Perforator and the Edge of a Valve Leaflet to the Perforator Lumen ........................................................................................................................................ 47
Figure 4.4 Average Peak Systolic Velocity (cm/s) Detected in Medial Calf Perforators following Distal Augmentation in Different Positions and Split by Zone .............................................................. 48
Figure 4.5 Venous Blood Flow (mL/min) in the Different Positions and when split into Zones ........................ 49
Figure 4.6 Spectral Doppler Ultrasonographic Image demonstrating Spontaneous Flow in a Venous Perforator at Rest from Superficial to Deep Compartment .................................................................................................................. 50
Figure 4.7 Example of a Spontaneous Perforator following Exercise ............................................................. 52
Figure 4.8 Spectral Doppler Venous Perforator Response during Planter Flexion in a Standing Position ....... 53
Figure 4.9 Pearson Correlation of PSV (cm/s) during Planter Flexion Compared with Distal Augmentation on Standing ........................................................................................................................................... 54
Figure 4.10 Spectral Doppler Pattern Types from Perforators along the Medial Calf on Distal Augmentation. ......................................................................................................................................................... 56

Figure 6.1 Regional Distribution and Mean Diameter (mm) of Competent Perforators Compared by Groups 78
Figure 6.2 Superficial Normal Perforator Communication Over Three Different Population Groups............ 80

Figure 6.3 Normal Deep Communication and the Venous Perforator across Three Population Groups........ 82

Figure 7.1 A Below Knee Amputated Limb with a Medial Calf Outline of the Great Saphenous Vein (GSV). .... 89

Figure 7.2 Dissected Area of Tissue Along the Course of the Great Saphenous Vein (GSV)......................... 89

Figure 7.3 Tissue Dissection of a More Extensive Superficial Vein Network.................................................. 90

Figure 7.4 Partial Tissue Maceration of a Perforator (arrowhead)................................................................. 90

Figure 7.5 B-Mode Image of a Venous Perforator with Two Distinct Valves Observed Deep to the Fascia..... 93

Figure 7.6 Resin Cast of Both the Great Saphenous Vein(GSV) and the Posterior Tibial Vein (PTV).............. 94
Chapter 1:

1 Introduction

Varicose veins are an extremely common condition\(^1\). They continue to be a significant problem in health care management. It is well recognized that chronic venous insufficiency (CVI), which results from varicose veins, can lead to venous ulceration in the lower limb\(^2,3\).

Over the centuries varicose veins have created many questions when it comes to optimal management, not only what is the most effective means of dealing with this problem; but also, how the high levels of recurrence of varicose veins following treatment be avoided. This includes determining the role of treating venous perforators which contribute to varicose veins\(^4\).

The beginning of our understanding of the venous system goes back a long time. In 1452, Leonardo de Vinci sketched images of veins of both upper and lower limbs. However, the growth of knowledge of the function of the venous system has been slow to advance. In more recent times there has been a resurgence in research towards bettering our understanding of the venous system and the causes of both varicose veins and CVI\(^5,6\). This includes sorting out the problem of the venous perforators and their role \(^4\).

One of the dilemmas, for example, is that surgical ligation of incompetent perforating veins (IPV) has been reported to offer long-term positive results in managing varicose veins and venous ulcers\(^7,8\). Numerous descriptions of perforators have been recorded in the surgical literature for more than a century as a guide for surgical procedures on how to best ligate them\(^9\). However Akesson et al and Stuart et al, had demonstrated that with the correction of saphenous reflux alone, without ligation of any incompetent perforators at the time of surgery, would result in the once incompetent perforators reverting back to normal function without causing any further problem\(^10,11\). Others have found incompetent perforators not ligated at the time of surgery would continue to remain incompetent and again play a significant role in
varicose veins recurrence\textsuperscript{[12]}. Our own work showed that despite ligation of only large incompetent perforators the remaining residual smaller incompetent perforators did not disappear but rather the number of incompetent perforators increased\textsuperscript{[4]} \textsuperscript{[4]}. Even the quite extensive subfascial ligation procedures of the past, such as that described by Linton and Cockett were associated with recurrence of perforators \textsuperscript{[13, 14]}. The cause for this recurrence of perforators could be the result of a number of possibilities including, the previously competent perforators becoming incompetent, the appearance of missed incompetent perforators at initial diagnosis or during surgical treatment, and even new reconnections of these perforators by neovascularisation\textsuperscript{[15]}.

The perforating veins are the focus of this thesis. These perforating veins course between the superficial and deep venous compartments of the lower limb\textsuperscript{[16, 17]} \textsuperscript{[16, 17]}. The earliest description of the perforating vein of the lower limb was given by von Loder in 1803, however little had advanced for a significant time period\textsuperscript{[13]} \textsuperscript{[13]}. In 1855 Verneuil described the presence of the perforator veins connecting the superficial veins to the deep venous system and stated they had valves within their lumens, their function was to facilitate the flow of blood and to also prevent blood flowing outward from the deep venous compartment toward that of the superficial compartment. There are said to be over 150 perforators in the lower limb however most significance has been placed on those that are located on the medial aspect of the leg and particularly that of the calf region \textsuperscript{[13, 18, 19]} \textsuperscript{[13, 18, 19]}, probably because the distribution of incompetent perforating veins (IPV) is predominantly located within the medial calf \textsuperscript{[20, 21]} \textsuperscript{[20, 21]}. Cockett noted that the lower third of the medial calf was the most important\textsuperscript{[14]} \textsuperscript{[14]}. Linton also showed that 80 – 90\% of cases of perforators within this medial calf (gaiter region) also had poor surrounding muscle content and therefore lacked structural support\textsuperscript{[14]} \textsuperscript{[14]}. It was felt that this lack of muscular structure contributed to the incompetent perforator placing extra stress upon the surrounding tissue and resulting ulceration.
Perforators are known to be of two types, those that directly enter the deep veins, which account for over half of those identified. The other being the indirect perforator with a course via a muscle group prior to joining the deep axial venous system\cite{14, 19}. Perforators are also located in the foot however they are known to have bi-directional flow and are devoid of valves. They were not examined in this thesis and therefore will not be referred to again. Another feature in at least some perforators is the presence of valves. Valves were first written about in 1547 by Fallopius who stated that Canano had described the presence of what was referred to as valve like folds in the azygos vein within the abdominal cavity. However these valve like folds were not observed by others; and later when Vesalius was unable to locate these valvular folds within the anatomical dissection of the vein; it was concluded that none were present and so the venous valve was dismissed and considered nonexistent for many years. Then during a public dissection in 1579, Hieronymus Fabricius showed the presence of a venous valve in the flesh. Fabricius became convinced that the venous valves played an important role in the prevention of retrograde blood flow down the limb. The once elusive valve was again in the limelight. Then in 1585 Saloman Alberti became the first person to show a drawing of the valve leaflet within the vein. Fabricius also concluded that blood flow within the venous system of the lower limb should be in an antegrade direction, back toward the heart. The greatest of all vascular discovery, was when William Harvey in 1628, showed in the animal model how the circulation of blood occurred. He then showed in the human model that the presence of valves within the vein allowed only the unidirectional flow of the blood, back toward the heart\cite{14}. The venous system, having to contest with gravity, required the veins to have along their course a number of valve leaflets to control firstly the direction of blood flow and also to ensure the regulation of venous pressure within the distal veins, especially in the lower limb\cite{22-25}.

Lurie in 2002 demonstrated through the use of ultrasound how the venous valves behave in cycle like phases, depending on the position of the body. In the standing position, the valves
appear to open and close in a rhythmic behavior, at a rate of approximately eighteen to twenty cycles per minute and match that of the respiratory cycle. In the supine position the rate of valve cycling was noted at approximately 34 to 36 cycles per minute. In this position the valve appeared to be influenced by both the respiratory and cardiac cycles[26-29].

The venous valves are covered with a single layer of endothelial cells over a thin intima, covering a reinforcing core of connective tissue and usually with a bicuspid leaflet shape. The valve is extremely strong and more elastic than the vein wall. The locations of valves are more concentrated toward the distal end of the limb when compared to the femoral vessels[30].

Table 1.1 Normal distribution of venous valve numbers within the superficial and deep venous system of the lower limb.

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Number of Valves</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC</td>
<td>None</td>
</tr>
<tr>
<td>CIV</td>
<td>None</td>
</tr>
<tr>
<td>EIV</td>
<td>1 valve</td>
</tr>
<tr>
<td>CFV</td>
<td>1 valve</td>
</tr>
<tr>
<td>FV</td>
<td>1 – 4 valves</td>
</tr>
<tr>
<td>Popliteal v.</td>
<td>1 valve</td>
</tr>
<tr>
<td>GSV</td>
<td>2 – 13 valves</td>
</tr>
<tr>
<td>SSV</td>
<td>1 – 12 valves</td>
</tr>
</tbody>
</table>

*Based on number of valve found in cadaver studies[31, 32].*

There was also a widely held belief that veins with a diameter of less than 2mm, were devoid of venous valves[33, 34]. Nicholas Popoff in 1934 through his work on cadaveric dissection showed that veins with diameters of less than or equal to 2 mm had valves. He demonstrated this within small caliber superficial veins[35]. Even though Popoff was referring to the superficial venous system, the fact remains that since many perforating veins fall within this diameter range, his research asserted that it is possible that perforators could also have valves. The ability to identify the presence of valves within the venous system throughout different
areas of the body has been confirmed [31, 32, 35-38]. However the stance on the venous perforator and venous valve still remain confusing. This confusion ranges from the view that perforators may not always have valves, to the view that they all do but their function varies depending on the valve location within the perforator.

Work by Linton in 1938 described the functional understanding of perforators and asserted that valves must be present for the perforators to function, and to control flow between the superficial and deep pressure systems [39]. Raivio in 1948 showed that the location of the perforator valves in relation to the fascia determined their role. He suggested that a perforator with a valve superficial to the fascia allowed flows outward and if the valve was deep to the fascia then flows were directed inward toward the deep system[40]. Cockett (1956) and Dodd (1957) through the dissection of amputated legs described the location particularly of the medial calf perforators and stated that perforators had one if not more valves. They stated that each perforator valve controlled the direction of blood flow, from the superficial system toward the posterior tibial veins, but did not allow the blood flow in the reverse direction[41-43]. Hadfield in 1971 through a study of dissection in fresh post-mortem legs, claimed to show that small perforators did not have valves and only larger caliber perforators demonstrated valves, however these valves appeared insufficient. He stated that the arrangement of both the muscle and fascia aperture had an important role to play in the prevention of outward blood flow thereby controlling the pressure effect of the deep venous system with that of the superficial system upon muscle contraction[44, 45].

Since then the direct examination of the venous system for valves has been primarily in the area of gross visual anatomy of cadavers and through the use of venography to the lower limbs. Popoff’s work revealed the presence of valves within small diameter veins, however in 1963, Pirner[46] showed the presence of valves within the perforator. He observed that not only did these perforators have valves, but also on occasion there were several valves noted in a single perforator. He also demonstrated through dissection that in the majority of
perforators that had multiple valves, these valves were all observed deep to the fascia. Pirner not only found valves in the perforators he examined, but also went on through their dissection to observe that the valves were bicuspid in appearance\textsuperscript{[46]}. Hamish Thomson in 1979 observed valves to be readily identified in the perforators sampled from 60 cadaver legs that he studied. He demonstrated this by releasing the perforator from the surrounding tissue, and stroking the vessel in both a backward and forward motion. Any residual blood in the perforator would form a dilation in the perforator, which on further dissection was at the site of a valve. Histology results from his work also confirmed these findings\textsuperscript{[19]}. McMullan, Coleridge-Smith and Scurr (1991) showed using duplex ultrasound, that when a perforator valve was located superficial to the fascia, then, that valve position denoted outward flows within that perforator\textsuperscript{[47]}. In contrast when the perforator had its valve deep to the fascia then blood flow was directed in an inward fashion, from superficial toward the deep venous compartment. However this was in the early days of ultrasound application in venous assessment. The quality of images acquired with ultrasound technology at that time still held obvious limitations especially in relation to image resolution in the superficial venous compartment of small caliber vessels.

Ghali in 2005 while addressing the problem of skin flaps failure in reconstructive plastic surgery over open tibial fractures, made the observation while selecting suitable tissue for grafts that approximately a quarter of all perforating arteries had more than one accompanying perforating vein. His work involved dissection on twenty cadavers, along the vicinity of the medial aspect of the tibia border of the lower limb. He performed a fasciocutaneous flap and observed all vessels that accompanied the perforating artery could be inspected. He found that each perforating artery had mainly one perforating vein and in some cases there were up to two perforating veins accompanying the artery. In only one sample
from this study did he show a situation where there were three perforating veins accompanying the artery\textsuperscript{48}.

The assessment by high-resolution Duplex ultrasound provides another approach to assessing the superficial and deep venous system, and to explore the location of valves and leaflets within them. Even with the advances of high-resolution ultrasound, the insonation of perforator veins, and the ability to observe their presence and determine the function of venous valves within them remains difficult\textsuperscript{49-51}. The consensus within the vascular society is that the sensitivity of duplex ultrasound over techniques like continuous wave Doppler has confirmed an accurate understanding and clarity of function and outcomes on venous interventions\textsuperscript{52}. Ultrasound as a modality in detecting accurate quantification in venous function is not always optimally applied\textsuperscript{53}. Its full potential will be limited in situations where either patient position or limited use of all the ultrasound modalities to obtain an understanding towards function would over simplify our interpretation of the venous system. However duplex ultrasound that is optimally applied can ensure real time quantification of venous function\textsuperscript{52, 54}. The advancement of real time high-resolution ultrasound has allowed the opportunity to best understand, through an accurate, safe system of assessment, the live function of both the entire deep and superficial venous system of the lower limb and the influence of the venous perforators in CVI\textsuperscript{4, 15}. This will further our advancement and understanding of this complex system.

Yet another approach to detecting the presence and location of valves in the venous system has been to make casts of it. In particular there has been the development of resin casting, which allows very detailed imaging of valves even to the extent of scanning electron microscopy (SEM) of the resin corrosion casts. This has allowed the identification of valves in even very small veins (40 \mu m; \& 100–300 \mu m)\textsuperscript{38}. 
1.1 Role of the fascia in perforator function

It has been suggested that the fascia, separating the superficial venous system from that of the deep venous system (Figure 1.1), may play a role in determining the direction of blood flow within the perforating veins.

It was observed by Sander in 1959 that the perforators have three different types of fascia openings, from a simple hole, to a funnel, to a slit\cite{34, 40}. The simple hole appeared like that of the opening within the diaphragm for the inferior vena cava. Sander observed that its structure only offers support but with no significant compliance to allow narrowing or widening of the fascia aperture and he concluded therefore that this type of opening would have no functional impact on the venous perforator. The second type, the funnel shaped openings were most commonly observed where the deep muscle was attached to an inter-muscular septum. This opening was observed not to have any obvious change in the opening shape, even when tension was applied to the fascia. Finally the slit type, which was the least common but also appeared to have the most influence on the perforator function, was only seen where the perforator entered the deep system at an acute angle. This type was observed around the muscle belly and so when the fascia was relaxed, the perforator was opened and filled with blood and this also appeared to widen the slit. Then on muscle contraction the perforating vein was compressed pushing the blood out so no blood flow was present. It appears these slit openings of the fascia could be acting as a kind of venous valve mechanism\cite{55}.
Figure 1.1 Gross anatomy showing a cross-sectional image of the GSV within the superficial compartment.

There are also some smaller superficial veins (SV) within the hypodermal layer of the superficial compartment. The PTV is seen as a cluster of four veins surrounding a highly calcified PTA, within the deep compartment. The fascia layer is clearly seen as a dense layer, which clearly separate both compartments. (Kindly supplied by Associate Professor Greg Jones, Department of Surgery).

1.2 Anatomy of the perforator vein wall

The walls of the veins are usually composed of 3 layers referred to as the tunica intima, media, and adventitia. Histological sections of the perforating veins do not appear to differ from larger veins, with the epifascial region of the perforator resembling the GSV and the subfascial region resembling that of the PTV when looking at the vein wall structure. The perforating veins appear to more closely resemble with the superficial veins than the deep with regard to having less collagen, more vasa vasorum, and greater shrinkage\textsuperscript{[56]}. 

Figure 1.2 Gross anatomy of a venous perforator within the lower limb.

Outlying both direct and indirect perforation are seen coursing between the superficial and deep compartment. Histology images of veins within section: Upper Rt. histology of the GSV, Lower Rt., histology of a direct perforator, Upper Lt. Histology of an indirect perforator. Lower Lt. Histology of the posterior tibial vein (PTV). Note the varying thicknesses of the tunica media and adventitia. The thickest adventitia is observed surrounding the PTV (a capacitance vessel), which is in contrast with the relatively thin adventitia observed surrounding the indirect perforator. (Kindly supplied by Associate Professor Greg Jones, Department of Surgery).

1.3 Venous Physiology

The advancement of understanding venous physiology has also been difficult and lags behind in clarity when compared to the arterial system. Determinants on venous blood return within the closed circuit are first based on the mean systemic filling pressure and the mean right atrial pressure. The greater the difference in the determinant then the greater is the venous return. This system is often referred to as the primary determinant of venous blood return. However this system of return is most effective with increased cardiac activity; it therefore requires other factors to aid with return such as the respiratory venous pump and the skeletal muscle venous pump.
The respiratory system plays an important role in aiding venous blood return. This is achieved with the effect breathing has on both the intra-thoracic and abdominal veins. The respiratory pump aid is an important component of venous return.

The veins have the ability to collapse and dilate making them an effective capacitance system. The fluid mechanics of “collapsible tube” of the venous system is quite different to the arterial system.

The muscle pump also plays an important role in the venous return of blood. Lower in 1669, became the first to link peripheral muscle tone and its pumping effect on the blood flow within the venous system[42]. With the contraction of the muscle, veins within that muscle are compressed and therefore can compel blood flow back toward the heart. The pressures within the veins of the leg are determined by the hydrodynamic effect related to the pressure generated by the calf muscle pump. In the standing position the venous pressure within the veins of the lower leg may reach 80 – 90 mm Hg[58]. On muscle contraction during ambulation the pressure increases within the deep veins, and with relaxation and the effect of competent venous valves and collapse of the veins the pressure is reduced about 30 mm Hg. Arnoldi in 1962, demonstrated that the pressure exerted within the deep vein (PTV) was greater on muscle contraction and fell on muscle relaxation. The PTV was noted to have greater pressure levels on contraction when compared against the GSV and popliteal vein (Figure 1.2). The healthy calf muscle pump allows a regulated controlled pressure gradient which is not maintained in cases of CVI[59].
1.4 The Physiology of the Perforator

The conceptual understanding of the venous perforator is to allow blood to flow from the superficial venous compartment in towards the deep venous compartment\(^9\). The impression is that of the venous perforator playing the role of a pressure valve - that once a muscle contraction is commenced then the pressure of the deep compartment triggers the perforating venous valve to close and prevent venous blood being directed from the deep compartment towards that of the superficial compartment. If the perforators were found to be incompetent then the high pressure of the deep venous compartment, especially the PTV would be directed towards that of the superficial venous system (GSV). The calf muscle pump and its efficiency are considered to reflect the venous disease severity, as it is considered that an increased venous pressure (\(\Delta V\) Pex) is seen when poor venous function is found\(^{14, 22, 60}\).

![Diagram of calf muscle pump pressure profile observed within deep and superficial veins](image)

*Figure 1.3 Calf muscle pump pressure profile observed within deep and superficial veins*
1.5 Investigations of the Venous System

There are a number of modes available to assess the venous system by both invasive and non-invasive methods. The main invasive methods that have been used include venography and pressure measurements and more recently CT venography and contrast magnetic resonance venography. The non-invasive methods are by the various plethysmography systems (air, Strain gauge and photo), continuous and pulse wave Doppler studies, and in more recent times B-mode ultrasound in combination with Doppler technology (duplex and colour flow imaging)\(^{[61]}\).

1.5.1 Phlebogram

The Venogram (or phlebogram) was first used in the 1920s, however it was hampered mainly due to the chemical nature of the contrast media. It was not until 1938 that phlebography became more standardized, when dos Santos performed the ascending method, demonstrating the deep and superficial venous system by injecting the contrast into the veins on the dorsum of the foot\(^{[62]}\). Luke in 1941 used descending phlebography by injecting the contrast into the common femoral vein and observing the response to the valsalva maneuver\(^{[63]}\). The main objective of this method was to show whether the venous valves were intact or if they were incompetent and the extent of this down the deep system\(^{[9, 64]}\). A technique called varicography can be used when looking for communication of perforators between compartments. However the earlier radiological techniques were time consuming due to table repositioning to guide filling in both a proximal and distal direction in the vein to find the perforators. In addition they were not readily repeatable because of radiation exposure and reaction to the media\(^{[65]}\).
1.5.2 Computer Tomography and Magnetic Resonance Imaging

The advancement of Computer Tomography and Magnetic Resonance Imaging has contributed to venous management in more complex disease. Each have limitations including cost, static imaging, time consuming ad hoc analysis and lack of functional information. However MRI for venous assessment has more recently developed a modality that allows demonstration of flow and flow dynamics without the need for intravenous contrast material\[66\]. However at the present this system of assessment is limited in that it often over estimates poor function and therefore limits its use in planning interventional management.

1.5.3 Ambulatory Venous Pressure (AVP)

AVP was used to supplement and extend the understanding of the anatomic findings that were provided by phlebography. This invasive test arose out of research which measured venous pressures by cannulation of leg veins, as part of the study of venous hemodynamics. The phenomena of reduced venous pressure on walking and recovery on standing were critical elements in the indication of function. From the 1970s to 1980s AVP was used as the gold standard in interpretation of venous function, and also used to set the standards for the new development of other non-invasive techniques\[67\]. AVP has its own limitations, with set up complexity, invasiveness and inability to identify which vessel is the major contributor to the venous problem and so over time has lost favor when compared to newer methods of assessment. However it is still felt by many to be the most reliable method to assess venous hypertension\[68\].

1.5.4 Non-invasive Plethysmography

The opportunity to understand venous function response via a non-invasive method came about through the use of Plethysmography. The word is derived from the Greek word “plethysmos”, meaning overly full or fullness and “graphy” to record. Plethysmography is
the measurement of volume changes. When applied to the limb, it is normally a measure of alterations in the arterial and or venous blood flow.

Venous plethysmography can be used to measure either the whole limb, a segment of the limb or simply a local volume change. Plethysmography has provided an excellent approach to functional evaluation of the venous system.

1.5.4.1 Air Plethysmography (APG)

APG is a method of assessment based on volume changes detected by an air chamber that has been applied to the lower limb from below the knee to the level of the ankle. This system of assessment allows an understanding of several components of venous physiology including venous reflux, venous obstruction and calf pump muscle function\(^{69}\). Functionality is derived from changes in volume – for example the Venous Filling Index (VFI), which measures the rate of filling of the limb on standing. A VFI of < 2mL/s is found in normal limbs where the veins fill slowly from the arterial system. The VFI however can increase to over 30 mL/s in persons with back fill due to severe venous reflux. VFI has a strong specificity and sensitivity (100% & 73% respectively) when used to identify limbs with venous ulceration\(^{69, 70}\). This method of assessment has allowed a better understanding of overall venous function, but only provides a global measure and does not identify the site of impaired function. It is therefore less helpful in determining perforator function.

1.5.4.2 Strain Gauge or Impedance plethysmography (SGP)

SGP was first developed in 1953 by Whitney to assess arterial blood flow; and was later used for the assessment of the venous system\(^{71}\). This is based on the accurate measurement of changes in circumference of the limb as a surrogate for volume change using the electrical impedance of an elastic mercury-filled tube attached around the limb. It only reflects changes of a slice of the limb and is less readily extrapolated to the whole limb.
1.5.4.3 Photoplethysmography (PPG)

PPG is a qualitative indirect method of accessing changes in venous volumes. The PPG probe placed on the skin contains an infrared light source (805 nm) directed at the skin and a photodiode that measures the reflectivity of the skin. The light transmitted into the skin is absorbed and scattered into the immediate surrounding tissue. Since blood is more opaque than the surrounding tissue, it attenuates the reflected light in greater proportion and therefore results in more reflected light in areas of greater blood density. The PPG method of assessment is used to measure refilling time and not volume. When the presence of reflux is noted then a fast refill curve is generated. However, PPG cannot be relied on to identify the anatomical distribution of venous disease. An updated method of PPG has since been developed, which is quantitative digital PPG. This method measures both time and amplitude curves, but again is limited in the anatomical quantification\textsuperscript{[72, 73]}.

1.5.4.4 Liquid Crystal Thermography

Liquid Crystal Thermography is an indirect volume measurement based on changes in temperature that accompany changes in flow\textsuperscript{[74]}. The changes in temperature are observed as colour changes in thermographic plates held in close proximity to the limb. The liquid cholesterol crystal in the thermography plate changes colour with change in temperature. It is not quantitative and has very limited application.

1.5.5 Ultrasound

When a piezoelectric crystal is excited to vibrate at its resonant frequency, it generates ultrasound waves of known frequency. When these are directed at moving red blood cells from a probe they are reflected back and detected at a different frequency by a second piezoelectric crystal in the probe. This change in frequency is proportional to the velocity of
the moving red cells (the Doppler effect) and can be registered as an audible sound or recorded electronically. The signal is complex with many velocities across a vessel, which is smoothed out to give an average velocity. Direction of flow can also be determined.

1.5.5.1 Continuous Wave Doppler

Hand-held vascular continuous wave Doppler probes (cw-Doppler) have been in use for many years, especially when examining the arterial system. In the venous system flows are slow and flow augmentation is used for diagnostic purposes. Examination of perforating veins in using cw-Doppler ultrasound is found to have both a low sensitivity and specificity when used along side clinical examination[9], and even lower when compared to duplex ultrasound[75, 76]. This simple method of assessment is inherently difficult, mainly because it is qualitative and so reflux severity cannot be established with cw-Doppler, and more importantly because it is difficult to know if it is a perforator vein that is being examined[9, 77]. Folse & Alexander in 1970, determined a method of assessment along the medial calf for detecting the presence of incompetent perforators[78]. A tourniquet is applied to the limb between the sites of compression and where the CW probe is placed. This removes confusion when detecting flows, as flow will only be detected in the superficial vein if incompetent perforators are present. Unfortunately this technique is neither sensitive nor specific[78].

1.5.5.2 Duplex Ultrasound

The development of Duplex Ultrasound [52] has created a modality of preferred choice for venous assessment as it removes most of the limitation of cw Doppler[52]. As well as being a non-invasive modality, in gray scale (B-mode) it has the ability to identify all veins both superficial and deep in real time with exact placement of the Doppler sample[79-82]. This allows individual interrogation of the desired venous vessels, especially the venous perforators[18, 83] (Figure 1.4).
The perforator is seen traversing the deep fascia separating the superficial and deep venous compartment.

Duplex ultrasound is a combination of gray scale imaging, colour and spectral Doppler that detects blood flow, which became an important system of assessment in the mid 1980s, especially with the introduction of colour Doppler. In the hands of an experienced vascular technician, ultrasound is a useful assessment tool prior to venous intervention, in that it ensures confirmation of venous problem sites prior to any management plan\cite{84}. This method of assessment should therefore result in better outcomes following surgery, especially in reducing the incidence of recurrence of varicose veins\cite{85}. Smith in 2002, tested the theory using two patient groups, both of which had ultrasound of the venous system, but only allowing one of the groups’ results to be made available to the surgeon prior to clinical examination and planned management; that it would best reflect the usefulness of the modality\cite{85}. From this research it was noted that ultrasound did not improve outcomes.
Recurrence rates were still raised at all sites and also at the site of the perforators, which had a recurrence rate of 3%\(^{(85)}\). However since then it has become apparent that venous disease is more a progression disease\(^{(6)}\), and in longitudinal studies ultrasound has allowed the collection of accurate data in relation to venous changes and their outcomes\(^{(4, 15)}\). The use of duplex ultrasound is now regarded as the standard for the assessment of the venous system\(^{(81, 82, 86, 87)}\). This modality is most effective as it also allows a detailed hemodynamic, live response to be recorded at the time of the examination\(^{(88, 89)}\).

B-mode ultrasound (Brightness-mode) is the display of a 2D-map of B-mode data, currently the most common form of ultrasound imaging. The ultrasound signal is used to produce various points whose brightness depends on the amplitude of the returning echo for the tissue. Sweeping a narrow ultrasound beam through the area of tissue being examined while transmitting pulses and detecting echoes along closely spaced scan lines produces B-mode images. The vertical position of each bright dot is determined by the time delay from pulse transmission to the return of that echo. The returning sound pulses in B-mode have different shades of darkness depending on their intensities. The varying shades of gray reflect variations in the texture of internal organs. This form of display (solid areas appear white and fluid areas appear black) is also called gray scale. The ultrasound transducer is passed across the site of interest, to display the anatomic position within the limb. A pulsed Doppler signal can then be superimposed into the B-mode gray scale image at the point where flow velocity is to be measured. The direction is determined and changes observed in real time. This alone can be adequate in understanding venous function\(^{(90)}\), however spectral Doppler allows a more detailed quantification of duration, the blood velocity and a true confirmation of the direction of blood flow\(^{(91)}\). Colour Doppler is a system whereby a quick impression of function can be determined. This imaging modality, superimposes a blood flow image on the B-mode standard image, and results in an instantaneous visual assessment of blood flow. The difference of colour imaging from B-mode is that colour uses Doppler shift information, time
of flight and amplitude. The direction of blood flow can be determined by the display colour, for example red might be coded for blood flow toward, with blue colour away from the transducer. However it should always be kept in mind that the colour processor displays motion relative to the ultrasound beam, from each of the beam lines forming the flow image. Therefore different parts of the vessels are interrogated from different beam directions, either by orientation of the vessel or transducer scan format that is used.

![Image](image_url)

**Figure 1.5 Colour and Spectral Doppler image of a perforating vein.**

*The colour red denotes flow from the deep to the superficial compartment; Spectral Doppler outlining retrograde flow following a distal augmentation within an incompetent perforator (IPV).*
The presence of venous incompetence is easily identified using colour and Spectral Doppler, in association with distal augmentation and the valsalva maneuver (Figure 1.5). Ninety-five percent of venous valves will close in response to these procedures within a 0.5 second interval\[^{92}\]. Therefore retrograde flow > 0.5 seconds is generally used to represent significant reflux and venous valve incompetence\[^{51, 87, 92}\].

The 0.5 second criteria has been applied to both the superficial and deep venous system, however it is considered that > 0.35 second duration is best suited to the perforating veins especially within the calf \[^{91}\]. Although duplex ultrasound can be used to localize incompetent perforators there is still considerable controversy as to its ability to adequately assess their haemodynamic significance\[^{18, 76}\].

Even though a great deal has been determined regarding functional aspects within both the deep and superficial venous system using duplex ultrasound, this is limited when it comes to the perforating veins. Our understanding of perforators remains controversial. What more can be gained from the use of duplex ultrasound about the roles of perforators in the flow of venous blood in normal subjects and in venous disease? Are all perforators functionally the same in the leg? How does having varicose veins affect these perforators and what happens after they are treated?

This thesis sets out to understand through the use of duplex ultrasound these and other questions surrounding perforator characteristics.
Chapter 2:

2 General Methodologies for Clinical Studies

This chapter describes the basic methods used in the studies that follow in subsequent chapters of this thesis. In the past imaging assessments of the venous system have been performed using invasive techniques that involved the use of an iodine contrast; that for many patients caused a severe adverse reaction. However with the development of duplex ultrasound, including B-mode, colour and spectral Doppler, has now provided for a more comprehensive, non-invasive, detailed assessment of the venous system to be performed\[80, 85\]. Through the use of B-mode we are able to perform a detailed anatomical assessment of the venous system. With the advancement of colour and spectral Doppler we are now also in the comfortable position of performing, with confidence, detailed assessments of venous functionality in real time. This technique has enabled a significant advancement toward a reliable, reproducible method of assessment\[8, 93\]. Duplex ultrasound is the basis for the evaluation of the venous system of the lower limb used for this thesis.

2.1 Ultrasound Imaging and Quantitative Measurements

A Siemens (Antares) ultrasound machine (Siemens Medical Solutions, Inc. Mountain View, California, USA) was used for examinations of all normal participants within this study\[94-96\]. Both 4-7 & 12–15 MHz linear array transducers were used to optimally assess the venous system. An ATL 5000 using a 7 - 4 MHz/ 12 - 5 MHz linear array (Phillips Medical Systems) was used in the assessment of the venous disease population. Both machine offer the same level of resolution and therefore will have no effect on the overall quality of my results.
All B-mode pre sets were optimized when viewing the deep and superficial venous system and perforators of the lower limb. Both colour and spectral Doppler were set at an optimal pulse repetition frequency (PRF) and low filter setting to ensure the detection and quantification of low blood flow velocity and direction. Pulse repetition frequency is the number of acoustic pulses transmitted per second when using ultrasound and is especially useful in application of colour and spectral Doppler and velocity of blood flow.

### 2.2 Ultrasound Examination Protocol for all Study Groups

#### 2.2.1 Ultrasound Criteria for Venous Assessment

This detailed venous assessment was performed on both the deep and superficial systems to identify residual venous thrombus, anatomical variation and any other anatomical features. Flow measurements and in particular the functional response to distal calf augmentation and valsalva maneuver were assessed in multiple sites to determine normality. A reverse blood flow of > 0.5-second duration was used as the cutoff to quantify reflux in large veins [51, 87, 92]. Similarly reverse flow of > 0.3 second duration was used to define incompetence within perforators of the normal subject population [91]. All sites of perforators were recorded in detail [97]. The communication with both the deep and superficial venous compartments was recorded in detail for each perforator [17]. The perforator diameters were measured at the point where they crossed the fascia plane, with the calipers placed to the inner margin of the perforator vein wall (Figure 2.1).
2.2.1.1 Spectral Doppler

Spectral Doppler allows for both the confirmation of blood flow direction and quantification of its velocity, including maximum peak venous velocity, following a distal augmentation (Figure 2.2). A study by Ogawa in 2002 on 25 healthy subjects found that the measurement of velocity flows with ultrasound was repeatable when the sample volume, angle of insonation and cross sectional area of the vessel was optimal\textsuperscript{[96]}. He found that a larger gate on the sample volume settings reduced the error on velocity obtained; conversely errors can also occur if the sample volume gate is set too large resulting in sampling from adjacent vessels in the surrounding tissue. More modern ultrasound machines are found to have an
error of < 6% in relation to volume flow measurements\[^95\]. Reliability of sampling may therefore become questionable in very small diameter vessels like that of the venous perforator\[^98\].

![Spectral Doppler Ultrasonographic Image demonstrates Venous Flow Direction](image)

*Figure 2.2 Spectral Doppler Ultrasonographic Image demonstrates Venous Flow Direction.* Following a distal augmentation within an incompetent vein. The point of onset of distal augmentation is shown at site (a). From this we can see a negative Doppler shift. This response demonstrates a normal blood flow in an antegrade direction. At point (b) on completion of the distal augmentation stimulus there is an immediate positive Doppler shift. This is indicative of a retrograde reverse flow following augmentation. This perforator demonstrates incompetent function as the duration of reverse flow over time is > 0.3 sec\[^91\].

To obtain the Peak Venous Velocity, the spectral Doppler sample cursor was placed into the perforator lumen at the point where it crossed the fascia, (Figure 2.1). The sample volume gate was adjusted to match the diameter of the perforator from both walls of the inner lumen. The angle of insonation to sampling the venous blood flow was not in excess of 60° to avoid errors in measurements as mentioned above\[^96\].

The ultrasound examination was performed in two phases. The participant was placed on the examination couch and prepared for all body weight to be applied to the contra-lateral limb. Then the participant was tilted into a 90° reverse trendelenburg position. The limb for examination was externally rotated with no body weight applied. The first phase of the examination involved a detailed assessment of the thigh. This was performed from the common femoral vein (CFV) to the distal medial thigh femoral vein (FV) and then examined
along the medial thigh great saphenous vein (GSV), from the distal thigh towards the SFJ. While coursing the thigh GSV in B-mode, observations were made for the presence of perforators. These were identified in B-mode as they crossed the fascia (Figure 2.1) and marked on the skin with an indelible marker. On completion of the deep and superficial compartment, all perforators that had been identified were then assessed for function using a distal augmentation. The location of each perforator that was identified was then measured from the superior border of the patella, anterior from either the lateral or medial aspect of the thigh.

Accessory veins observed in the anterior medial or posterior lateral thigh were then assessed for function with both colour and spectral Doppler. Again, when insonating these veins in B-mode, attention was made to the presence or absence of perforating veins from the superficial to the deep compartment. The lateral aspect of the thigh was not assessed in this research, unless veins were identified to course in this region.

Following the completion of the thigh assessment the participants were then seated with their limb extended over the side of the examination couch and their foot placed on the seated sonographer’s leg. Again the deep venous system, from the proximal popliteal to the distal to calf veins, were assessed along with the SPJ, SSV, calf segment of the GSV and any accessory superficial veins. Like before all locations of perforators were identified and this involved a 360° assessment of the calf\cite{99,100}.

### 2.2.2 Distal Augmentation

Distal augmentations were performed with the use of a calf pneumatic cuff, which was placed around the calf (gaiter region) of the lower limb. This cuff was attached to a pneumatic pump that supplied a constant, controlled, set pressure with a quick inflation followed immediately by a quick deflation\cite{92}. This allowed an effective, consistent and controlled calf squeeze from
the augmentation\textsuperscript{92,101}. The response following augmentation was to simulate the calf muscle pump.

2.2.3 Valsalva Maneuver

The valsalva maneuver was performed by applying a moderately forceful exhalation against a closed airway. It is most effective as a means to quantify retrograde flows when the participant is assessed in the erect position as shown by Lagattolla in 1997. His finding showed that reverse flow > 0.5 sec duration while performing a valsalva maneuver was needed to determine reflux, a < 0.5 sec was predominantly found in subjects with normal venous function\textsuperscript{102}.

2.2.4 The Research Subjects

Each study group will be described in the following chapters for each of the research projects. Subject recruitment was by advertisement within the local newspaper, staff bulletin and sourced from personnel on the university campus. Patients within the venous disease population were referred to the vascular laboratory and following their venous assessment were approached to participate in a larger longitudinal study within the vascular laboratory. All participants across the board were given the opportunity to read the research study outline and were followed up by a phone call approximately two to three days later, to confirm if they wished to participate in the study.

2.2.5 Ethical Approval

The Lower South Regional Ethics Committee reviewed and approved these projects. Each participant received an information sheet informing them of all their rights and conditions of
the research. Consent was obtained from all subjects prior to commencement of the ultrasound examination. (Appendix A)

2.2.6 Data Security and Privacy of the Participants

The NZ Privacy Act 1993 along with the NZ Health Information Privacy Code 1994 are all abided to and followed. The participants are not identified. A unique identifier is used to allow review of the raw data with the results. The findings in this project have been used for publication in the scientific literature, and at both national and international presentations. All data were held within the vascular laboratory’s Filemaker Pro database. All statistical analysis was performed with Stat View software (Berkeley, California). The values unless otherwise specified were described as mean ± standard deviation (SD) for continuous variables (Student t-test). An analysis of variance (ANOVA) was the test to observe for significant differences between means. Statistical significance was assigned at $P \leq .05$. Only the student and supervisors have access to the raw data obtained during this study. All raw data have been stored within the Department of Surgery, and on a secure server within the University of Otago.
Chapter 3

3 The Distribution of Venous Perforators in Normal Subjects

While much has been written about the distribution of perforators this is largely confined to anatomical cadaver studies\textsuperscript{[19]}, clinical observation, phlebography and limited ultrasound particularly in patients with venous disease. This study seeks to answer the question, “what is the distribution of venous perforators in normal limbs as observed with duplex ultrasonography?” To my knowledge there are no known previous systematic studies of the venous perforator that have included spectral analysis.

The aim was to also describe other anatomical characteristics of the perforators - their size and both their deep and superficial connections.

3.1 Methods

3.1.1 Research Subjects

Only subjects over the age of eighteen years, and who had no evidence of venous disease (i.e. varicose veins) were recruited to participate in this study. Persons who were found to have the presence of varicose veins, previous venous intervention or a history of deep vein thrombosis were excluded from the study. The decision to assess only one limb for the study was for both patient comfort and time constraints. The right limb was chosen for assessment for comfort of both the participant and sonographer. The ultrasound examinations took approximately one hour and thirty minutes each. As outlined in chapter two of this thesis; a detailed venous ultrasound examination was performed.
3.1.2 Results

A total of 20 subjects participated in the first study, ranging in age from 22 – 60 years. The mean age was 36.9 ±12 years. There were a total of thirteen females and seven males. An additional three subjects were excluded from the research once they were found to have superficial venous disease following the detailed venous assessment. The subjects with superficial venous incompetence had a detailed report compiled and were referred back to their general practitioner (GP) for consultation and further referral to a specialist surgeon if they so wished.

In the 20 limbs, 283 perforators were identified. Following distal augmentation none of the right lower limb perforators were found to be incompetent, with all perforators demonstrating inward flow on distal augmentation and valsalva. There were 14.2 perforators identified per limb (range 8 to 21; median, 13). The mean diameter of these perforators was 1.3 ± 0.56 mm, (range 0.4 to 3.5 mm; median, 1.2 mm).

The distribution of perforators of the lower limb as observed through Duplex ultrasound is shown in Figure 3.1. The majority of the perforators were located in the lower leg and of these more were located in the medial calf (i.e. Para-tibial and posterior tibial region)[41]. Remarkably few perforators (9%) were identified in the thigh of twelve normal subjects with none seen in eight thighs. One subject had three thigh perforators.

The diameter of the perforators across each of the regional locations was not significantly different (Table 3.1, Figure 3.1).
Table 3.1 Regional Perforator Location and Diameter (mm).

<table>
<thead>
<tr>
<th>Region</th>
<th>Total Count (n= 283)</th>
<th>Paratibial (n= 53)</th>
<th>Posterior Tibial (n= 50)</th>
<th>Medial Gastroc (n= 34)</th>
<th>Lateral Gastroc (n= 16)</th>
<th>Lateral Calf (n= 80)</th>
<th>Anterior Calf (n= 38)</th>
<th>Femoral Canal (n= 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.3±0.5</td>
<td>1.5±0.8</td>
<td>1.5±0.5</td>
<td>1.4±0.5</td>
<td>1.3±0.4</td>
<td>1.0±0.3</td>
<td>1.4±0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>1.2</td>
<td>1.2</td>
<td>1.4</td>
<td>1.3</td>
<td>1.2</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0.4 – 2.6</td>
<td>0.4 – 3.5</td>
<td>0.5 – 2.8</td>
<td>0.8 – 2.4</td>
<td>0.4 – 2.9</td>
<td>0.5 – 2.5</td>
<td>0.5 – 2.2</td>
</tr>
</tbody>
</table>

There was no statistical significance found between perforator diameters and their regional location. (p value was set at < 0.05).

Figure 3.1 Regional Distribution and Diameters (mm) of Perforators within a Normal Population of Rt. Lower Limb

3.1.3 Perforators and their Superficial Communications

The communication of the perforators from the superficial compartment is shown in Figure 3.2. The majority drained the superficial lateral vein network of the lateral calf, 40% [16, 17].
On the medial aspect of the calf drainage was directly from the GSV in 28% (n= 79) and a further 20% of the perforators (n=58) were found to drain in a more convoluted manner in the subcutaneous tissue from the GSV. It was not possible to identify a discrete posterior accessory great saphenous vein (PAGSV) as described in the literature\[14\]. This is a superficial accessory vein seen coursing posterior to the GSV, which may be located to either the thigh or calf region of the lower limb\[14\]. Relatively few perforators (6%, 16) were observed connecting with the Short Saphenous Vein (SSV) and the thigh GSV (4%, 12). In the thigh there were occasions where the perforator drained directly from superficial vein networks. (Figure 3.2)

![Figure 3.2 The Percentage of Perforator Communication with the Superficial Compartment of the Lower Limb of Normal Subjects. Great Saphenous vein (GSV) Accessory GSV (AGSV); Lateral Superficial Vein (LSV), Short Saphenous Vein (SSV) & Thigh GSV](image)

**3.1.4 Perforators and Deep Venous Communications**

The communication of the venous perforators with that of the deep venous system is shown in Figure 3.3. These connections of the perforators to the deep system followed the expected
anatomical regional drainage with the medial calf to the posterior tibial vein (36%), the lateral calf to the peroneal veins (28%) and anterior tibial veins (13%). The communication into the lateral (6%) and medial (13%) gastrocnemial veins lying within the respective muscles were mostly relatively short and direct from the deep aspect of the SSV. These findings are supported by both our own and others researcher along with anatomy dissections[14, 17, 103, 104].

![Diagram showing percentage and number of perforator communication with the deep venous compartment.](image)

**Figure 3.3 Percentage and Number of Perforator Communication with the Deep Venous Compartment.**

Posterior tibial Vein (PTV), Peroneal Vein (PV), Anterior Tibial Vein (ATV), Medial Gastrocnemius Vein (MGV), Lateral Gastrocnemius Vein (LGV), Femoral Vein (FV)

### 3.1.5 Discussion

From this initial assessment of the normal lower limb, we have demonstrated the presence of a greater number of perforators per limb by ultrasound or by phlebography than has been previously reported by others[105, 106]. Even so this is far fewer than has been shown though cadaver work with the description of over 150 perforators per limb[18]. Even with an
experienced sonographer, a methodical system of assessment and high quality ultrasound resolution, we were unable to detect similar numbers. Our ability to identify with ease perforators in the diameter range of 0.4 mm demonstrates the quality of the ultrasound resolution. Below this (<0.3 mm) however detection ability is lost and may account for some of the difference in numbers. The beam width and pulse length, will determine the apparent size and resolution of the perforator image. With such small vessels the ability to scan for them over the large area of the deep fascia and maintain the correct insonation also limit numbers. Further to this, even with augmentation maneuvers, flows may be well below that detectable.

The distribution of the perforators in the regions of the leg match up well with that described by other work\(^{17}\). Similarly, so are the vessels into which they drain in the deep system. Less well understood is the exact territory from which the perforators drain. Most are in the calf and most are to the medial aspect of the calf, the site considered most affected by incompetent venous perforator. Of the 283 perforators identified 103 or almost 30%, were located in the medial calf. Even through perforator diameters did not appear to be of a greater size, however, the greater concentration of perforator numbers may have influence on the venous pressure profile if applied to the diseased population\(^{25, 107}\).

Communication of the venous perforators, especially within the superficial compartment, did not match with the literature; this was especially seen in relation to the posterior accessory great saphenous vein (PAGSV). None of the perforators were found to communicate with the PAGSV in this sample group\(^{107}\). The main communication in the medial calf was with the GSV and a small accessory GSV. Is it possible that in a normal functioning venous system the PAGSV is not dominant and is represented as a small inter-saphenous vein within the superficial compartment? There is the possibility that the numbers in this research are limited and therefore would need further numbers to confirm and support these findings. There is also the limitation of not having the diameter measurements of the superficial veins in the
vicinity of all the perforators that communicated with the accessory GSV. Possibly the remaining superficial veins that connected with the accessory GSV were also connecting with a much smaller PAGSV?

The finding of the deep compartment communications lied with the PTV. The PTV and its known high pressure profile may play a role in the relationship of incompetent perforators along the medial calf\cite{13,24,43}.
Chapter 4

4 A Detailed Examination of the Medial Calf Perforators in Normal Subjects

In the evaluation of varicose vein disease and venous insufficiency most significance has been placed on the perforators that are located on the medial aspect of the calf region \([13, 18]\). Most research studies emphasize that there is not only a greater number of incompetent perforating veins in this region of the leg, with over 80-90% of cases located in this region, but also implied that these are related to greater severity of disease\([108]\). Consequently this is the region where most perforator interventions occur.

This study focuses in detail on the characteristics and function of the perforators in this area in normal limbs with the aim to determine factors that may be distinctive and influence their role in venous disease\([13]\). This study therefore involved a more detailed assessment of both the tibial and paratibial regions, which constitute the commonly described medial calf.

4.1 Methods

4.1.1 Medial Calf Perforator Identification

The numbers of perforators along the tibial and paratibial region of the medial calf were identified, marked with an indelible marker, and measured along the medial calf as outlined previously in Chapter 2. The medial calf was then divided into three equal zones coursing from the inferior border of the medial malleolus to the superior margin of the medial calf, just inferior to the knee joint. These three medial zones will be referred to as the lower, mid and upper zones throughout this chapter. The dividing of the medial calf into zones was to allow
for ease of reference and comparison of perforators but more importantly to distinguish possible functional differences in the vertical positioning associated with changing hydrostatic and muscle pump actions and relationships to deep vessels.

### 4.1.2 Quantification of Venous Perforator Blood Flow

Spectral Doppler allows for both the quantification and confirmation of both maximum blood velocity and blood flow direction following a distal augmentation. The maximum peak venous velocity flow (PVVF) was obtained from all subjects’ perforators in the tibial and paratibial aspect of the medial calf.

### 4.1.3 Peak Venous Velocity Flow

The peak systolic velocity was used to quantify the venous blood flow through the perforator, as it is the most consistent expression of flow\(^{[109]}\). This involved insonation of the perforator at the point where it crossed the fascia (Figure 2.1). With the use of spectral Doppler the sample volume gate was adjusted to match the diameter size of the perforator. The angle of sampling was not in excess of 60° to avoid error in measurements\(^{[96]}\). Three independent distal augmentations were performed on each of the identified venous perforators and the peak venous velocity flows were recorded. The mean velocity from the three measures was calculated. The diameters of each of the perforating veins in the medial calf were obtained as outlined in Chapter 2. The main duplex parameters that were used to quantify the blood flow within each of the perforators was the peak venous velocity (cm/s) and the peak flow (mL/s) calculated using the equation:

\[
\text{Peak Flow} = \text{Peak Velocity} \times \text{Area (}\pi r^2\text{)}.
\]

The vessel cross sectional area was calculated from the diameter making the assumption that the vessel was circular in shape.
It was decided to use the peak venous blood flow as a measure in order to reduce error in the results. Optimal insonation of blood flow through perforators where the time average mean velocity could be obtained is open to sampling error in the case of small vessels < 2 mm in diameter\textsuperscript{98}. A sample error could also result from a larger spectral Doppler gate setting\textsuperscript{96}. Time average mean velocity would be more suited for larger caliber vessels, like the GSV and deep venous system, in situations where there is spontaneous flow. The velocities acquired from these perforator groups have had a distal augmentation response. The diameter sizes of each of the perforators were also in a range that also made accuracy questionable with regard to determining volume flow.

4.1.4 The Participants Examination Position

The normal venous participants were assessed in three different positions to observe the functional effects of each position in the medial calf venous perforators when a distal augmentation was used. Three positions were used as venous function is known to be affected when in these different positions\textsuperscript{54}. In the standing position the level of pressure to the lower limb ankle region is about 85 mmHg, when compared to sitting where pressures are at 56 mmHg; and only 12 – 18 mmHg in the supine position\textsuperscript{110, 111}. Valsalva maneuver was not used in this part of the research, as no effect to the distal veins is detectable when the proximal venous system is normal in function\textsuperscript{102}.

4.1.4.1 Upright Standing Position

The participant lay supine on the examination couch. They were then tilted with the use of a tilting examination couch into a standing position. The participants were then required to transfer their entire body weight onto the contra-lateral limb, with no body weight to the right
limb. The right limb was externally rotated to allow ease of assessment of the medial calf perforators.

4.1.4.2 Sitting Position

Each participant sat with their limb extended over the side of a raised examination couch. The limb for examination was positioned horizontally and supported on the examining sonographer’s leg. This leg position was found to be most comfortable for both the participant and sonographer during the examination. The thigh was rested on the couch, with no impingement in venous flow as it was held supported^{112}.

4.1.4.3 Supine Position

The participant lay supine on the examination couch with their right leg externally rotated. No body weight was applied to the limb during the entire examination whilst in this position.

4.1.5 Distal Augmentation via a Foot Stimulus

Distal augmentations were performed with the use of a meta-tarsal cuff, which was placed around the dorsum of the foot. This cuff was attached to a pneumatic pump that supplied a constant, controlled, set pressure with a quick inflation followed immediately by a quick deflation^{92}. This allowed an effective foot squeeze on distal augmentation. The response following distal augmentation was to simulate the foot muscle pump and the dorsum of the foot. This was repeated three times in all three positions for each perforator.

4.1.6 Exercise effect on medial calf perforators

The effect of exercise on the medial calf perforators was also assessed during this study. The venous pressure varies greatly in the lower limb when walking - this is influenced by the
planter venous system and muscle pumps. It has been shown that the venous pressure increases from 85 mmHg when standing and drops to 20 – 30 mmHg on walking.

The subject was studied in the upright standing position as described and non-weight bearing of the right leg. The foot simply rested on the examination couch footplate. The most distal perforator was always identified first (in contrast to the randomized order applied to the remaining study). Prior to exercise each perforator was examined for the presence of spontaneous blood flow, if spontaneous activity was present then a spectral Doppler waveform of this was recorded for analysis. The subject was then transferred to the Star-Trac treadmill and undertook a five-minute walk at a rate 4 km/h, with a 10° elevation on the treadmill (Unisen Inc. USA) [110]. Insonation of the perforators was not possible during the exercise, due to limb movement and inability to maintain adequate transducer contact with the perforator during the activity. Immediately on completion of the exercise, the participants were repositioned back into a standing position on the examination couch as previously described. The perforators were then again insonated and the profile of the venous velocity was recorded. This system of evaluation was repeated for each of the identified distal to proximal medial calf perforators in each of the twenty subjects. All subjects required multiple bouts of exercise to evaluate each of the individual perforators along the medial calf; a five-minute interval was enforced between each individual perforator exercise performance.

4.1.7 Isometric Planter Flexion Test

Planter flexion was performed when examining each of the medial calf perforators in a standing position, to observe its effect on velocity flow. This observation was also used to see if there was any correlation between this isometric action and a distal augmentation[9]. Each individual perforator was insonated with the subject in a standing position on the tilted examination couch. No weight was applied to the leg under examination, however the foot
was placed lightly against a platform and the subject was instructed to firmly plant the forefoot as a planter flexion contraction and then to relax. This was performed three times for each of the perforators and the velocity changes were recorded. The perforators were insonated in order from the distal to proximal medial calf.

4.2 Results

The twenty subjects who participated in the previous study in Chapter 3 also agreed to participate in this section of the research. In the twenty limbs 105 perforators were identified and assessed along the tibial and paratibial medial aspect of the right leg, of which none were found to be incompetent following distal augmentation and valsalva. There were 5.3 perforators per limb along the medial calf (range 4 - 8; median 5) with a mean diameter of 1.5 ± 0.71 mm, (range 0.4 - 3.1mm; median1.3 mm).

4.2.1 Statistical Analysis

The values unless otherwise specified were described as mean ± standard deviation (SD) for continuous variables (Student t-test). An analysis of variance (ANOVA) was the test to observe for significant differences between means. Statistical significance was assigned at $p \leq .05$.

4.2.2 Perforator Diameters of the Medial Calf

4.2.2.1 Gender Effect

There were thirteen females and seven males with 5 and 5.7 perforators respectively per limb, with their respective perforator diameters as shown in Table 4.1. While it appeared that males
had large perforator diameters when compared with the female group, there was no statistically significant difference (Figure 4.1).

<table>
<thead>
<tr>
<th>Gender</th>
<th>Female (n=13)</th>
<th>Male (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforator number</td>
<td>65</td>
<td>40</td>
</tr>
<tr>
<td>Perforator per medial limb</td>
<td>5.7</td>
<td>5</td>
</tr>
<tr>
<td>Mean Diameter ± SD</td>
<td>1.4± 0.7</td>
<td>1.6 ± 0.8</td>
</tr>
<tr>
<td>Range</td>
<td>0.4 – 3.0 mm</td>
<td>0.5 – 3.1 mm</td>
</tr>
</tbody>
</table>

*Table 4.1 Medial Calf Perforator Diameter (mm) in Males and Females*

*Figure 4.1 Medial Calf Perforator Diameters (mm) Split by Gender.*
4.2.3 Vertical Zones

The distribution of perforator size by zone in the lower leg is shown in Table 4.2. Perforators were found to have a large caliber in the lower zone of the medial calf. The diameter of the perforators within the lower zone was $1.7 \pm 0.8$ mm. The perforators in the upper and middle zones were smaller and of similar diameters to each other (Table 4.2).

Table 4.2 Medial Calf Perforator Diameter (mm) by Zone as seen on Ultrasound.

<table>
<thead>
<tr>
<th>Perforators n =105 (20 Limbs)</th>
<th>Lower n = 39</th>
<th>Mid n= 32</th>
<th>Upper n= 34</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>1.7±0.8*</td>
<td>1.4±0.7</td>
<td>1.4±0.6</td>
</tr>
</tbody>
</table>

$t(71) = 1.9, p = .05$ *

4.2.4 Direct Vs Indirect Venous Perforators

The perforators of the medial calf passed into deep axial vessels either directly or by a more circuitous indirect course. The diameters of the direct and indirect perforators shown in Table 4.3 were not significantly different $t(103) = 0.58, p = 0.56$.

Table 4.3 Medial Calf Perforator Diameters (mm), Direct and Indirect.

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Direct Perforator (n= 88 )</th>
<th>Indirect Perforator (n= 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>1.5± 0.73</td>
<td>1.4± 0.63</td>
</tr>
<tr>
<td>Median</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Range</td>
<td>0.4 - 3.1</td>
<td>0.6 – 2.9</td>
</tr>
</tbody>
</table>
The majority of direct perforators were in the ‘gaiter region’ of the lower and mid zones with closer proximity to the PTV (Table 4.4). All of the 88 direct perforator communications were found to be with the PTV. The majority of indirect perforator communications (n= 11) were seen in the upper zone of the calf, the region of greater muscle mass where they were all observed to communicate with the MGV (Table 4.4 & Figure 4.2). Of the two indirect perforator communications in the lower calf, one was observed to communicate with the Soleus sinus and the second perforator to the MGV. Of the four indirect perforators of the mid zone in the medial calf, two were found to communicate with the MGV. The third perforator communicated via the PTV and the Soleus sinus, with the fourth perforator seen communicating only with the soleus sinus.

Table 4.4 Distribution of the Direct and Indirect Perforators when Split by Zones along the Medial Calf

<table>
<thead>
<tr>
<th>Zone</th>
<th>Direct Perforators</th>
<th>Indirect Perforators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Mid</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Lower</td>
<td>37</td>
<td>2</td>
</tr>
</tbody>
</table>
Figure 4.2 Venous Perforator Anatomy - Tissue Cross Section. (a) Indirect perforator (b) Direct Perforator.

Note there are a number of PTV surrounding a highly calcified PTA.
4.2.5 Valves Identification of Perforator valves by duplex ultrasound

A total of eighteen of 105 (17%) venous perforators along the medial calf were identified as having a valve present when examined by B-mode ultrasound (Table 4.5 & Figure 4.3). Seventeen of these valve-containing perforators were direct connections with the PTV and all were observed to take a short course from the superficial to the deep compartment. They were all found in the distal medial region of the lower leg. Only one of the perforators observed with a valve was seen with an indirect connection to the soleus sinus.

Twelve of the valved perforators were the first perforator identified from the inferior border of the medial malleolus. The six remaining perforators with valves were the second perforator up from the inferior border of the medial malleolus. The diameters of the eighteen perforators identified with valves were found to be significantly larger, with a mean diameter of 2.1 mm compared with 1.4 mm of those perforators not seen to have valves $t(103) = 3.9, p = 0.0006$ (Table 4.6).

Table 4.5 Ultrasound B-mode Finding of Venous Perforators With and Without Valves.

<table>
<thead>
<tr>
<th></th>
<th>Direct</th>
<th>Indirect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valves</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>No Valves</td>
<td>72</td>
<td>16</td>
</tr>
</tbody>
</table>

$\chi^2(1, N=105) = 0.09, p = 0.001$.

Table 4.6 Diameter (mm) of Perforators with and without Valves

<table>
<thead>
<tr>
<th></th>
<th>Valves</th>
<th>No Valves</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD (mm)</td>
<td>2.1 ± 0.67</td>
<td>1.4 ± 0.66</td>
</tr>
<tr>
<td>Median (mm)</td>
<td>2.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Range (mm)</td>
<td>1.0 – 3.1</td>
<td>0.4 – 3.0</td>
</tr>
</tbody>
</table>

$t(103) = 3.9, p = .0006$
Figure 4.3 B-Mode Ultrasonographic Image Demonstrates a Venous Perforator and the Edge of a Valve Leaflet to the Perforator Lumen.

Leaflets are shown by the arrows

The difference was also observed between perforators with valves and without valves when split into zones, p = 0.001. These findings suggest that ultrasound detectable valves most frequently occur in larger, direct perforators at the ankle.

4.2.6 Perforator Peak Systolic Velocity (PSV)

The peak systolic velocity in the perforators following a distal augmentation is shown in (Table 4.7). In general the PSV in perforators was greater in the standing position, less in the sitting and least in the supine positions $F(2,312)=6.7, \ p = .05$ (1 way ANOVA). This significance held when split into zones (Table 4.8). The lower zone demonstrated the greatest PSV especially in the standing position (Figure 4.4).
Table 4.7 Peak Systolic Velocity (cm/s) in Medial Calf Perforators in Different Positions.

<table>
<thead>
<tr>
<th>Perforator</th>
<th>Standing</th>
<th>Sitting</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=105 (20)</td>
<td>15±14*</td>
<td>11±14</td>
<td>8.6±11</td>
</tr>
</tbody>
</table>

F(2,312)=6.7, p = .05*. 1 way ANOVA.

Table 4.8 Peak Systolic Velocity (PSV) cm/s in Medial Calf Perforators in Different Zones

<table>
<thead>
<tr>
<th>Perforator n = 105</th>
<th>Standing</th>
<th>Sitting</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower (n = 39)</td>
<td>19±16</td>
<td>14±18</td>
<td>11±14</td>
</tr>
<tr>
<td>Mid (n = 32)</td>
<td>13±11</td>
<td>12±12</td>
<td>7.9±8.3</td>
</tr>
<tr>
<td>Upper (n = 34)</td>
<td>13±15</td>
<td>7.4±8.1</td>
<td>6.4±7.4</td>
</tr>
</tbody>
</table>

F(8,306) = 3.14, p = 0.002

Figure 4.4 Mean Peak Systolic Velocity (cm/s) Detected in Medial Calf Perforators following Distal Augmentation in Different Positions and Split by Zone

4.2.7 Peak Venous Flow (PVF)

Peak venous flows (mL/min) varied considerably in different positions. Within the medial calf perforators PVF was greatest through the lower zone perforators in all three positions and most evident in the standing position. (Tables 4.9 & 4.10, Figure 4.5).
Table 4.9 Peak Venous Blood Flow (mL/min) through the Perforators following a Distal Augmentation.

<table>
<thead>
<tr>
<th>Perforators</th>
<th>Standing</th>
<th>Sitting</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 105</td>
<td>4.3±6.4*</td>
<td>3.5±7.4</td>
<td>2.3±4.9</td>
</tr>
</tbody>
</table>

$t(208)=2.53, p=.05$ *standing versus supine.

Table 4.10 Peak Venous Blood Flow (mL/min) in Medial Calf Perforators in Different Zones

<table>
<thead>
<tr>
<th>Zone</th>
<th>Standing</th>
<th>Sitting</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower</td>
<td>6.7±8.5</td>
<td>5.7±11</td>
<td>3.7±7.2</td>
</tr>
<tr>
<td>Mid</td>
<td>2.9±3.8</td>
<td>3.1±5.2</td>
<td>1.6±2.4</td>
</tr>
<tr>
<td>Upper</td>
<td>2.8±4.5</td>
<td>1.3±2</td>
<td>1.2±2.4</td>
</tr>
</tbody>
</table>

$F(8, 306) = 3.59, p = .0005.$

Figure 4.5 Mean Venous Blood Flow (mL/min) in the Different Positions and when split into Zones. $F(8, 306) = 3.59, p = .0005.$

4.2.8 Direct Vs Indirect Peak Velocity Flows

There was no difference in PVF between direct and indirect perforators the postural differences were similar for each (Table 4.11).
Table 4.11 Peak Venous Flow (mL/min) when Comparing Direct and Indirect Perforators.

<table>
<thead>
<tr>
<th>Peak Velocity Flow mL/min</th>
<th>Standing</th>
<th>Sitting</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct (n= 88)</td>
<td>15±15</td>
<td>11±14</td>
<td>8.6±11</td>
</tr>
<tr>
<td>Indirect (n = 17)</td>
<td>16±12</td>
<td>11±11</td>
<td>8.7±8.5</td>
</tr>
</tbody>
</table>

$t(103) = .59, p = >0.05.$

4.2.9 Spontaneous Perforator Blood Flow

Along the medial calf 47.6% of the perforators were found to have spontaneous flow when observed prior to any activity. These were distributed equally in each of the three zones from the lower to the upper zones (Tables 4.12 & 4.13, Figure 4.6). The spontaneous flows within the perforators were all inwards and appeared to be influenced by the arterial pulsations with a phasic (approx 60/min) spectral Doppler effect as observed in Figure 4.6.

![Figure 4.6 Spectral Doppler Ultrasonographic Image demonstrating Spontaneous Flow in a Venous Perforator at Rest from Superficial to Deep Compartment.](image)

Table 4.12 Proportion of Perforators with Spontaneous Flow in the Medial Calf at Rest

<table>
<thead>
<tr>
<th></th>
<th>Total 20(105)</th>
<th>Lower</th>
<th>Mid</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>n= 50 (47.6%)</td>
<td>19</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Non-Spontaneous</td>
<td>n = 55 (52.4%)</td>
<td>20</td>
<td>17</td>
<td>18</td>
</tr>
</tbody>
</table>
Table 4.13 Spontaneous Blood Velocity (cm/s) in the Medial Calf Perforators of Normal Limbs Pre Exercise Split by Zone

<table>
<thead>
<tr>
<th>Perforator n=50 (20 Limbs)</th>
<th>Lower n=19</th>
<th>Mid n=15</th>
<th>Upper n=16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Exercise Spontaneous Flow</td>
<td>4.6±3.7</td>
<td>4.1±1.9</td>
<td>3.9±3.3</td>
</tr>
</tbody>
</table>

4.2.10 Exercise Effect on Spontaneous Flow and Flow Pattern

Following five minutes of treadmill walking at a 10° gradient exercise induced spontaneous flow was detectable in 71.5% of the perforators Table 4.14. When compared by zones there was no significant difference along the medial calf. There was also no significant found between zones when compared to the resting group; p = > 0.5

Compared as a total group there was significance with a small increase in perforator velocities along the length of the medial calf from 4.2 cm/s to 5.6 cm/s within this sample population (Table 4.15, Figure 4.7).

Table 4.14 Spontaneous Blood Flows (cm/s) in the Medial Calf Perforators of Normal Limbs following Exercise Split by Zones

<table>
<thead>
<tr>
<th>Perforator n = 75 (20 limbs)</th>
<th>Lower</th>
<th>Mid</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise Effect</td>
<td>5.5± 2.8</td>
<td>5.8±2.4</td>
<td>5.5±2.4</td>
</tr>
</tbody>
</table>

t(204)=1.9, p = >.05
Table 4.15 Percentage of Spontaneous Flows seen to Perforators following Exercise along the medial calf.

<table>
<thead>
<tr>
<th>Spontaneous Velocities</th>
<th>Perforator Number</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower</td>
<td>(26 / 75)</td>
<td>34%</td>
</tr>
<tr>
<td>Mid</td>
<td>(21 / 75)</td>
<td>28%</td>
</tr>
<tr>
<td>Upper</td>
<td>(28 / 75)</td>
<td>37%</td>
</tr>
</tbody>
</table>

Table 4.16 Pre and Post Exercise Spontaneous Perforator Velocities (cm/s) of the medial calf.

<table>
<thead>
<tr>
<th>Perforator (20 Limbs)</th>
<th>Pre-Exercise n = 50</th>
<th>Post Exercise n = 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD</td>
<td>4.2±0.44</td>
<td>5.6±0.29</td>
</tr>
</tbody>
</table>

$ t(123) = 2.737, p > 0.007$

Figure 4.7 Example of a Spontaneous Perforator following Exercise

The image has not been inverted. Inward flow is demonstrated with a phasic response similar to the spontaneous flow observed in Figure 4.6.

4.2.11 Isometric Planter Flexion Effects

Isometric planter flexion was performed with the participant in the standing position and a spectral Doppler recorded at each perforator (Figure 4.8). There was no flow in the perforator during the active isometric contraction phase (muscle pump systole) but sudden inflow on release with relaxation (muscle pump diastole). Where there was previously spontaneous flow in Figure 4.8 this was shut off by the isometric contraction only to accelerate to a peak
with relaxation. This peak was similar to a pattern frequently seen on augmentation (Figure 4.8).

![Figure 4.8 Spectral Doppler Venous Perforator Response during Planter Flexion in a Standing Position.](image)

Blood flow was induced across 103 perforators (20 limbs) with the level of activity only slightly more in the lower zone, however this was not significant, neither was the difference when compared against distal augmentation in the three positions (Table 4.16).

### Table 4.17 Comparing PSV (cm/s) on Planter Flexion to a Standing Distal Augmentation.

<table>
<thead>
<tr>
<th></th>
<th>Lower n=39</th>
<th>Mid n=33</th>
<th>Upper n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planter Flexion</td>
<td>14±7.9</td>
<td>11±5.4</td>
<td>11±6.7</td>
</tr>
<tr>
<td>Distal augmentation Standing</td>
<td>19±16</td>
<td>13±11</td>
<td>13±15</td>
</tr>
</tbody>
</table>

\[ F (2,102) = 0.95, p = 0.389 \]
Peak velocity was correlated between that induced following isometric planter flexion with that achieved by distal augmentation in each perforator. There was no correlation for the 103 perforators, suggesting different mechanisms (Figure 4.9).

![Planter Flexion Vs Distal Augmentation Standing](image)

*Figure 4.9 Pearson Correlation of PSV (cm/s) during Planter Flexion Compared with Distal Augmentation on Standing.*

(r = 0.04)

4.2.12 Spectral Doppler Pattern Type On Distal Augmentation

Each individual perforator was stimulated by a distal augmentation as this is the standard test of competence used to determine the normal blood flow response within perforators. There were three main spectral Doppler trace patterns observed following this stimulus. The different trace patterns were labeled as type one, two and three respectively as shown in Figure 4.10. In each of the different postures it was observed that pattern types one and three were the most common in the medial calf (approximately 40%) Table 4.17.
Table 4.18 Spectral Doppler Pattern Types following Distal Augmentation in Different Positions

<table>
<thead>
<tr>
<th>Position</th>
<th>Total</th>
<th>Pattern Type One</th>
<th>Pattern Type Two</th>
<th>Pattern Type Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>105</td>
<td>42 (40%)</td>
<td>20 (19%)</td>
<td>43 (41%)</td>
</tr>
<tr>
<td>Sitting</td>
<td>103</td>
<td>42 (40.7%)</td>
<td>16 (15.5%)</td>
<td>45 (44%)</td>
</tr>
<tr>
<td>Supine</td>
<td>101</td>
<td>56 (55%)</td>
<td>7 (6.9%)</td>
<td>38 (37.6%)</td>
</tr>
</tbody>
</table>

Type one was assigned as the pattern type when flow was observed in one direction only following a distal augmentation; pattern type two was assigned when flow was observed in an inward flow, followed immediately by outward flow; type three was assigned when flow was observed as an initial inward flow, followed by an outward flow and then a second inward flow as observed in Figure 4.10.
Figure 4.10 Spectral Doppler Pattern Types from Perforators along the Medial Calf on Distal Augmentation.

Spectral Doppler demonstrating inward flow on distal augmentation. These went from a uni-directional to a multi-directional complex appearance. (a) Type 1 (b) Type 2, (c) Type 3. All spectral traces have been inverted. A negative shift (upwards) demonstrates inward flow.
The pattern types in the sitting position were found to be significantly different when compared to diameter as shown in Table 4.19. There was no difference seen between the diameter and pattern types in the other two positions.

Table 4.19 Spectral Doppler Compared to Diameter (mm)

<table>
<thead>
<tr>
<th>Position</th>
<th>Total</th>
<th>Pattern Type One</th>
<th>Pattern Type Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>42/43</td>
<td>1.34± 0.69</td>
<td>1.6± 0.72</td>
</tr>
<tr>
<td>Sitting</td>
<td>42/45</td>
<td>1.17±0.57</td>
<td>1.71±0.67*</td>
</tr>
<tr>
<td>Supine</td>
<td>56/38</td>
<td>1.42± 0.67</td>
<td>1.56±0.76</td>
</tr>
</tbody>
</table>

$F (4, 519) = 8.22, p = 0.0001$ *

The peak velocity was found to be significantly different between pattern types in the standing and sitting position Table 4.20.

Table 4.20 Spectral Doppler Pattern Types Compared to Peak Systolic Velocity (cm/s)

<table>
<thead>
<tr>
<th>Position</th>
<th>Pattern Type One</th>
<th>Pattern Type Two</th>
<th>Pattern Type Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>8.42±8.87</td>
<td>29.9±18.14</td>
<td>14.87±11.84</td>
</tr>
<tr>
<td>Supine</td>
<td>5.0±0.23</td>
<td>13.51±13.25</td>
<td>18.4±20.95</td>
</tr>
</tbody>
</table>

$F (3,182) = 11.02, p = 0.0001$
4.3 Discussion

The importance of the medial calf perforator continues to be consistently seen as playing a major role in the function and severity of chronic venous insufficiency [13, 18]. This may simply have resulted from the fact that the greatest concentrations of incompetent perforators are located in the medial calf, as will be outlined in Chapter 6[20, 21], and most of the understanding of perforator functions historically concluded from subjects with abnormal venous function[106]. There is a need therefore to go back and better understand how the venous perforator might behave in the medial calf in a population of normal subjects. This study has been an attempt towards this, using duplex ultrasound assessment.

One measure of normal function has been the diameter of a perforator. It has been said that perforators < 3 mm are unlikely to be abnormal. However this is a simplistic view and there is more to diameter than this. Perforator diameters in the medial lower leg in our study may be greater in males, but this is not statistically significant with a relatively small sample.

Perforators in the lower region of the medial calf are larger, and pass more directly into the deep system and therefore this may be relevant as these are the sites where most incompetent perforators and ulceration occur in the diseased population. Could this slight size difference be a reflection of the greater pressure placed on the gaiter region, as observed by Bjordal[24] when assessing pressure profiles in the PTV? These gaiter region perforators are all in direct communication with the PTV. They incidentally were the only perforators in which an obvious valve could be identified on B-mode ultrasound and had the largest flow rates with distal augmentation. This suggests that in this region the perforators perform a greater role in
redirecting superficial venous blood flow, and may have greatest susceptibility to incompetence, with possibly far greater consequence.

This same region of the medial calf was found to have no obvious difference in relation to venous blood velocities on distal augmentation in the standing position when compared to a planter flexion / isometric contraction. This in itself is significant as it demonstrates that perforators act in a similar way when we produce a stimulus and perform a planter flexion.

If we were to apply the new theories viewing venous insufficiency more as an ascending condition, as suggested by Bernardini [113], then could the level of hydrostatic pressure and diameter size of the perforators in the lower region of the medial calf be a reflection of this process to endure greater workload? The foot pump activates the planter muscles and so results in a greater expulsion of blood forward within the superficial venous system[9].

The point where the venous perforator traverses the fascia plane is agreed as the most optimal site to determine true function when insonated in both colour and Spectral Doppler[51]. In this research it was observed that the spectral Doppler waveforms produced following distal augmentations were mainly composed of three pattern types. Although these three pattern types were not shown to be statistically significant when compared to perforator diameter, they however may simply denote a normal functional response of perforators at the point of insonation. Diameter was only significant in the sitting position, which may demonstrate a pressure difference while sitting which causes more pooling due to compression on sites within the deep venous system, especially around the region of the adductor hiatus. These spectral Doppler findings may best represent the response of the perforator and its valve when blood is passed over it. Forty percent of all spectral Doppler waveforms were either mono-phasic or tri-phasic patterns. A level of reverse flow is evident in normal perforators on distal
augmentation, however I am suggesting that this is simply valve closure versus blood flow along a short vessel segment. This reinforces the importance of always using spectral Doppler to quantify both direction and time when assessing function rather than relying on a visual observation and colour Doppler.

The peak velocity was found to be significant in the standing and sitting positions when compared to their pattern types. This may simply be a response to the distal augmentation in relation to the perforator location.

Spontaneous flow along the medial calf was found in 50% of perforators when in a resting state. This is interesting in that the superficial system may constantly be emptying its venous volume, and these perforators may therefore have a different function when in an active state.

The relationship of the standard compression test to normal physiological function must be challenged by some of the observations, at least when compared to an isometric plantar contraction. The time relationships are quite different. Although the magnitude of peak velocity and flow achieved through each perforator could be expected to have some correlation, disappointingly this was not the case. The relevance to abnormal function (incompetence) has yet to be examined.
Chapter 5:

5 The Fate of Venous Perforators following Varicose Vein Surgery

Whatever the correct approach, there is no doubt that incompetent perforators recur after treatment and that more incompetent perforators mean worse disease severity\textsuperscript{[114]}. Unfortunately, little is known about the frequency and origin of “recurrent” perforators. Are these previously competent perforators, or missed incompetent perforators, or are they possibly the result of neovascularization \textsuperscript{[15]}? Understanding this would provide better insights for prevention. In the past, the invasive methods of venography did not permit serial evaluation of recurrence; this is now possible with detailed, meticulous, ultrasound assessment\textsuperscript{[15, 93, 100]}. The aim of this prospective observational study was to determine the causes of perforator recurrence and their relative importance following varicose vein surgery.

5.1 Method

All patients between the age of 20 and 75 years referred to the vascular laboratory for venous assessment before varicose vein surgery were invited to participate in a larger prospective study of the long-term outcomes of varicose vein surgery. Patients unable to attend follow up and those with obstructed venous outflow were excluded.

This study is an analysis of the perforator veins in the first 104 consecutive patients (145 limbs) who gave informed consent and then had venous surgery. All major varicosities and incompetent perforators were marked pre-operatively by using duplex ultrasound.
The surgery was primarily for saphenofemoral junction ligation, with stripping of the great saphenous vein (GSV) to the level of the knee, and avulsions of varicosities. Ligation of all incompetent perforators was done in an identical fashion by short incision directly over the marked sites and ligation at the fascia. No subfascial endoscopic perforating vein surgery (SEPS) was used.

Any incompetent perforators remaining after surgery that had been previously identified were noted, and ultrasound-guided sclerotherapy was offered to obliterate these. Treatment was considered complete when all previously marked incompetent perforators were obliterated.

5.1.1 Patient assessments
All patients were assessed pre-operatively, and then scanned again at the time of the vein marking session, on the day of surgery and post-operatively at 1, 6, 12 and 36 months. Venous assessment included a full Duplex ultrasound scan and physiologic tests with air plethysmography (APG) as described previously.[100]

5.1.2 Definition of Perforators
An incompetent perforator was defined as a perforator that allowed either an outward flow or a bi-directional flow to both distal and proximal augmentation of > 0.3 seconds. Both colour and spectral Doppler was applied to quantify incompetence. The foot was not assessed during this study. The locations for incompetent veins only were subsequently confirmed by ultrasound and marked on the skin immediately preoperatively to guide the surgeons.

The definitions of the types of perforator for the purpose of the study were:
Original – any perforator noted at the pre-operative assessment.
Obliterated – an incompetent perforator noted pre-operatively and no longer present after treatment.
Missed – a previously incompetent perforator remaining at the one month assessment that had not been surgically ligated. These were subsequently to be treated by sclerotherapy.

New – any perforator, which can either, be normal or incompetent, not previously seen at the pre-surgical assessment.

Recurrent – any perforator, which can either, be normal or incompetent appearing at the site of previous successful treatment defined as being within 1 cm of the obliterated perforator. These are attributed to neovascularization.

Absent – a perforator previously observed but no longer identifiable.

The later three types could be either competent or incompetent.

5.1.3 Statistical Analysis

Statistical analysis was performed using Stat View software (Berkeley, California). The Students t test was used for continuous variables. The values are described as mean ± standard deviation (SD). Differences in proportions were evaluated with the $\chi^2$ test. Statistical significance was assigned at $P \leq 0.5$

5.2 Results

There were 104 patients (68 female, 36 male; age 53.0 ± 10.6 years; body mass index [BMI], 28.3 ± 5.9) whose limbs had a range of severity of venous disease features typical of our surgical varicose vein practice (Table 5.1). In the 145 limbs, 1206 perforators were identified of which 850 were incompetent and targeted for surgical ablation. There were 5.8 ± 3.0 of these incompetent perforators per limb (range 1 - 16; median 5) with a mean diameter of 3.50 ± 1.21 mm, (range 1 - 12 mm; median 3.2 mm).
Table 5.1 Comparison of Limbs Preoperatively to Limbs with and without Incompetent Perforators Three Years Following Surgery.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (n=145)</th>
<th>Total (n=145)</th>
<th>No Incompetent Perforators (n=35)</th>
<th>Incompetent Perforators (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous surgery (%)</td>
<td>63 (41.4)</td>
<td>63 (41.4)</td>
<td>2 (5.7)*</td>
<td>61 (47.2)</td>
</tr>
<tr>
<td>CEAP grades 1-3 (%)</td>
<td>85 (58.5)</td>
<td>86 (59.3)</td>
<td>27 (77.1)*</td>
<td>59 (53.6)</td>
</tr>
<tr>
<td>CEAP grades 4-6 (%)</td>
<td>60 (41.5)</td>
<td>59 (40.7)</td>
<td>8 (22.9)*</td>
<td>51 (46.3)</td>
</tr>
<tr>
<td>Deep reflux (%)</td>
<td>9 (5.8)</td>
<td>8 (5.5)</td>
<td>1 (2.8)</td>
<td>7 (6.3)</td>
</tr>
<tr>
<td>VFI ml/sec</td>
<td>5.26 ± 4.08</td>
<td>1.9 ± 1.7</td>
<td>1.4 ± 0.9*</td>
<td>2.08 ± 1.8 ‡</td>
</tr>
<tr>
<td>VFI&gt;2ml/sec (%)</td>
<td>107/131 (81.6)</td>
<td>49/129 (38.0)</td>
<td>6/26 (23.1) †</td>
<td>43/103 (41.7) **</td>
</tr>
<tr>
<td>VFI&gt;4ml/sec (%)</td>
<td>62/131 (47.3)</td>
<td>11/129 (8.5)</td>
<td>0 (0)*</td>
<td>13/103 (12.6) ‡</td>
</tr>
<tr>
<td>Incompetent Perforators per limb</td>
<td>5.8 ± 2.9 [1-16]</td>
<td>2.5± 1.9 [0-11]</td>
<td>0</td>
<td>3.4 ± 2.3 [1-11] ‡</td>
</tr>
</tbody>
</table>

Data is represented as counts (as a percentage) or mean ± Standard Deviation [range]

* Comparison with preoperative and 3 year incompetent limbs p<0.001
† Comparison with preoperative and 3 year incompetent limbs p<0.01
‡ Comparison with pre-operative limbs p<0.001
§ Comparison with pre-operative limbs p<0.01

5.2.1 Disease Severity and the number of Incompetent Perforators

The total number of incompetent perforators studied in limbs with clinical CEAP class 1-3 and CEAP class 4-6 limbs were equal, although limbs with more incompetent perforators had more severe disease (Table 5.2). The competent perforators recorded were fewer at 356 (2.3 ± 2.0/limb, range 0 - 8; P < .005), had a smaller diameter (1.9 ± 0.7 mm, P < .001) and were distributed proportionally less in the paratibial and medial gastrocnemius regions compared to the incompetent perforators.
Table 5.2 Comparison of Disease Severity in Limbs with Six or more Incompetent Perforators Preoperatively to Limbs with less than Six Incompetent Perforators.

<table>
<thead>
<tr>
<th></th>
<th>6 or more Incompetent Perforators (n=67)</th>
<th>Less than 6 Incompetent Perforators (n=78)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.8±9.9</td>
<td>52.8±10.9</td>
<td>n.s</td>
</tr>
<tr>
<td>BMI</td>
<td>29.0±5.3</td>
<td>27.4±6.0</td>
<td>n.s</td>
</tr>
<tr>
<td>CEAP (class 4-6)</td>
<td>32/67</td>
<td>28/78</td>
<td>n.s</td>
</tr>
<tr>
<td>Venous Filling Index</td>
<td>6.8±4.1</td>
<td>4.1±3.8</td>
<td>0.0002</td>
</tr>
<tr>
<td>(ml/sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous Filling Time</td>
<td>39.0±24.9</td>
<td>60.6±41.0</td>
<td>0.0006</td>
</tr>
<tr>
<td>(sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcer Index</td>
<td>129.1±115.9</td>
<td>256.4±569.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ejection Volume (ml)</td>
<td>89.0±30.9</td>
<td>68.3±33.4</td>
<td>0.0004</td>
</tr>
<tr>
<td>Venous Volume (ml)</td>
<td>172.5±61.3</td>
<td>127.5±44.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Residual Volume (ml)</td>
<td>68.2±41.2</td>
<td>52.2±33.4</td>
<td>0.02</td>
</tr>
</tbody>
</table>

n.s., not significant; VFI, venous filling index; VFT, venous filling time.

Following surgery, 44 incompetent perforators had been missed (4.7%) of which 8 had become competent - a surgical failure rate contributing to recurrence of 3.8%. Sclerotherapy in those patients who agreed to this meant that a total of 841 incompetent perforators were obliterated (99%) at the commencement of the longer-term follow up (Table 5.3). A number of competent perforators had diminished, of which some could no longer be seen (“absent perforators”), and two had become incompetent. Even at this initial postoperative assessment, however, 30 new incompetent perforators were already apparent.
Table 5.3 Comparison of Diameter among Perforator Types preoperatively and at Three Years.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Competent perforators (mm)</strong></td>
<td>1.9± 0.7</td>
<td>1.8± 0.6</td>
</tr>
<tr>
<td>Total</td>
<td>n = 356</td>
<td>n = 1047</td>
</tr>
<tr>
<td><strong>Incompetent perforators (mm)</strong></td>
<td>3.50± 1.21*</td>
<td>2.79± 0.96</td>
</tr>
<tr>
<td>Total</td>
<td>(1.0 – 11.4)</td>
<td>(0.9 – 7.8)</td>
</tr>
<tr>
<td></td>
<td>n = 850</td>
<td>n = 380</td>
</tr>
<tr>
<td>New (mm)</td>
<td>-</td>
<td>2.65± 0.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.9 – 6.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 225</td>
</tr>
</tbody>
</table>

Surgical missed incompetent perforators at 3 years (3) are included only in the total.

* Different to all other groups p<0.0001,
† Different to all incompetent groups p< 0.0001
‡ Different to similarly marked groups p<0.0001,
§ Diameter of those obliterated incompetent perforators that recurred by 3 years compared to those that did not recur p< 0.0001

After 3 years 576 (67.8%) of the ligated perforators remained obliterated. In the intervening time, from 6 months onwards, a gradual reappearance of incompetent perforators was noticeable at the sites of previous surgery (Table 5.4). The rate of this neovascular recurrence was 29.9%; but only 152 of 252 of these neovascular perforator veins were incompetent; hence, the neovascular incompetence rate following ligation was 17.8 % at 3 years. This includes incompetence after recanalization, also a form of neovascularization, of 15 (41%) of 37 perforators closed by sclerotherapy compared with 15% of those surgically ligated (P< 0.01). As other incompetent perforators also appeared during the same time, neovascular recurrence accounted for only 152 (40.4%) of all 376 incompetent perforators. The most prevalent incompetent perforators (58.8%) were new incompetent perforators (Table 5.4). These newly developing incompetent perforators were distant from the surgical sites. Only a few were due to incompetence developing in competent perforators observed preoperatively. Most were due, presumably, to other competent perforators becoming incompetent with continuing venous insufficiency.
Table 5.4 The Progression of Incompetent Perforators in 155 Limbs.

<table>
<thead>
<tr>
<th>Status</th>
<th>Original</th>
<th>New</th>
<th>Neovascular Recurrence</th>
<th>Missed (uncorrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>850</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1 month</td>
<td>-</td>
<td>30</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>6 months</td>
<td>-</td>
<td>47</td>
<td>9</td>
<td>43</td>
</tr>
<tr>
<td>1 year</td>
<td>-</td>
<td>83</td>
<td>12</td>
<td>71</td>
</tr>
<tr>
<td>3 year</td>
<td>-</td>
<td>209</td>
<td>16</td>
<td>152</td>
</tr>
</tbody>
</table>

Number of the initial surgical failures not dealt with by sclerotherapy

Development of incompetent perforators in a limb was associated with onset of more severe venous reflux compared with limbs in which no incompetent perforators had arisen (Table 5.1). Factors at the time of surgery, including age, gender, side of limb, BMI, or the presence of deep reflux did not predict the appearance of incompetent perforators. Previous varicose vein surgery (P < 0.001), clinical class (CEAP 4-6), and venous filling index (6.4 ± 4.4 mL/s vs 3.7 ± 2.9 mL/s, P < 0.005) did predict the development of incompetent perforators. None of these factors were either predictive of, or associated with, the development of the specific type of incompetent perforator, new or recurrent.

At the time of surgery the diameter of the incompetent perforators was substantially greater than at any other time in the study (P < 0.001). As new perforators developed, the diameter of the competent ones was unchanged despite the large change in numbers seen (Table 5.3). The neovascular recurrences had diameters that were significantly larger than the new incompetent perforators, and they occurred at sites where the incompetent perforators before surgery were larger (Table 5.3).
5.2.2 Anatomical Distribution

The anatomical distribution of the two major types of new incompetent perforators was quite different. Neovascular recurrence occurred predominantly in the paratibial region (64%), whereas new incompetent perforators occurred there in only 35% (P < .01). In contrast, new incompetent perforators arose proportionately more in the lateral leg (26% vs 11%, P < .01). The regional distribution of the new incompetent perforators was the same as for the competent perforators both before surgery and at 3 years.

5.2.3 Ultrasound Grapher Expertise and Possible Bias

Also noted at the 1 and 3 year follow-up periods was a surprising increase in the number of competent perforators (Table 5.3), and correspondingly, the number of competent and incompetent perforators per limb increased. The possibility of a time bias resulting from improving ultrasound grapher expertise and equipment or a patient selection bias was excluded by comparing the demographics and frequency of perforators recorded in a cohort at the beginning and at the end of the study. No significant bias was observed.

During the study 2437 individual perforators were identified. Despite careful documentation of location, some perforators seen at one assessment could not be located on the next. At the 3-year assessment, 450 perforators were absent. During the study, a small number of perforators were competent at one assessment and incompetent at the next and vice versa. These were assigned the status observed on the day, and did not affect the overall observations.
5.3 Discussion

To our knowledge, this research presents for the first time, evidence that the phenomena of neovascular recurrence occurs following ligation of venous perforators in varicose vein surgery and that it is not unique to the saphenofemoral junction. Recurrence occurred at the site of ligation in 32.2% of perforators. These appear to be the same sites as ligation by careful repeated measurement and by the appearance of scar tissue and typical tortuosity. Also, we took biopsies of these recurrent perforators and observed the appearance of neovascular channels in the specimens[15]. Just as with other sites of venous surgery, neovascular recurrence is much more common than previously realized[15, 115, 116]. This is not surprising, as angiogenesis is a normal component of healing of the ligated perforator and produces the focus for normal vessel formation. These enlarge to form new venous channels that reconnect the deep and superficial venous compartments.

These recurrent perforators occur predominantly in the paratibial region on the medial aspect of the lower leg. Most are incompetent (63%), and after 3 years these are larger than the incompetent new perforators, suggesting that reflux through them is more severe. In situ hemodynamic performance measurements, as described by Delis et al[117], would be required to confirm this however. Not surprisingly, development of recurrence by neovascularization was associated with worsening reflux and clinical disease. Those incompetent perforators that were larger before surgery or in the paratibial location were more likely to recur. The preoperative likelihood of recurrence was greater in legs with severe clinical disease, worse venous reflux, and more incompetent perforators. This recurrence was also more common in the perforators closed by sclerotherapy, and invariably, these neovascular channels became incompetent. The numbers in this study were too few to make much of this observation, however. It is consistent with the lesser durability of sclerotherapy than of surgery[118].
The commonest incompetent perforators occurring after surgery derived from pre-existing competent perforators (60%). A small proportion (1 - 2%) was from those that were observed before surgery, but most arise from pre-existing perforators not observed before surgery. These two types of new incompetent perforator together are characterized by being the most numerous (60% of all incompetent perforators 3 years after surgery) and distributed in the leg in a general pattern similar to competent perforators, are found away from sites of surgical activity, and are smaller in diameter compared with neovascular recurrence.

The other type of incompetent perforators is the one missed in surgery. Despite detailed ultrasound assessment, accurate pre-operative marking and experienced surgeons, the surgical miss rate in this study was still significant at little less than 5%. The configuration of vessels in the vicinity of the incompetent perforators can be complex, and care in identifying the entry through the fascia is critical. Factors contributing to this failure include difference in position at time of marking and at surgery as well as obesity of the limb. Intra-operative ultrasound may reduce the miss rate.

A new and unexpected observation in this ultrasound-based study was the increasing number of new competent perforators appearing during the 3-year period after surgery. Only a few perforators have been anatomically described and labeled with eponyms\(^42,104\). Similarly with standard ultrasound techniques, relatively few perforators are detectible. In limbs with venous disease, only 2.9 per limb with 55% incompetence were found in one report\(^2\) - but as many as 8.3 per limb and 70% incompetence are shown in this study, bringing the detection limit down to 0.8 to 0.9 mm by using both a 12-5 MHz linear array probe with colour and spectral Doppler modalities and a time – consuming protocol to ensure a full leg scan.
In contrast, we know from detailed anatomic dissections that there may be as many as 60 perforators in the normal lower limb, therefore many smaller venous perforators remain undetected by ultrasound because of their size and competence. However, these same small perforator vessels, as they enlarge and remodel under the influence of changing venous hemodynamics, will become detectable. It is therefore my hypothesis that worsening venous function and flow load on perforators is the cause of the large increase in the number of new ultrasound-detectable competent perforators observed in this study (2.5/limb preoperative vs 7.1/limb at 3 years).

The increase in the number of new incompetent perforators observed in this study can also be understood with this hypothesis. As further dilatation in some of the newly detectable perforator veins occurs, incompetence will result. The relationship of perforator incompetence with increased size is well described. The valves present in these veins, of quite small size (down to 0.1mm diameter), become incompetent, and in those perforators without valves, which normally allow to and fro flow, the “shutter effect” at the fascia interface becomes less effective.

This study has important limitations. Although ultrasound has been validated for guiding surgical intervention with a sensitivity of 82% and specificity of 100% of predicting the site of perforating veins at the medial side of the lower leg, this has not been done for competent and smaller incompetent perforators.

Our own experience in this study has been comparable. Identifying each of the 2437 perforators and following these over several assessments during the study was a demanding exercise. Localizations are affected by technique, patient habitus and posture. Despite this,
reproducibility was very good and best for recurrence of ligated vessels, where scarring at the fascia interface provided extra assistance.

The choice of criteria for assigning incompetence continues to be debated. It is further made difficult by the realization that some normal competent perforators allow both inward and outward flow\cite{108}. The primary aim of the study was to observe what happened to ligated perforators, however, and we considered that the study design of ligating all perforators with reflux time of > 0.3 seconds, regardless of size, served that purpose.

These findings only describe events out to 3 years and doesn’t allow us to say whether the increase in numbers has reached a plateau, nor whether more would become incompetent. Similarly, no comparisons could be made with the natural history of untreated incompetent perforators.

These findings highlight the frequency with which incompetent perforators develop after surgery and the predictors of this are the same as for recurrence at the saphenofemoral junction\cite{4}. The clinical relevance of this is that, as we have shown, the greater the number of perforators, the worse the reflux and the greater the clinical severity of the venous disease. For the surgeon, this provides evidence for better informing patients about the possible later reappearance of varicose veins after surgery, and that this is less a matter of the adequacy of surgery and more a result of the underlying disease. Limbs that do not develop recurrent incompetent perforators are those having a first operation for mild disease (CEAP Class 1-3) with modest reflux (Venous Filling Index < 4 mL/s).

The types of incompetent perforators that appear after surgery also have clinical relevance in directing efforts towards preventing recurrence. For the surgical approach, minimal tissue disturbance should be aimed for to reduce the angiogenic response and neovascularization.
The new technologies of laser and radiofrequency venous endoablation are directed toward reducing neovascularization by avoiding transecting veins. A similar intent to reduce perforator recurrence with subfascial endoscopic perforator ablation, unfortunately, has not avoided recurrence\textsuperscript{[122]}.

The most common postoperative incompetent perforators arise from pre-existing perforators with persistent venous hemodynamic disturbance, and preventing this may be a more difficult challenge. Fortunately, the least common incompetent perforator is the result of missed ligation. Better imaging, mapping and marking, as well as intra-operative ultrasound provide scope for improvement.
Chapter 6

6 The characteristics of perforators in limbs with varicose vein disease.

Having described the distribution and features of perforators in normal subjects it is pertinent to examine how this may differ between patients with varicose veins and those who have had previous varicose vein surgery. There is a suggestion from the earlier work that perforators, even when competent, may differ in those with varicose veins when compared to normal subjects.

6.1 Method

Comparisons were made between the features of perforators in normal limbs as described in Chapter 3 and in the limbs of subjects with varicose veins as described in Chapter 5. The perforators were compared for regional distribution, diameter, deep and superficial communications, and seasonal effect.

Data acquired from study one was compared against the varicose vein patients in the longitudinal study. Comparisons were primarily of competent perforators and in the varicose vein group competent perforators both before surgical intervention and after 3 years. The incompetent vessels were also compared for completeness. In addition, it was possible to examine the seasonal effect on the diameter of the normal perforators in the large cohort of patients. This was done by selecting and sorting each subject group into the time of day and date of vascular laboratory assessment. This was then sorted to the seasonal calendar.
6.2 Results

As referred to earlier in Chapter three, there were 14.2 perforators identified per limb in normal subjects, this was greater than in the diseased group where 8.4 & 10 perforators per limb respectively were detected in the Pre-op VV and 3 year post-op VV as seen in Table 6.1.

<table>
<thead>
<tr>
<th></th>
<th>Normal Limbs n =20</th>
<th>Pre-op Limbs n = 144</th>
<th>3 yr Limbs n =141</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Perforator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number n</td>
<td>283</td>
<td>1212</td>
<td>1415</td>
</tr>
<tr>
<td>Average</td>
<td>14.2</td>
<td>8.4</td>
<td>10</td>
</tr>
<tr>
<td>Range</td>
<td>8 - 21</td>
<td>2 - 20</td>
<td>1 - 23</td>
</tr>
<tr>
<td>Median</td>
<td>13</td>
<td>8</td>
<td>10</td>
</tr>
</tbody>
</table>

There was a significant difference between the normal subjects’ perforator diameter and pre-op and 3 years post-op varicose veins groups. The diameters of each perforator group are outlined in Table 6.2. The normal subjects had a mean diameter of 1.3± 0.6mm compared against the Pre-op VV and 3 years follow-up in relation to both the normal and incompetent perforators with mean diameter of 1.9 ± 0.65mm & 1.8 ± 0.64mm respectively. These were all significantly different.
All incompetent perforators were then removed from the two diseased groups and residual competent perforator compared against the normal population. Again the normal population perforator diameters were significantly smaller than that of the pre-op and 3 years post-op varicose veins group (Table 6.2).

### 6.2.1 Distribution of Perforators across Three Groups

The regional distributions of all the perforators groups are shown in Figure 6.3. Few perforators (12 limbs, 9% of the perforators) could be identified in the thigh of normal subjects when compared to the pre-op and three years post-op varicose veins groups. There was an increase of medial and lateral calf perforators from the normal group when compared to the three years post-op population. The comparison of the normal population against the pre-op varicose vein group and their normal function perforator number was the same in the remaining regions of the lower limb.
Table 6.3 Regional Distribution of Normal Perforators Across Three Groups.

<table>
<thead>
<tr>
<th></th>
<th>Paratibial</th>
<th>Posterior Tibial</th>
<th>Medial Gastroc</th>
<th>Lateral Gastroc</th>
<th>Lateral Calf</th>
<th>Anterior Calf</th>
<th>Femoral Canal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>n = 53</td>
<td>n = 50</td>
<td>n = 34</td>
<td>n = 16</td>
<td>n = 80</td>
<td>n = 38</td>
<td>n = 12</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.3±0.5</td>
<td>1.5±0.8</td>
<td>1.5±0.5</td>
<td>1.4±0.5</td>
<td>1.3±0.4</td>
<td>1.0±0.3</td>
<td>1.4±0.6</td>
</tr>
<tr>
<td>Median</td>
<td>1.2</td>
<td>1.2</td>
<td>1.4</td>
<td>1.3</td>
<td>1.2</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Range</td>
<td>0.4 – 2.6</td>
<td>0.4 – 3.5</td>
<td>0.5 – 2.8</td>
<td>0.8 – 2.4</td>
<td>0.4 – 2.9</td>
<td>0.5 – 2.5</td>
<td>0.5 – 2.2</td>
</tr>
<tr>
<td>Pre-op</td>
<td>n = 49</td>
<td>n = 56</td>
<td>n = 50</td>
<td>n = 27</td>
<td>n = 94</td>
<td>n = 33</td>
<td>n = 44</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.9±0.6</td>
<td>1.8±0.6</td>
<td>2.0±0.7</td>
<td>1.8±0.6</td>
<td>1.9±0.7</td>
<td>1.8±0.6</td>
<td>1.9±0.7</td>
</tr>
<tr>
<td>Median</td>
<td>1.8</td>
<td>1.8</td>
<td>2.0</td>
<td>1.8</td>
<td>1.8</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Range</td>
<td>1 – 3.8</td>
<td>0.7 – 3.2</td>
<td>0.8 – 4.8</td>
<td>0.8 - 3</td>
<td>0.8 – 4.6</td>
<td>1 – 3.5</td>
<td>0.7 – 3.6</td>
</tr>
<tr>
<td>3 Years Post-op</td>
<td>n = 266</td>
<td>n = 22</td>
<td>n = 102</td>
<td>n = 56</td>
<td>n = 338</td>
<td>n = 168</td>
<td>n = 95</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.8 ± 0.68</td>
<td>1.8±0.7</td>
<td>2.1±0.9</td>
<td>1.9±0.6</td>
<td>1.8±0.6</td>
<td>1.6±0.5</td>
<td>2±0.7</td>
</tr>
<tr>
<td>Median</td>
<td>1.7</td>
<td>1.9</td>
<td>2.0</td>
<td>1.8</td>
<td>1.7</td>
<td>1.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Range</td>
<td>0.6 – 5.1</td>
<td>0.6 – 3.0</td>
<td>0.7 – 5.4</td>
<td>0.8 – 3.5</td>
<td>0.8 – 3.7</td>
<td>0.5 – 3.1</td>
<td>0.3 – 3.4</td>
</tr>
</tbody>
</table>

There was statistical significance found between regional locations (p value was set at < 0.05).

The regional distribution of normal perforators over all three groups outlined that normal subjects had perforators that were of a smaller diameter. A significant increase in perforator numbers in the medial and lateral regions of the calf were recorded at the 3 years post-op phase. The overall diameters of these regions however remained unchanged (Figure 6.1).
Seasonal effect on perforator diameter was also compared. There was no seasonal effects observed either within or across the groups. (Table 6.4).

**Table 6.4 Normal Perforator Diameters (mm) in Three different Venous Populations and their Season Effects.**

<table>
<thead>
<tr>
<th></th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1±0.6</td>
<td>1.3±0.5</td>
<td>1.4±0.6</td>
<td></td>
</tr>
<tr>
<td>Pre-op</td>
<td>3±1.3</td>
<td>3.2±1.5</td>
<td>3.1±1.3</td>
<td>2.8±1.1</td>
</tr>
<tr>
<td>3 years post-op</td>
<td>3.1±1.0</td>
<td>2±0.8</td>
<td>2±0.8</td>
<td>2.2±0.9</td>
</tr>
</tbody>
</table>

**6.2.2 Perforators and their Superficial Communications**

The communication of the perforators from the superficial compartment across the three venous groups is shown in Figure 6.2. The majority drained the superficial lateral vein network in the lateral calf - 39%, 34% and 47% in the normal, pre-op and 3 year post-op.
varicose veins groups respectively. On the medial aspect of the calf, drainage was directly from the GSV in 24%, 29% and 31% respectively across the three groups. In the normal group, as shown in Chapter 3, 17% of perforators were found to drain in a more convoluted manner in the subcutaneous tissue from the GSV. It was not possible to identify in the normal group a discrete PAGSV as described in the literature. Seventeen percent of these communications observed in the normal population were short links with the GSV prior to diving to the deep compartment.

However 6% and 7% respectively of normal functioning perforators were observed to drain from the PAGSV in the pre-op varicose vein and 3 year post-op varicose vein populations. Relatively a few perforators, 16%, 19% and 12% respectively across the three groups, were observed connecting with the short saphenous vein (SSV). However, in the thigh, the GSV perforators were observed at 4% in the normal group, compared to 12% in the pre-op varicose veins group and 3% at three years post-op varicose vein surgery (Figure 6.3). In the thigh there were a small number of occasions where the perforator drained directly from a superficial vein networks in all population groups.

Incompetent perforators and their superficial communications were mainly with the calf GSV, with 41% and 50% incompetent perforators seen to the medial calf in the pre-op and post-op groups respectively. This was also consistent in the lateral calf with 20% and 25% respectively at the two time periods. The incompetent thigh perforators were lower at the three year phase with only 4% observed compared to 8% at the pre-op phase (Figure 6.4).
Figure 6.2 Superficial Normal Perforator Communication Over Three Different Population Groups.

Normal, pre-op varicose vein and three years post-op varicose vein surgical groups. Great Saphenous Vein communication (GSV, thigh, calf and accessory) Posterior Accessory Great Saphenous Vein (PAGSV), Short Saphenous Vein (SSV), Lateral calf Vein (Lat. V. calf)
6.2.3 Perforators and Deep Venous Communications

The communication of the venous perforators with that of the deep venous system is shown in Figure 6.5. These connections of the perforators to the deep system followed the expected anatomical regional drainage with the medial calf to the posterior tibial vein as observed in Chapter 3. These findings are supported by both our own and others’ research along with anatomy dissections\textsuperscript{[14, 17, 103, 104]}. 

Incompetent perforators and their deep communications were mainly with the calf PTV, with 41% and 44% incompetent perforators seen in the medial calf with a PTV communication in the pre-op and three years post-op venous surgery groups respectively.

In the lateral calf between 15- 21% were seen to communicate with the PV at the two time periods. The communications in incompetent thigh perforators had greater numbers however at three years, with 11% observed compared to 8% at the pre-op phase (Figure 6.3).
Figure 6.3 Normal Deep Communication and the Venous Perforator across Three Population Groups.

Normal, pre-op varicose vein and three years post-op varicose vein surgical groups. Posterior Tibial Vein (PTV), Medial Gastrocnemius Vein (MGV), Lateral Gastrocnemius Vein (LGV), Peroneal Vein (PV), Anterior Tibial Vein (ATV) Femoral vein (FV)
6.3 Discussion

From this initial assessment of the normal lower limb, we have demonstrated the presence of a greater number of perforators per limb when compared against the two diseased populations. This demonstrates that many perforators are not clearly seen even in a diseased population, even with a known higher venous pressure in the garter region of the medial calf. This may be explained by the fact that many patients with venous disease may also have a more significant impact on imaging due to severe induration, pigmentation and ulceration. The fact remains however that the two diseased populations had competent and incompetent perforators, which are generally of a larger caliber, and should be easier to identify.

The regional distribution of the perforators across all three groups was comparable and from this we can be reasonably confident that this represents a fair and accurate map of the lower limb perforators\cite{17}. Similarly, so are the vessels into which they drain in the deep system. Less well understood is the exact territory from which the perforators drain as referred to in Chapter three. As previously demonstrated, most perforators are in the calf, particularly at the medial aspect of the calf, the site considered having the most influence and impact toward venous disease still continues to hold out. Across all three groups the medial calf perforators identified have a significant increase in numbers just among the normal functioning perforators. There is a doubling in perforator numbers just to the medial calf.

Even though perforator diameters did not appear to be of a greater size, however, the greater concentration of perforator numbers must, influence the venous pressure profile when applied to a diseased population\cite{25,107}.

As discussed in Chapter three, when we compared the communication of the venous perforators, especially within the superficial compartment, it did not match with the literature;
as seen in relation to the posterior accessory great saphenous vein (PAGSV). However in both diseased populations 6% and 7% respectively of the normal functioning perforators were observed communicating with the PAGSV and 8% and 10% respectively of the incompetent perforators [107]. The main communication in each of the diseased groups in the medial calf still remained with the GSV in both the competent and incompetent perforators. The possibility that in a normal venous system the PAGSV is not obvious may be a fair conclusion to reach, and perhaps the PAGSV only becomes obvious when venous incompetence is present within the superficial compartment? The findings of the perforators and their deep compartment communications were with that of the PTV. The PTV and its known association with a high venous pressure profile must play a role in the relationship of the number of incompetent perforators along the medial calf [13, 24, 43].
Chapter 7

7 Identification of Perforating Veins and their Valves using Resin Casting

The venous system is both complex and variable and has numerous valves that are essential for the prevention of blood flow reversal\(^{[23]}\). As reviewed in the introduction, there remains a great deal of debate regarding the presence of valves in the perforators, their direction and whether there are other valve-like mechanisms. Unfortunately the duplex ultrasound studies in normal subjects infrequently identified valves. This left the question of perforator valves still very much up in the air.

To add some further light another mode of demonstrating possible valves in perforators was found which could be compared with duplex ultrasound appearance. This involved the use of retrograde resin venography, a technique developed in the Department of Surgery.

7.1 Methods

7.1.1 Subjects

The vascular surgeons approached patients who required an amputation of their lower limb for reasons not related to venous disease and who also appeared not to have clinical venous disease. An initial verbal consent was obtained. An information sheet was then supplied to the patient (Appendix A) giving them the opportunity to read the outline of the project. Written consent was then obtained.
7.1.2 Ethical Approval

Ethical Approval was obtained from the Lower South Regional Ethics Committee for the casting of the veins in the amputated limbs.

7.1.3 Ultrasound Assessment

The limb to be removed underwent a detailed venous duplex ultrasound prior to surgery. The medial calf perforators were all examined and recorded, to including investigation of the presence or absence of valves within the perforator and the functional direction of the blood flow within the perforator as seen on both colour and spectral Doppler with augmentation.

The course of the GSV within the medial calf was also mapped and its relationship to the medial calf perforators (Figure 7.1). This was to aid in the later identification of the communication of the perforators following the maceration of the tissue and the formation of the resin cast. Each of the perforators was also characterized according to which superficial and deep veins they communicated with. This was also to assist in the identification of each perforator post-maceration of the tissue.

Following the amputation of the lower limb, the tissue was processed and prepared for vascular corrosion casting.

7.1.4 Resin Casting Process

This procedure was carried out by Associate Professor Greg Jones and involved cannulation of the distal end of the GSV at the level of the medial malleolus using a 14 gauge IV catheter. The vessels were then flushed with sufficient amounts of normal saline (typically 100 – 150 mL) to remove any remaining blood clots from within the vein lumen. The GSV was then
injected with Batson’s Number 17 resin (Polysciences Inc. Warrington PA, USA) until the resin was observed freely flowing out of both the deep and superficial veins at the proximal cut surface of the amputation specimen. These outflow vessels were then clamped with artery forceps and the resin further injected until the GSV was fully filled, as indicated by a clear increase in the pressure required to perfuse the vein (typically a further 20–30 ml of resin). Care was taken not to force resin into the veins once the initial pressure rise occurred.

The resin kit consists of a “base solution” - plastic monomer, a catalyst and a promoter to allow curing at room temperature following injection. The three components were mixed within a fume hood as recommended by the manufacturer. A blue pigment was added to the resin solution to denote the vein.

Immediately prior to injecting the resin solution the components were mixed together and left to rest for approximately five minutes to allow any air bubbles trapped within the resin to rise to the surface. The resin then had a working time of 30 to 45 minutes to complete the injection process. The resin was then polymerized (hardened) over 2 to 3 hours at room temperature.

Resin was injected in a pro-grade flow direction, which is the direction of normal venous blood flow (from the medial malleolus toward the proximal segment of the amputated limb). This allows the resin to course along the vein in the normal flow direction of the vessel. Injecting in this manner allowed the valve to rest along the wall of the vessel injected. The clamping of the proximal GSV allowed the resin to course from the superficial venous system into the deep venous system via the perforators within the region of the medial calf. The medial calf perforators and GSV were the vessels of choice in this study (Figure 7.1). In order to obtain the best possible quality of vascular casts we did not attempt to create casts
from the SSV region, or the lateral calf region. This decision was made to avoid poor filling of the resin within the selected veins, and to avoid collapse of the GSV and the perforators along its path (Figures 7.2 & 7.3).
Figure 7.1 A Below Knee Amputated Limb with a Medial Calf Outline of the Great Saphenous Vein (GSV).

2 small tributaries off the GSV with connections to perforators as denoted in red marking based on duplex scan.

Figure 7.2 Dissected Area of Tissue Along the Course of the Great Saphenous Vein (GSV).

The same limb as Fig 7.1. Demonstrates the resin filled vessels following resin injection. Superficial fascia (SF) of the saphenous track along the medial calf.
Figure 7.3 Tissue Dissection of a More Extensive Superficial Vein Network

Resin cast of the superficial veins of the medial calf; Great Saphenous Vein (GSV) along a straight course, with the Posterior Accessory Great Saphenous vein (PAGSV) prior to tissue maceration. Perforators are denoted with red dot based on preoperative duplex ultrasound.

Figure 7.4 Partial Tissue Maceration of a Perforator (arrowhead).

Perforator as it courses from the superficial toward the deep venous compartment. Notice the valve (arrow) directing flow towards the perforator, and the suture material tied around the vein indicating where the presence of a perforator has been marked on the surface during ultrasound.
7.1.5 Tissue Maceration Process

Prior to maceration the GSV was partially dissected (Figures 7.2 & 7.3) and the superficial veins beneath skin sites marked as ultrasound-detected perforators were labeled using a nylon suture looped and tied around the vein (Figure 7.4).

A standard tissue maceration protocol was then performed on all specimens\(^5\). The tissue was immersed in a large (sealable) plastic container filled with distilled water at 50°C overnight. The water was then replaced with a macerating solution (15% NaOH) and incubated for a further 24 hours at 50°C. Additional periods of maceration were conducted depending on the volume of tissue. The NaOH was carefully decanted off and the tissue rinsed with hot tap water to remove any adhering tissue debris. The container was again refilled with NaOH and placed back in a 50°C oven. This process was repeated until all tissue was removed and the maceration process completed (Figure 7.4). On completion of the maceration the resin cast was again rinsed several times in warm water and placed in a clean container and allowed to dry in an oven at 50°C. The resin casts were all then photographed along their entire length using a digital camera (Figure 7.6).

7.1.5.1 Resin Cast Examination

The vascular casts were examined over an x-ray box providing a suitable light source. The superficial, deep and perforating veins were confirmed and all venous valves within the perforators were pinpointed and recorded. Once located, all valves within the perforator had the valve leaflet fold direction described. All perforators were then matched against the pre-recorded data from the ultrasound examination. The use of suture material, which was applied to the superficial vein to pinpoint out the location of the ultrasound identified perforators as they crossed the fascia (Figure 7.4) was highly useful in matching the ultrasound to resin cast observations. A number of the deep venous communications were damaged during the maceration process as the cast collapsed under its own weight, thereby
limiting the ability to describe all perforator–deep system connections in two (11%) of the perforators.

7.2 Results
A total of six subjects participated in this study. There were three males and three female patients who required amputation for conditions unrelated to venous disease. Five of the subjects required a below knee amputation, with one requiring an above knee amputation.

Table 7.1 Ultrasound-derived Perforator Diameters Prior to Surgical Amputation.

<table>
<thead>
<tr>
<th>Number of Subjects (n=6)</th>
<th>Ultrasound Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforators detected n= 24</td>
<td>Mean ± SD: 2.1 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>Range: 0.6 - 7.0</td>
</tr>
<tr>
<td></td>
<td>Median: 1.75</td>
</tr>
</tbody>
</table>

7.3 Perforator Communication

7.3.1 Ultrasound Findings
The majority of perforators that were observed by duplex ultrasound communicated within the superficial compartment with the GSV via a short segment of a superficial venous tributary. The communications of these same perforators with the deep venous compartment were predominantly with the PTV (19/24, 79%). A further five perforators were noted to communicate both with the PTV and medial soleus sinus vein.
Table 7.2 Perforators and Valves Detected by B-mode Ultrasound Prior to Amputation.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Operation Type</th>
<th>No. Perforators Detected (n=24)</th>
<th>No. Valves Identified (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1037</td>
<td>BKA</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1038</td>
<td>AKA</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>1057</td>
<td>BKA</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1012</td>
<td>BKA</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>1078</td>
<td>BKA</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1061</td>
<td>BKA</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

BKA = below the knee amputation, AKA = above the knee amputation

Figure 7.5 B-Mode Image of a Venous Perforator with Two Distinct Valves Observed Deep to the Fascia.

The two leaflets of the superficial (arrowheads) and deeper (arrows) valves are indicated.

7.3.2 Resin Caste Appearance

A total of 19 resin cast perforators were preserved following amputation and completion of the maceration process. Communication was observed clearly to the PTV. None were clearly viewed to the soleus, as they appeared to have sapped during the maceration process.
Table 7.3 Perforators and Valves Detected in Resin Casts Post Maceration.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Operation Type</th>
<th>No. Perforators Detected n=19</th>
<th>No. Valves Identified n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>1037</td>
<td>BKA</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>1038</td>
<td>AKA</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1057</td>
<td>BKA</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>1012</td>
<td>BKA</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>1078</td>
<td>BKA</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1061</td>
<td>BKA</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

BKA = below the knee amputation, AKA = above the knee amputation

7.4 Perforator Valve Identification

7.4.1 Ultrasound Findings

In the perforators observed using high-resolution ultrasound, only seven perforators were seen to have a valve present. These perforators followed a direct course from the superficial venous compartment to the deep venous compartment (Figure 7.5 page 92). Those with valves were of a larger diameter ranging from 2.6 - 7.0 mm. The remaining perforators, in which no valves were detected by ultrasound, were of a smaller diameter ranging from 0.6 – 2.5 mm.

7.4.2 Resin Caste Findings

In the 19 perforators that were present following resin cast formation a total of 31 valves were identified. All resin cast perforators had at least one valve, with four perforators having two valves and only one perforator having four valves. This perforator had a dual channel as shown in Figure 7.6.

Two small resin cast perforators did not maintain contact with the deep compartment following completion of the maceration process and so some valves may have been missed.
7.5 Multiple Perforator Channels

7.5.1 Ultrasound Findings
On ultrasound examination, all the perforators that were identified were seen as a single channel. No multiple channels were observed in either B-mode or colour Doppler.

7.5.2 Resin Cast Findings
On completion of the resin casts, five (26%) of the perforators were seen as dual or multi-channels\(^\text{[12]}\) (Figures 7.6 – 7.8). These perforator channels appeared as a greater caliber channel with an accompanying smaller companion. The companion perforators were found to also have valve leaflets.

![Figure 7.6 Resin Cast of Both the Great Saphenous Vein (GSV) and the Posterior Tibial Vein (PTV).](image)

*Two perforators seen between SAGSV and PTV. These perforators are seen as dual perforator channels (*). Suture material shows the point where the perforator is closest to fascia opening to the deep compartment (lighting flash).*

95
Figure 7.7 a & b Close Up of a Resin Cast Perforator with Valve Leaflets seen within the Perforator.

a) Top image is of a single channel perforator, b) Lower image dual perforator channel.
7.6 Valve Leaflets Appearance

7.6.1 Ultrasound findings
The valve leaflets that were seen under ultrasound appear as bicuspid in each of the five perforators. One of these perforators had two bicuspid valves noted as shown in Figure 7.5.

7.6.2 Resin cast Appearance
In all of the resin cast perforators all the valve leaflets all appear as bicuspid with the leaflet fold direction toward the deep compartment. None of the leaflets appeared shortened or malformed in any of the resin casts (Figure 7.9).

Figure 7.8 Subject HC1037; Vascular Cast Demonstrating Multiple Perforator Channels (arrowheads).
Figure 7.9 Magnified View of a Vascular Cast of a Venous Perforator Valve (*). Arrows indicate direction of blood flow.

7.7 Discussion

Even with the advancement of high-resolution ultrasound, optimal spatial and lateral resolution, we are still unable to fully insonate all areas of the venous perforator. Our ability to insonate and identify the superficial and deep venous system has advanced and we have reasonable confidence in our interpretation of the functional response of these veins when they are challenged\textsuperscript{[91]}. However, in the much smaller veins and especially the venous perforators this is much more difficult and hence less reliable. The primary difficulty encountered when using ultrasound to identify perforator vessels and their valves, is the diameter of the vessel in question. The majority have a smaller diameter (1-2 mm) and it is generally felt that lateral resolution will be less reliable to differentiate clearly, two distinct interfaces in such small torturous vessels. Dodd & Cockett long ago showed how the medial calf perforators had at least one, if not more, valves. But this has more recently been questioned by Hadfield, who said that small perforators simply did not have valves\textsuperscript{[125]}. My high-resolution ultrasound findings were able to confirm the presence of valves in the
perforators with a larger diameter, but I was unable to demonstrate this in the smaller caliber vessels. Those perforators that were seen with a valve all had a direct short course to the PTV. In one perforator I was able to observed two valves using B-mode imaging, as shown in Figure 7.2. These large valve-containing perforators were observed in the gaiter region of the medial calf, where the depth of tissue between the superficial and deep system was minimal. Resolution was optimized in this region due to the ability to use a high frequency transducer and view the perforators using a perpendicular angle of insonation. However as the venous perforators were assessed along the length of the medial calf, the need to insonate the vessel at a greater depth, through a much more tortuous path, required a reduction in probe frequency, along with a shift in line of site from perpendicular and as a result a reduction in clarity of image. In some cases these perforators were coursing close to the tibial bone, in a posterior plane to the muscle or around the side edge of the muscle. This appeared to contribute to difficulty in obtaining the optimal window to insonate the entire length of these perforating veins.

In contrast, however, the valves were demonstrated clearly within all perforator resin casts. The perforator resin casts confirmed the presence of at least one valve, with a number of perforators showing more than one valve per vessel. In addition casts proved conclusively that perforators have valves that are bicuspid in appearance. This supports the finding of earlier work performed by Pincer\textsuperscript{126}. Furthermore, valve leaflets were all directed from the superficial towards that of the deep compartment. Therefore, the statement that perforators allow bi-directional flow as a normal function does not appear consistent with the resin cast appearance of the perforators and their valves as observed in this series. The presence of the valves were noted along the course of the perforators deep to the fascia and not just at the fascia plane\textsuperscript{40, 126}. No examples of perforators with valve leaflets superficial to the fascia were observed in this series of resin casts\textsuperscript{44}. At no time throughout the ultrasound
examination, within the limited group of amputated limbs examined, were any multiple-channel venous identified. And yet, within matching resin casts of these same perforators approximately a quarter (5/19) had appeared to have dual channels (Figures 7.6 - 7.8). These resin cast findings compare well with observations by Pirner & Gohel identifying multiple perforator existence at the site of a single perforation of the fascia\textsuperscript{[126, 127]}. We could also clearly identify the dual appearance of a number of perforators where they divided and communicated with both the PTV and soleus veins at a deep level within the tissue. All these configurations had been accounted for when casting was completed\textsuperscript{[124]}. The accompanying perforators were generally of a much smaller caliber, and this factor may best explain the miss rate on ultrasound, with the resolution unable to show separation of tissue interfaces in such smaller vessels. Indeed, we have previously observed a similar inability to accurately detect small, but physiologically significant, venous channels in the context of saphenofemoral junction recurrence when compared with histological and vascular corrosion cast methods of assessment\textsuperscript{[15]}.

These perforator cast findings may also explain the sudden appearance of new perforators following venous surgical ligation\textsuperscript{[103]}. Could these ‘new’ perforators be the result of neovascularisation or simply a remodeling of pre-existing small caliber perforators? These findings demonstrate the limitation of ultrasound as a modality in defining the presence of all vessels within the lower limb venous system.

These findings also appear consistent with those of Ghali, who, on reconstruction surgery, reported that a quarter of all perforating arteries had more than one accompanying perforating vein, with some having up to three perforating veins\textsuperscript{[124]}.
7.8 Limitations of this study

This journey of the venous perforator and the question of valve presence can now be answered by our findings. However in this series, we have not yet performed adequate numbers of perforator resin casts to allow a clear understanding of all possible valve combinations within the perforators of the lower limb venous system.

7.8.1 Resin Cast Limitations

The study had some limitations, especially as the perforator casts were only from the mid and distal medial calf. This was simply due to the nature of the below knee amputation. Not all of these perforators, which had been identified under ultrasound, were preserved following surgery due to the need to preserve suitable tissue to aid in the formation of the residual limb stump. The proximal medial calf may hold the key to the location of bi-directional perforators. We have observed bi-directional flow along this region in previous venous assessment of one normal subject, apparently acting as a release valve or collateral circulation pathway, but this could not be investigated in this study. The other possibility of bi-directional flows lies not so much with the individual direct perforator but in those perforators that have a fork like communication. Could it be that these perforators, especially those that communicate with both the soleus and gastrocnemius muscle, have valves that simply allow blood flow in the reverse direction?

Finally it is clear that further research is required and that this would need to include the examination of more perforators of both the posterior and lateral aspect of the calf and, if possible, from more extensive amputations. The examination of a population of amputated limbs, which are known to have venous disease, would also be relevant in observing perforator valve location, their number and the valve leaflet fold appearance.
Chapter 8

8 Conclusion

The perforators between the superficial and deep compartments of the venous system of the lower leg remain difficult to truly understand. It remains true that there are a large numbers of them, and only a small number are detected using the preferred clinical method of assessment - duplex ultrasound. Our findings compare well for the regional distribution of perforators described using other methods. With careful technique and high-end equipment we have been able to describe larger numbers than previously described using ultrasound. This thesis describes the size distribution in the normal population and their deep and superficial communications not previously described in this level of detail in ultrasound studies.

The focus of the thesis has been the medial perforators of the calf because of their prominence in clinical venous disease. We found that distal medial calf perforators in the normal population, were of a larger diameter, have a greater blood flow and demonstrate higher velocities. This may suggest that this group of perforators exist in a more demanding environment and are more susceptible to failure. Similarly they may play an especially key role in maintaining normal venous function. Therefore incompetence in this region could be of a greater significance in a diseased population.

This study has shown that perforator valves can be consistently identified by ultrasound in some perforators. Identification of venous valves is more clearly visualized in the gaiter region of the medial calf. The reason for this may be due to their greater size and shorter
direct route into the PTV of the deep compartment. This leads to the possible suggestion of the increased propensity of lower medial calf perforator incompetence in venous disease.

However not all perforators could be shown to have valves by ultrasound even though they were all competent. Hence the resin casting study to correlate ultrasound with the anatomical reality. This novel technique demonstrated valves where ultrasound could not “see” but also demonstrated the complexity of perforators with duplications, tortuosity and branches not appreciated by ultrasound. This provided a cautionary message as to the limitations of even the best in diagnostic ultrasound.

During this research anatomical dogma was also challenged with the ultrasound approach. Our inability to detect the PAGSV of the calf in the normal population could not be clearly explained. Small venous connections were observed between the perforator and the GSV, yet none appeared to connect with a PAGSV. Yet in the diseased population this vessel was clearly apparent! Was this simply due to the inability to detect this vessel when very small in the normal population? What it does suggest is that venous remodeling occurs with changes in flow in the diseased state.

Our study does not yet directly inform the question of which perforators are important in surgical decision-making – which to leave and which to treat. However we were able to document some original observations as to what happens to perforators following surgical ablation. It was shown that following venous surgery, perforator numbers in the lower limb increased significantly suggesting remodeling of smaller, often previously undetectable, perforators and enlarging in response to continuing venous haemodynamic demand. Even more interesting was to see the phenomena of neovascularisation and reconnection of the deep and superficial system at the same site of those that were obliterated. These ultrasound -
based observations confirm the biological basis for recurrence and provide a helpful message for the surgeon and his/her patient.

### 8.1 Further Research

These findings open up additional avenues for research that could further advance our understanding of venous perforators and their function:

1. Confirm, in other regions of the lower limb, detailed responses to diameter, blood flow and venous velocities, which may identify other perforators that also have a more demanding environment.
2. This could then be extended to confirm whether these relationships also hold in the diseased population.
3. Investigate a functional test for muscle contracting versus an external squeeze compression in both a normal and venous-diseased population.
4. Further resin casts of a complete lower limb would provide answers to total perforator numbers and their valve appearance. It would also provide a wonderful teaching tool for medical, vascular sonographer and anatomy students.
5. The impact of the GSV and its removal for CABG would allow an opportunity to understand the remodeling of the superficial venous compartment and the perforating veins in an already confirmed normal venous population.
9 References


75. Wienert, V., *Diagnosis of incompetent perforating veins - value of the methods*.


“I have read and understand the information sheet for volunteers participating in the study designed to investigate the anatomy and valve location of perforating veins along the inner aspect of the calf.

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care.

I agree for my information to go to my GP if any finding is noted of importance toward my general health and wellbeing.

GP Name:………………………………………………………………
Medical Centre:……………………………………………………

I also understand that my participation in this study is confidential and that nothing which could be used to identify me will be used in any reports in this study.

I ………………………………………………………………….. (Full Name) hereby consent to take part in this study.

Date:…………………………………………
Full Names of Researchers:
Professor Andre van Rij
Vascular Consultant & Director of the Vascular Laboratory

Dr. Greg Jones
Senior Lecturer

Mrs. Gerry Hill
Vascular Technologist

Project explained by: ......................
Project role: ................................

Signature: ....................................
Date: ..........................................
Features of Vein Perforators in the lower Leg of both Normal and Disease Participants.

“I have read and understand the information sheet for volunteers participating in the study designed to investigate the function of veins in the leg.

I have had both the opportunity to discuss this study and ask questions which have been explained and answered to my satisfaction.

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care.

I agree for my information to go to my GP if any finding is noted of importance toward my general health and wellbeing.

GP Name: …………………………………………………...
Medical Centre: ……………………………………………..

I also understand that my participation in this study is confidential and that no material that could be used to identify me will be used in any reports in this study.

I also understand that investigation will cease if it should appear harmful to me.

I ………………………………………………………………….. (Full Name) hereby consent to take part in this study.

Date: ………………………………
Signature: ..................................

Full Names of Researchers:

Professor Andre van Rij
Vascular Consultant & Director of the Vascular Laboratory

Dr. Greg Jones
Senior Lecturer

Mrs. Gerry Hill
Vascular Technologist

Project explained by: .........................
Project role:

Signature: ...............................
Date: ..........................
The Characteristics of Perforating Veins in the Lower Leg.

We would like to invite you to take part in a study to look at the function of veins in the legs. This study will involve looking at people who have no varicose veins and normal vein function, and comparing them against a group with varicose veins.

The function of veins is to return blood to the heart after it has supplied nutrients to the tissues of the body. In the legs the veins must return the blood against the force of gravity; therefore veins have valves to ensure the forward movement of the blood toward the heart. Varicose veins are a very common problem within New Zealand with over 25% of men and 40% of women having this problem.

This study will examine the function of the perforating veins, which connect superficial veins to the veins deep within the leg.

Understanding how these veins work will provide the basis for identifying which perforators may play the most important role in vein function. This may give further clues to the cause of varicose veins.

We will use Ultrasound (a non invasive examination) to see what your veins look like. Your veins will be examined with you in the sitting, lying and standing positions. An exercise test will also be performed. This will involve you walking on a treadmill for 5 minutes after which the perforators will be looked at again. A total of 3 hours of your time will be required to participate in this research project. Gerry Hill an experienced vascular technician will perform all the ultrasound examination.

Participation in this study is voluntary and you may withdraw at any time. Your involvement is confidential and no material that could identify you will be used in any publication of this study.

All participants may have a report of findings go to their GP if any finding is noted of importance toward their general health and wellbeing.

In the unlikely event of a physical injury as a result of your participation in this study, you will be covered by the accident compensation legislation within its limitations. If you have
any question about ACC please feel free to ask the researcher for more information before you agree to take part in the study.

If you would like advice as to your rights as a participant in this study you may approach the Health and Disability Consumer Advocates, Dunedin. Tel: (03) 479 0265 or 0800 377 766.

If there is a specific Maori issue/concern please contact Linda Grennell at 0800 377 766.

This study has been approved by the Lower South Island Regional Ethics Committee.

Investigators:

Professor Andre van Rij
Vascular Consultant & Director of the Vascular Laboratory

Dr. Greg Jones
Senior Lecturer

Mrs. Gerry Hill
Vascular Technologist
Masters Student

Contact: Mrs. G Hill on Tel: 474 0999 Ext 8851
We would like to invite you to take part in a study to look at the anatomy and features of veins in the leg. This study involves the examination of the lower limb veins of patients who are to undergo amputation for reasons unrelated to varicose veins.

The function of the lower leg veins is to return blood to the heart. These veins are required to do this against the force of gravity; therefore they have valves to ensure the upward movement of the blood toward the heart. Along with the obvious veins seen on the limb there are also veins deep in the leg. Connecting these deep and superficial veins are veins called perforating veins. It is still not clear whether these perforators have valves or not, where they are located, and how they might work.

This study is designed to give us answers about this.

Prior to going to the operating theatre we will perform a routine ultrasound examination of the leg to exclude varicose veins. The ultrasound examination will be performed by Gerry Hill within the vascular laboratory. It will take approximately 40 minutes to perform the ultrasound examination.

After your leg has been amputated, it will be taken to the laboratory and a special resin will be placed in the veins. All residual material will be disposed of by incineration.

Subsequently the resin cast of the veins will then be examined under an electron microscope.

Participation in this study is voluntary and you may withdraw at any time. Your involvement is confidential and no material that could identify you will be used in any publication of this study.

All participants may have a report of findings go to their GP if any finding is noted of importance toward their general health and wellbeing.

In the unlikely event of a physical injury as a result of your participation in this study, you will be covered by the accident compensation legislation within its limitations. If you have
any question about ACC please feel free to ask the researcher for more information before you agree to take part in the study.

If you would like advice as to your rights as a participant in this study you may approach the Health and Disability Consumer Advocates, Dunedin. Tel: (03) 479 0265 or 0800 377 766.

If there is a specific Maori issue/concern please contact Linda Grennell at 0800 377 766.

This study has been approved by the Lower South Island Regional Ethics Committee.

Investigators:

Professor Andre van Rij
Vascular Consultant & Director of the Vascular Laboratory

Dr. Greg Jones
Senior Lecturer

Mrs. Gerry Hill
Vascular Technologist
Masters Student

Contact: Mrs. G Hill on Tel: 474 0999 Ext 8851