"Optimisation of intermittent compression for the improvement of vascular inflow and outflow proximal to a wound site"

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Abstract

Ulceration of the lower limb is a chronic, debilitating condition affecting an increasing percentage of the adult and elderly populations. Conservative treatment options are limited, and generally result in surgery or amputation. The purpose of this research was to investigate the feasibility of using intermittent pneumatic compression for the treatment and management of chronic non-healing leg ulcers. The aim was to develop a system capable of improving the healing of leg ulcers of varying causes through improving distal blood flow; whilst also being comfortable and easy to use, to encourage patient compliance.

Using Doppler ultrasound, it was demonstrated that intermittent pneumatic compression was capable of producing a distal blood flow response in the limb of a healthy volunteer. Further investigations examined the effect on this distal response of altering the cuff design, pressure and cycle duration; in order to determine the optimal compression regime for enhancing the distal circulation; the ultimate objective being to use intermittent pneumatic compression to improve the healing of chronic leg ulcers by improving distal blood flow.

The optimal sequence involved a 3-chamber thigh cuff, using a pressure of 60mmHg and a short sequential cycle which was operated within a 2 minute on and off sequence. The optimal system was investigated for distal blood

flow effects in a group of 20 healthy volunteers, and 14 patients with leg ulcers of differing aetiologies.

A distal hyperaemic response was achieved during the 2 minutes without compression, consequent upon changes induced in the venous circulation during the 2 minutes of compression. A greater response was detected in the patient group as compared with the healthy volunteer group.

A 3 month case study of the clinical effects of the new system resulted in the complete healing of the patients long standing non-healing leg ulcer. Further case studies are required to determine the significance of this finding.

Contents

Introduction

Chronic non-healing leg ulcers are a considerable source of morbidity and a potential huge resource problem to the NHS, impinging on an increasing percentage of the population, with prevalence figures of approximately 1% in the adult populace, and 3-5% in the populace over 65 years of age, (Mekkes et al. 2003).

Leg ulcers commonly arise due to impaired blood flow, as a result of atherosclerosis (occlusive arterial disease) or venous insufficiency. The presence of a painful, malodorous, unsightly leg ulcer is not only disconcerting and restrictive to the patient, but the current management and treatment of the ulcer is protracted and inconvenient.

The treatment of ulceration involves improving the circulation of blood. For ischaemic and diabetic ulcers, conservative treatment options are few, generally resulting in some form of surgery, ultimately an amputation, which incur associated risks and complications, (Montori et al. 2002). The current treatment of venous ulceration involves compression bandaging, which can be labour intensive for the nursing staff, varying in efficacy dependant on the skill of the health care professional in application of bandaging, relying on patient compliance for a treatment that can be uncomfortable, unsightly and inconvenient. Consequently, improved ulcer healing techniques are indicated, which incur greater efficacy.

Intermittent pneumatic compression (IPC) is a technique which has been successfully used in the past for the prophylaxis of deep vein thrombosis (DVT), for the reduction of oedema and improvement of venous return, and for the symptomatic reduction of peripheral arterial disease, (Chen et al. 2001). Various degrees of pressure are transmitted to the underlying subcutaneous tissue, muscle and blood vessels during the 'cyclic mechanical compression of the limb', (Sayegh 1987) resulting in a range of physiological effects. The ability of IPC to assist in the management of vascular diseases, lies, not only in mechanical effects, which initiate alterations in the dynamics of blood flow, but also in its ability to stimulate the release of biochemical mechanisms of the circulation, (Chen et al. 2001). The consequences of IPC may be summarised as oedema reduction, increased blood flow, and in acute ischaemia, the use of IPC encourages the formation of collateral circulation, (Koch 1997). However, arterial and venous applications have developed separately, with different cuff designs, pressures and compression sequences.

Although the number of studies examining the application of IPC to the treatment of ulcers are limited, and their reliability is questioned, (Mani et al. 2004), it is known that IPC has the ability to enhance vascular fluid flow, which essentially is the basis for initiating ulcer healing; consequently, IPC devices may represent an 'effective and safe limb salvage therapy for patients with wounds and critical limb ischaemia', (Montori et al. 2002). The advantages of IPC, namely its non-invasive nature, and ease of use with minimal associated risks, along with good patient compliance (Kumar and Walker 2002), would be

beneficial for patients with chronic non-healing leg ulcers, if it is found through investigation to be efficient in enhancing the wound healing process by improving the distal circulation.

The aim of this research was to investigate the feasibility of using intermittent pneumatic compression for the treatment and management of chronic non-healing leg ulcers of varying aetiologies.

A review of the literature relating to leg ulcers and intermittent pneumatic compression is included in chapter 1 of the thesis; chapter 2 describes the equipment used in the research.

Chapters 3 and 4 relate to the preliminary investigations which were carried out on a single healthy volunteer; chapter 3 refers to those experiments conducted with the two different uniform compression cuffs, and chapter 4 to the two multiple chamber compression cuffs.

Investigations on a group of healthy volunteers are reported in chapter 5, whilst those investigations on patients with leg ulcers of differing causes are referred to in chapter 6. A small number of case studies were also attempted to conclude the research which are detailed in chapter 7.

Chapter 1: Literature Review

1.1 Introduction

A review of the literature relating to the pathophysiology and management of chronic leg ulceration, and intermittent pneumatic compression and its application to vascular diseases has been composed. However, a synopsis of the cardiovascular system has been included prior to the main subject matter of the review, due to the central role occupied by the characteristics of blood flow in this research.

1.2 The Cardiovascular System

The cardiovascular system is a continuous circuit, responsible for the 'rapid convective transport' of substances, such as oxygen, nutrients, waste products and heat around the body, (Levick 2000). The system involves two distinct circulations, namely the pulmonary circulation and the systemic circulation. The pulmonary circulation is a short circuit extending from the heart to the lungs and back to the heart again, enabling gaseous exchange by diffusion between the blood and the alveoli of the lungs. The systemic circulation is responsible for the transportation of oxygen and nutrients to all other organs and tissues of the body, and the removal of carbon dioxide and other waste products, (Marieb 2001).

This research is concerned primarily with the systemic circulation; the anatomy and physiology described therefore concentrates predominantly on this element of the cardiovascular system.

1.2.1 Arteries

On contraction of the left ventricle of the heart, high pressure blood is ejected into the largest artery, the aorta, before progressing through a branched system of arteries of continually diminishing calibre, (Levick 2000).

Leaving the left ventricle, the aorta veers downwards at the aortic arch, from which branches supply the head, arms and heart. The visceral organs are supplied with blood from branches of the descending aorta, whilst the pelvis and legs are delivered with blood from the right and left iliac arteries,

bifurcations of the descending aorta, (Aaronson et al. 2004). Therefore, excluding the liver, the principal organs of the body are all supplied with blood from arteries which branch from the aorta. This 'parallel arrangement' of the systemic circulation guarantees an independent blood supply, driven at high pressure to each organ of the body, hence ensuring the delivery of highly oxygenated blood to each site, (Aaronson et al. 2004).

Within the lower limb, the external iliac artery continues into the femoral artery, which traverses down through the thigh and branches into the profunda femoris artery. The popliteal artery originates above the knee as a continuation of the femoral artery, branching into the anterior and posterior tibial arteries below the popliteus muscle. The anterior tibial artery descends anteriorly; lateral to the tibia bone. At the ankle, midway between the malleoli, the anterior tibial artery becomes the dorsalis pedis artery, which runs anteromedially supplying the foot. However, it is the posterior tibial artery which provides the principal blood supply to the foot, (Moore and Agur 1995). The posterior tibial artery descends the posterior lower limb inferomedially until reaching the ankle, where it runs posterior to the medial malleolus and into the foot, whilst its branch the peroneal artery travels along the medial side of the fibula and into the dorsum of the foot.

Arteries may be described as viscoelastic tubes, which are capable of altering their diameter, causing a resultant pulsatile pressure, (Nichols and O'Rourke 1990). There are different types of arteries, characterised by their size and by the varying compositions of the three layers making up the wall of the artery.

The three layers of tissue constituting the arterial wall are namely, the tunica interna, tunica media and the tunica externa or adventitia (Moore and Agur 1995). The tunica interna is an inner layer of endothelium, whilst the tunica externa is an outer layer comprising fibrous tissue. It is the composition of elastic and smooth muscular tissue in the middle layer, the tunica media which generally distinguishes one type of artery from the other.

Elastic arteries, such as the aorta and its major branches, are the largest type of artery, and as their name suggests are highly elastic, enabling expansion during cardiac contractions. The smaller muscular arteries however, encompass a high composition of circularly disposed smooth muscle fibres, which are capable of constricting the vessel lumen, thus controlling the distribution of blood to the various organs and tissues of the body as required.

The smallest category of artery is the arteriole, also termed a resistance vessel due to its ability to control the resistance to blood flow, (Levick 2000). Arterioles regulate blood flow and hence the degree of pressure within the arterial system by dilating (vasodilation) or constricting (vasoconstriction). The arterioles also control the flow of blood into the capillaries, thus impinging on capillary exchange, (Levick 2000).

1.2.2 The Microcirculation

The microcirculation is a collective term used to describe the flow of blood from the smallest arteriole, through a capillary bed to a venule. An important part of the cardiovascular system, the microcirculation is responsible for the

ultimate objective of the exchange of water, gases, nutrients and waste materials between the blood and tissue cells, (Smith and Kampine 1984).

Blood enters the microcirculation through small muscular arterioles, the tone of which controls the flow of blood entering the terminal arterioles and thus many capillaries. The terminal arterioles behave as precapillary sphincters for the capillaries into which they divide, regulated by local metabolic factors. Under basal conditions, the terminal arterioles exhibit vasomotion, a periodic constriction and relaxation of the arteriole walls, which results in rhythmic fluctuations in the flow of blood entering the capillaries, (Aaronson et al. 2004).

In some instances, there are through channels, called metarterioles, which run directly from the arteriole to the venule. Capillaries branch directly from the metarteriole, whilst precapillary sphincters at their point of origin control the inflow of blood, (Smith and Kampine 1984).

The capillaries are the smallest of the blood vessels, comprising a thin tunica interna only, which in some instances may be one endothelial cell thick. They function as a network called a capillary bed. Capillaries vary with respect to their anatomy and function dependant on their location within the body; however, in general there are three principal varieties. These are known as continuous, fenestrated and discontinuous capillaries. Each is identified with respect to 'the continuity of their filtration barriers', (Aaronson et al. 2004), such that the continuous capillaries have an uninterrupted wall of endothelial

cells, the fenestrated capillaries are similar, although some of their endothelial cells contain pores or fenestrations, whilst the discontinuous capillaries contain large intercellular gaps, (Marieb 2001). Hence, the continuous capillaries are permeable to small molecular substances and gases only, whilst the fenestrated and discontinuous capillaries allow the passage of large proteins and cells, (Aaronson et al. 2004).

Capillaries merge to form postcapillary venules, which merge to form venules. Postcapillary venules are composed of endothelium only and are highly porous, allowing fluid and white blood cells to move through their walls, whilst venules contain a few layers of smooth muscle cells, (Marieb 2001). It is the venules which unite to form veins.

1.2.3 Veins

Veins are responsible for the return of blood to the heart from the capillary beds. Veins from the organs and tissues of the body unite to form two major conduits returning blood to the right atrium of the heart; the inferior vena cava, collecting blood from organs in the lower body, and the superior vena cava, which amasses blood from the upper body, (Vander et al. 2001). In general, veins are located in close proximity to their corresponding arteries.

The veins have thinner walls than the arteries, although still consisting of the same three layers; and they have a larger lumen. The tunica media is thinner and weaker having less elastic and muscular tissue, whilst the tunica externa

is the thickest of the venous wall layers comprising longitudinal bundles of collagen fibres and elastic networks, (Marieb 2001).

The veins are highly compliant vessels at low pressures, consequent upon their thin walls, which allow the veins to collapse at low internal pressures, (Aaronson et al. 2004). The veins are also known as the capacitance vessels. With small changes in venous blood pressures the veins are capable of expanding considerably to accommodate large increases in blood volume, due to their large lumen and high expandability. However, there is a limit on the expandability of the veins. At high pressures, venous compliance decreases, preventing blood pooling, for example on standing, (Aaronson et al. 2004). Up to 65% of the total blood supply of the body may be found within the veins at any instant.

The return of blood to the heart is assisted by the contraction of muscles within the legs which squeeze the veins and force blood back towards the heart; whilst the presence of valves within the peripheral veins prevent the backflow of blood, (Aaronson et al. 2004). Venous valves are formed by a fold in the tunica interna, which is strengthened by connective tissue.

1.2.4 Blood Pressure

Blood pressure originates from the contraction of the ventricles. It is defined as the force per unit area exerted by the blood on the wall of the blood vessel, (Marieb 2001) and is measured in units of millimetres of mercury (mmHg) or in kilo Pascals (kPa).

The blood pumped out of the heart by the contraction of the ventricles has a pressure called the systolic pressure. When the heart is resting with no ejection of blood, the pressure of blood in the vessels is termed the diastolic pressure. Unless otherwise stated, 'blood pressure' implies systemic arterial blood pressure in the large arteries near the heart, (Marieb 2001). The blood pressure is recorded as the systolic value (maximum arterial pressure) over the diastolic value (minimum arterial pressure), and the difference between them is known as the pulse pressure. In a normal young adult, the blood pressure is usually 120/80mmHg.

Blood is maintained in perpetual motion by the pressure gradient that exists within the vascular system; from a high pressure within the arteries to the much diminished pressure within the venous side of the vasculature, (Levick 2000).

1.2.5 Arterial Blood Pressure

Pressure within elastic vessels is governed by the elasticity of the vessel and the volume of fluid contained within them, (Marieb 2001).

The rhythmic emptying of the left ventricle produces the pulsatile nature of blood flow within the large arteries. Blood ejected from the left ventricle strikes the column of blood already present within the ascending aorta, generating a pressure wave in the blood, which is rapidly dissipated towards the arterioles, (Aaronson et al. 2004). Pulsatile flow arises as the pressure wave progresses

along the large arteries, producing transient pressure gradients, driving blood locally forward in short bursts.

The elasticity of the arterial walls causes them to expand with the progression of the pressure wave. Recoil of the arterial walls assists in driving the blood forward along the arteries during diastole, and causes reverse flow in the peripheral arteries.

Effectively, the elastic arteries may be thought of as 'pressure reservoirs', storing some of the energy of the pressure wave during systole, and then transferring it back to the blood during diastole, (Marieb 2001). This has the effect of gradually damping the pulsatility of blood flow as it progresses along the arterial tree.

1.2.6 Arteriole Blood Pressure

The muscular arteries are active in vasoconstriction, due to the high composition of smooth muscle within their walls as compared with the elastic arteries; however, it is the smaller arterioles which demonstrate the highest resistance to blood flow. The contractile capability of the arterioles helps to control the flow of blood into the capillaries and helps to maintain arterial blood pressure. On constriction of the arterioles, blood flow and hence blood pressure are reduced, distal to the arterioles; whilst simultaneously arterial blood pressure is raised. These blood vessels are therefore known as the 'resistance' vessels.

The high blood pressures present in the large elastic arteries decline with progression through the systemic arterial system of ever decreasing calibre. This arises due to the drag present between blood and the vessel walls, and the diminishing elasticity of the vessel. Pressures within the arterioles may have values of between 40 and 60 mmHg, (Smith and Kampine 1984) as compared with pressures of the order of 120mmHg in the large elastic arteries.

1.2.7 Venous Blood Pressure

The pressure of blood within the veins is considerably lower than within the arteries. As a consequence of the large cross-sectional area of the venous system, the resistance to blood flow is greatly reduced as compared with the arterial system, and hence, the pressure gradient required to drive blood through the veins is relatively low; 15mmHg as compared with 80mmHg in the arterial system, (Aaronson et al. 2004).

1.2.8 Maintenance of Normal Blood Pressure

There are a number of factors involved in the maintenance of normal blood pressure; cardiac output, blood volume, peripheral resistance, arterial wall elasticity and venous return.

The stroke volume is the volume of blood ejected by the heart at each ventricular contraction, whilst cardiac output is defined as the volume of blood ejected by the ventricles every minute. An increased cardiac output results in

an increased blood pressure, however an increase in stroke volume raises the systolic pressure more so than the diastolic pressure.

In order to maintain blood pressure homeostasis, it is necessary to have a sufficient volume of blood circulating within the blood vessels. Typically, the total blood volume is approximately 5 to 6 litres.

As previously mentioned, the contractile capability of the arterioles facilitates in maintaining arterial blood pressure by altering the peripheral resistance to blood flow; vasoconstriction initiating an increase in arterial blood pressure, and vasodilation decreasing arterial blood pressure.

The elasticity of the arterial walls enables their distension and relaxation during fluctuations in the blood volume, hence sustaining normal blood pressure.

Cardiac output is dependant on the volume of blood returned to the heart by the superior and inferior venae cavae. The arterial pressure is not sufficient in itself to drive blood back to the heart; hence there are other factors which assist in venous return. Muscular contraction within inelastic compartments exerts pressure on the veins, which prevents blood stasis and aids venous return. Respiratory movements also assist venous return. During inspiration, the chest expands creating a negative intra-thoracic pressure, whilst the descent of the diaphragm increases the intra-abdominal pressure. Both of these effects are active in facilitating venous return. Another factor which aids

the return of blood to the heart is body position and hence gravity, assisting the return of blood from the head and neck, for example when standing.

Blood pressure is directly related to cardiac output, peripheral resistance and blood volume (since cardiac output is dependant upon blood volume. See equation 1.)

$$Blood\ Pressure = Cardiac\ Output \times Peripheral\ Resistance$$
$$BP = CO \times PR$$

Equation 1

Alterations in one of these variables, which threatens blood pressure homeostasis are compensated for by changes in the other variables, (Marieb 2001).

There are neural and hormonal controls within the body which determine cardiac output and peripheral resistance, and other local controls which help to regulate arterial blood pressure.

Local controls are mechanisms independent of nerves and hormones, by which vascular beds are capable of altering their own arteriolar resistances for the purpose of self-regulating their blood supply, (Marieb 2001). They have two principal functions.

1. Under basal conditions, local mechanisms regulate vascular resistance in order to maintain blood flow at a constant level for a range of arterial blood pressures; this is known as flow *autoregulation.*
2. When the metabolic needs of a tissue increase, local mechanisms initiate vasodilation to increase blood flow; this is known as *metabolic or active hyperaemia, and reactive hyperaemia.* An active hyperaemia refers to the increase in blood flow which arises in response to an increase in metabolic activity, whilst a reactive hyperaemia describes the dramatic increase in blood flow which occurs in response to the removal of a complete occlusion to the blood supply. (Aaronson et al. 2004).

There are two mechanisms involved in the process of flow autoregulation; a metabolic response and a myogenic response. Vasodilating metabolites produced during cellular metabolism, which are present in extracellular spaces, impart a direct effect upon the vascular tone of the nearby arterioles, (Aaronson et al. 2004). When blood flow increases, the vasodilating metabolites are removed from the tissues more rapidly than they are produced, resulting in constriction of the arterioles and a consequent reduction in blood flow, (Vander et al. 2001). Conversely, a reduction in blood flow leads to an accrual of metabolites, which initiates arteriolar dilation and a resultant increase in blood flow.

The vasodilation of flow autoregulation involves a similar metabolic mechanism to the vasodilation of active hyperaemia; it is the precipitating

factor which differs between the two local controls, whether an alteration in intravascular blood pressure or metabolic activity, (Vander et al. 2001).

The myogenic mechanism of flow autoregulation involves a vascular response to alterations in intravascular pressures. Arteriolar smooth muscle is believed to respond directly to alterations in stretch arising due to changes in blood pressure. When the blood pressure increases, arteriolar smooth muscle responds to the consequent increase in stretch exerted upon it by constricting; whilst a decrease in stretch arising due to a decrease in intravascular blood pressure leads to a reduction in vascular tone and dilation, (Vander et al. 2001).

In addition to the local controls there are also extrinsic controls which regulate arterial blood pressure. Extrinsic controls provide for the needs of the body as a whole, by diverting blood to the organs and tissues which require it the most, (Pocock and Richards 2006). Information concerning the blood pressure and blood volume throughout the cardiovascular system is conveyed to the brain through afferent nerves, whilst the autonomic nervous system and a variety of hormones form the efferent aspect of the regulatory circuit, initiating the appropriate response from the heart and vasculature.

The autonomic nervous system is an efferent system of nerves conveying signals from the brain for the regulation of the involuntary function of most organs, (Aaronson et al. 2004). Autonomic activity is capable of countermanding the action of the local controls for the benefit of providing for

the body as a whole. It is comprised of two divisions, the sympathetic and parasympathetic branches, which have their individual functions and anatomical origins, (Pocock and Richards 2006).

The sympathetic system originates from the intermediolateral column of the thoracic and lumbar regions of the spinal cord, (Pocock and Richards 2006). In general terms, the function of the sympathetic division of the autonomic nervous system is to prepare the body for activity. The parasympathetic branch of the autonomic nervous system derives from the brainstem and sacral segments of the spinal cord, whose function involves initiating restorative processes.

One of the principal roles of the autonomic nervous system entails the maintenance of blood pressure homeostasis. Autonomic innervations impart a basal level of vascular tone. Sympathetic neurons within arterioles release the hormone norepinephrine which causes vascular smooth muscle to constrict, (Vander et al. 2001). Altered activity of the sympathetic nerves can increase or decrease this level of tone in order to decrease or increase the flow and pressure of the blood. Sympathetic stimulation can also increase the heart rate and the force of ventricular contraction. Parasympathetic activity does not in general contribute any effect to the tone of the vasculature (although there are a few vasodilatory exceptions), although it does stimulate a reduction in heart rate, (Pocock and Richards 2006).

In addition to the activation of efferent nerves, there are also a number of hormones which upon their release into the circulation are capable of altering the tone of the vasculature. Epinephrine is a hormone which travels in the blood supply, capable of causing generalised constriction of the arterioles, except in skeletal and cardiac muscle, where epinephrine initiates vasodilation, (Marieb 2001). Norepinephrine, as previously mentioned, and angiotensin II are vasoconstrictive, whilst atrial natriuretic peptide (ANP) which is secreted by the heart atria has a vasodilative action.

Vascular tone may also be altered as a consequence of substances secreted from endothelial cells. In response to chemical and local stimuli, endothelial cells release paracrine agents which diffuse to the smooth muscle cells inducing either vasoconstriction or vasodilation, (Vander et al. 2001). Nitric oxide is an important paracrine vasodilator, which is released continuously in the arterioles, contributing to basal conditions. Shear forces between the endothelium and blood flow contribute to nitric oxide release, contributing to basal conditions and the local control of blood flow, (Aaronson et al. 2004). Prostacyclin is another vasodilator released by endothelial cells, whilst endothelin-1, if present in high enough concentrations can cause widespread vasoconstriction of the arterioles.

1.2.9 Blood Flow

Blood flows from regions of high pressure to regions of lower pressure, along a pressure gradient. The flow of blood across a vessel is not uniform. Normal resting blood flow is laminar; layers of blood which slide across each other at

different velocities. The slowest blood flow occurs at the vessel wall, whilst the faster blood flow is generally observed in the centre of the vessel.

If there is a significant increase in the velocity of blood flow, for example due to a stenosis, the streamline nature of resting blood flow is disturbed, and vortices arise.

The changes in blood flow across the vessel are referred to as the velocity profile. Flow profiles across a blood vessel are described as either blunt or parabolic. A blunt profile refers to blood which is moving at a similar velocity across the vessel diameter, whilst in a parabolic profile the central blood is at a higher velocity than the blood near the vessel wall. The variation in flow profile arises due to the viscous drag caused by the blood vessel walls, which causes the layer of blood at the wall to remain stationary, (Thrush 2003).

Viscosity is the internal friction between adjacent layers of a fluid which aim to resist flow. Blood flow is indirectly proportional to the viscosity of blood. Blood is classed as a non-Newtonian fluid, which implies that its viscosity decreases as the shear rate increases. Shear rate is the rate of change of velocity at which one layer of fluid passes over an adjacent layer. In the case of blood, shear rate is determined by the velocity of blood flow and by the size of the blood vessel. High shear rates are typically present in the large arteries where blood flow velocity is high, while low shear rates are typical in the microcirculation where blood flow velocity is lower. Viscosity also increases as the haematocrit and plasma concentration of blood increase. Therefore, under

basal conditions, the viscosity of blood within the circulation at any instant and any location varies depending upon the shear rate within that particular vessel and the cellular fraction of blood, (Eckmann et al. 2000).

Haemodynamics is the study of the relationship between blood pressure, the resistance to blood flow, and blood flow within the cardiovascular system, using physical laws which govern the flow of fluids through single tubes, (Aaronson et al. 2004).

Blood pressure is the pressure exerted by the blood and its magnitude varies throughout the vascular system. In order to determine blood flow, the difference in blood pressure between the relevant points and the resistance to blood flow should be known, (Vander et al. 2001). Blood flow, pressure and resistance are related by the following equation (equation 2).

$$Blood\ Flow = \text{Pr}essure\ Difference\ (between\ 2\ point s) \times Resistance$$
$$F = \Delta P \times R$$

Equation 2

The resistance to blood flow is dependant upon the viscosity of blood and the dimensions of the blood vessel, as given in equation 3.

$$Resistance = \frac{8 \times Fluid\ Viscocity \times Tube\ Length}{\pi \times Inner\ Radius\ of\ the\ Tube^4}$$

$$R = \frac{8 \times \eta \times L}{\pi \times r^4}$$

Equation 3
(Nichols and O'Rourke 1990)

From equation 3 it can be seen that the resistance is directly proportional to the viscosity and the length of the vessel, whilst it is inversely proportional to the fourth power of the vessel's radius. Since the length of blood vessels within the body is constant and if the viscosity of blood is considered to be constant, the flow of blood is dependant upon the radius of the blood vessel. Small changes in the radius of a blood vessel produce dramatic changes in blood flow. For example, at constant pressure, if the radius is halved, the resistance increases by a factor of 16, whilst blood flow decreases by a factor of 16. However, these relationships describe the flow of fluids through single tubes, and are therefore only an approximation of the dynamics of blood flow through the vasculature, where the radius of blood vessels is continually altering. Nevertheless, the principles still apply, such that small dilations or constrictions of the arterioles within the vascular beds can greatly adjust the flow of blood to that particular organ.

1.3 Leg Ulcers

Ulceration of the lower limb is a chronic, debilitating condition impinging on an increasing percentage of the population, with prevalence figures of approximately 1% in the adult populace, and 3-5% in the populace over 65 years of age (Mekkes et al. 2003).

An ulcer can be described as a 'local defect, or excavation, of the surface of an organ or tissue, which is produced by the sloughing of inflammatory necrotic tissue' (Negus 1995). Chronic ulceration develops when the normal wound healing process is interrupted.

Ulceration may arise due to various aetiologies. The principal origins include arterial and venous insufficiency; however infection, inflammatory disorders, congenital abnormalities, malignancy and trauma are also recognised causes of ulceration.

1.3.1 Arterial (Ischaemic) Ulcers

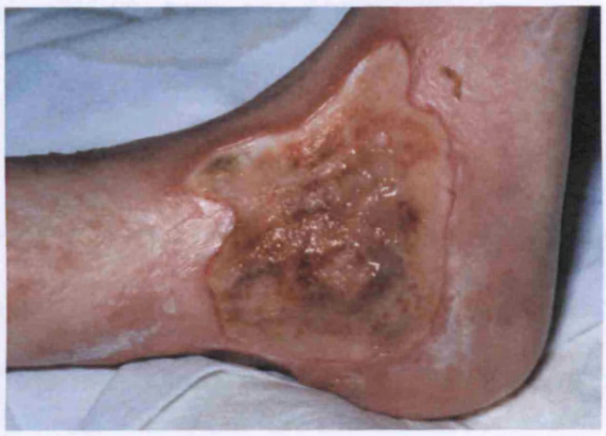


Figure 1.1 Example of an arterial ulcer.

(http://www.edu.rcsed.ac.uk/Wound%20Management/Leg%20Ulcer%20Arterial.htm)

Arterial disease is the consequence of an insufficient blood supply. Ischaemia, necrosis and subsequently ulceration may ensue.

Ischaemia is most frequently associated with arteriosclerosis. The term arteriosclerosis covers a variety of macrovascular conditions; atherosclerosis dominating under this heading. Atherosclerosis is a chronic, progressive disease, in which the arteries become increasingly narrowed and hardened. This arises as a consequence of an accumulation of fats, cholesterol, calcium, and other products on the intimal layer, due to endothelial dysfunction.

Endothelial dysfunction is believed to arise from a deficit in nitric oxide activity (Schulz et al. 2004). Nitric oxide, an effective vasodilator, also protects the intimal, endothelial lining from impairment. However, a surplus of oxygen free

radicals is considered to deplete the nitric oxide supply, promoting atherosclerotic damage (Taddei et al. 2004).

The accumulation of substances in the intimal lining is termed an atherosclerotic plaque, and continues to develop, restricting the vessel lumen and the flow of blood. The diminished blood flow influences the oxygen supply to the tissues of the lower limb. Intermittent claudication is the term used to describe pain in the leg muscles (most commonly the calf muscles) on exercise, and is a consequence of hypoxia.

Intermittent claudication may progress into rest pain; the final phase preceding gangrene. In this case, the oxygen demand exceeds the supply even when resting; distal tissues become ischaemic, and the patient experiences pain on rest. Controlled exercise may assist in alleviating the discomfort caused by claudication and rest pain, by encouraging the development of collateral circulation, without precipitating damage.

An intramural restriction or complete occlusion may arise, either due to extensive plaque formation, or thrombus development. A thrombus ensues when a plaque ruptures. The roughened surface of the plaque acts as a focus for an accrual of blood coagulation products. The amassing thrombus may entirely impede the blood vessel at the site of its formation, instigating an acute ischaemia. An embolus may also occlude the blood supply. This arises when a piece of the plaque becomes dislodged and travels in the blood flow until it becomes wedged in a smaller vessel.

When the required blood supply is not achieved, chronic or acute ischaemia ensues, and due to the depleted or inhibited perfusion of nutrients, necrosis and ulceration follow accordingly, distal to the site of the obstruction/occlusion. The risk factors for the development of arteriosclerosis include diabetes, smoking, hyperlipidaemia, hypertension, obesity and age, (Mekkes et al. 2003).

Ulceration can also develop due to ischaemia in the microvasculature. Thromboangiitis obliterans or Buerger's disease is one such condition. Buerger's disease afflicts smokers in the populace under 50 years of age, and involves ischaemia in the microvasculature of distal tissues and/or nomadic phlebitis, due to severe inflammation (Cutler and Runge, 1995).

Vasculitis is the term used to describe a class of conditions involving inflammation of the blood vessel walls. Various vasculitic disorders associated with autoimmune conditions such as rheumatoid arthritis and systemic lupus erythematosus (SLE) may lead to ulceration of the lower limb; as also will Raynaud's syndrome (vasospastic disease). Raynaud's syndrome involves a severe reaction to the cold. Arteriolar vasoconstriction occurs in the extremities, resulting in pallor (whiteness) and coldness. Cyanosis (blueness) may follow, due to an accumulation of deoxygenated haemoglobin. Minutes to hours later, when relaxation occurs and blood returns to the microcirculation, the extremities exhibit rubor (redness), and become very hot and painful. This reaction signifies the commencement of a chronic systemic disease, which

with advancement, may lead to the extremities becoming gangrenous and ulcerated.

Arterial ulceration usually arises distal to the obstruction/occlusion, at the extremities. Hence, ischaemic ulcers are commonly located on the toes, the dorsum of the foot and the heel; however they may also arise on the anterior lower limb or above the medial/lateral malleolus.

Clinically, an ischaemic ulcer has a pale base, with potential eschar (dry scab), and is free of exudates and oedema. The periphery is scantily epithelialised and is clearly delineated from the surrounding tissue; often described as having a 'punched out' appearance. Ischaemic ulcers can extend deep into the limb; in the acute instance revealing deep fascia and tendons. The surrounding tissue may be shiny, dry, free of hair, and inflammation is only apparent when infection prevails, (Sieggreen and Kline 2004).

Primary clinical tests for distinguishing ischaemic ulcers from other aetiologies include determination of skin temperature, as ischaemic tissue is cooler to the touch than the proximal skin; palpating pulses, and measuring the ankle-brachial pressure index (ABPI). Weak or absent peripheral pulses, and decreased blood pressure in the lower limbs is characteristic of patients suffering with arterial insufficiency. A normal ABPI has a value of greater than 1; arterial insufficiency is considered to be present for an ABPI of less than 0.8, although discrepancy exists in the exact cut off value, (Vowden and

Vowden 2002). For reduced ABPI values, the degree of ischaemia becomes increasingly critical. The need for a more extensive investigation would indicate the use of ultrasound, MRI or x-ray angiography.

1.3.2 Venous Ulcers

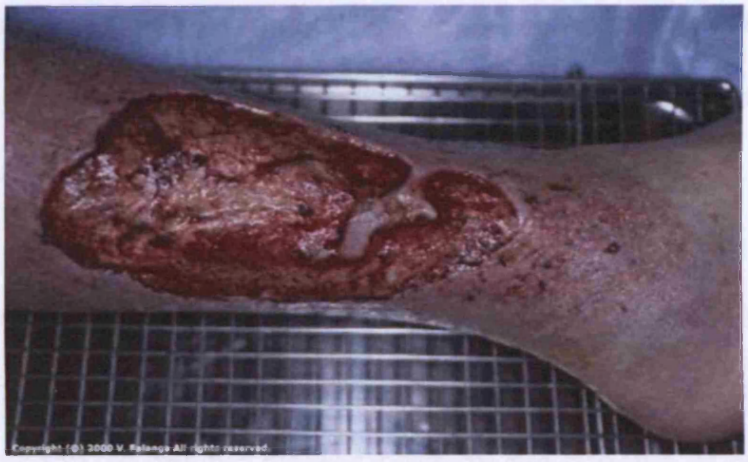


Figure 1.2 Example of a venous ulcer.

(http://www.bu.edu/woundbiotech/index.html)

Chronic venous insufficiency arises due to the incompetence of the mechanisms which aid venous return. Pathophysiological processes initiating venous hypertension precede chronic venous insufficiency, and the subsequent blood stasis within dilated, tortuous veins, concludes in oedema, anoxia and ultimately necrosis, (Sarkar and Ballantyne 2000).

There are three prime pathophysiological mechanisms by which venous hypertension may arise; perforating venous valve incompetence, deep venous thrombosis leading to post-thrombotic syndrome, and calf muscle pump

dysfunction. Regardless of origin, venous hypertension may be conveyed to the capillaries, resulting in their distension. A consequent increase in capillary permeability, leads to an accrual of fluid in the extravascular space. This oedema instigates the commencement of a progressive inflammatory process.

The route from oedema to ulceration involves dermal microcirculatory failure; however the precise pathogenesis is unclear. Nonetheless several hypotheses do exist.

In 1982 Browse and Burnand proposed the fibrin cuff theory. It was hypothesised that due to the distension of the capillaries, macromolecules, such as fibrinogen, (a soluble plasma protein), are capable of escaping from within. Extramurally, fibrinogen may polymerise to form pericapillary fibrin cuffs, which prevent the perfusion of oxygen and nutrients in surrounding tissues. Hence, necrosis and ulceration ensue. However, currently this supposition is believed to be an effect and not a cause of ulceration, as fibrin cuffs are detectable in other wound aetiologies, (Sarkar and Ballantyne 2000).

A further theory was suggested by Coleridge Smith et al. This notion implied that leukocytes could become deposited within the capillaries, subsequent to the decreased blood flow during venous hypertension. These 'trapped' leukocytes, once activated initiate the destruction of the capillary walls, hindering the filtration of nourishment to tissue. Another conjecture entails growth factor trapping. Falanga and Eaglstein postulated a theory which

considered fibrinogen and other macromolecules to ensnare growth factors and other homeostatic substances, extramurally. Due to the unavailability of reparatory substances, slight trauma could progress into chronic ulceration, (Valencia et al. 2001).

These are the principal theories; however others do exist, including arteriovenous shunting and combinations of those mentioned. The treatment and management of venous ulceration would benefit from elucidation of the precise processes involved.

Venous ulceration is preceded by a progressive inflammatory response to the inhibited nutrient perfusion. An area of erythema, due to congestion of the capillaries may be the primary clinical feature, followed by lipodermatosclerosis; an induration of the skin, due to tissue fibrosis. The definitive 'inverted champagne bottle' appearance can be attributed to a lipodermatosclerotic encircling of the limb, with oedema residing above.

The skin may acquire a red/brown hyperpigmentation, due to capillary leakage, followed by the development of eczema, and subsequent atrophie blanche. Atrophie blanche appears as small, smooth, ivory white plaques of scar tissue, interspersed with dilated capillaries, which are highly susceptible to ulceration.

Venous ulceration is commonly situated on the gaiter's area over the malleoli; most frequently on the medial side; either as a result of trauma or spontaneity.

The size of a venous ulcer can vary from a few centimetres, to circumferential around the entire area above the malleoli. The base of the wound is shallow, and irregularly shaped, with a pink/red colour due to the dilated capillaries. Venous ulcers are moist, often with a purulent exudate, an associated putrid odour; and are usually set amidst lipodermatosclerotic skin or atrophie blanche.

Patients at an increased probability of developing venous disease and subsequent ulceration include the overweight, women (often multiparous women), and those with familial tendency to develop varicose veins.

1.3.3 Diabetic Ulcers

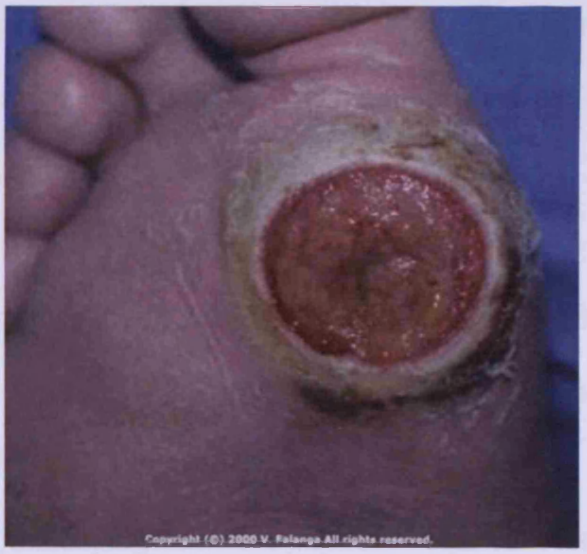


Figure 1.3 Example of a diabetic neuropathic foot ulcer.

(http://www.bu.edu/woundbiotech/index.html)

Plantar ulceration is a frequent complication of diabetes mellitus. It is estimated that 15% of all diabetic patients will acquire an ulcer at some stage during their lifetime, (Ulbrecht et al. 2004), which in the acute instance may conclude in amputation. The presence of diabetes mellitus not only increases the predisposition to ulceration, but also contributes precipitating factors for ulcer progression.

Diabetic neuropathy is a frequently attained complication of diabetes, considered to ensue secondary to prolonged hyperglycaemia, (or occasionally hypoglycaemia), and manifesting as peripheral nerve dysfunction, (Bhadada et al. 2001). Peripheral pain sensation may be lost as a consequence of sensory neuropathy, precipitating ulceration by incurring deficient patient awareness. Motor neuropathy of the muscles controlling foot motion results in abnormal plantar pressure loading, and combined with sensation loss in the lower limb, increases susceptibility to skin breakdown and subsequent progression into ulceration, (Jeffcoate and Harding 2003).

Autonomic neuropathy involving the lower limbs affects blood pressure regulation and perspiration. Thus, dysfunction of the autoregulatory response to changes in blood pressure leads to increased blood flow and arteriovenous shunting; capillary hardening due to calcium accrual follows, with subsequent oedema and diminished nutrient perfusion. Consequently, due to the ensuing ischaemia at the microvascular level, tissue necrosis commences. Decreased perspiration results in skin dryness, prone to fissure formation. Ulceration is imminent with the conjunction of these factors.

Charcot foot is a neuropathic arthropathy of the foot joints. Due to sensory and motor nerve dysfunctions, fractures or sprains of the foot may be overlooked. The consequences are vast, ultimately resulting in deformity, which if unrelenting, may lead to ulceration.

Neuropathy alone is not sufficient to instigate plantar ulceration; however, in combination with minor trauma, foot deformities or ischaemia, the threat of ulcer formation is significantly increased, (Jeffcoate and Harding 2003). Ulceration in diabetic patients may be broadly categorised as neuropathic, neuroischaemic or ischaemic; macrovascular ischaemic ulceration arising due to the aetiologies previously mentioned, and in the microvessels as a consequence of autonomic nerve dysfunction. Infection is also another causative factor for ulceration, the ensuing ulcer arising due to the altered ability of diabetic tissue to respond to mild infection.

Diabetic ulcers are prone to delayed healing, due to recurrent trauma with absence of awareness and due to secondary infection. Inadequate footwear is a common wound exasperator amongst patients with diabetic neuropathy, (Ulbrecht et al. 2004).

As previously mentioned diabetic ulcers typically occur on the plantar region of the foot, due to abnormal pressure bearing. However, ulcers may also appear distally on the toes, or on the dorsum of the foot if ischaemia is involved, (Negus 1995). Neuropathic ulcers may be readily differentiated from those ischaemic in nature as they tend to be painless, bleed easily, and are

surrounded by thick, dry skin. Both have a 'punched out' appearance; however, neuropathic ulcers generally have a pink base whilst ischaemic ulcers are very pale. The foot with a neuropathic ulcer is warm, pulses may be palpated and vein distension is apparent. Infectious ulcers are set amidst cellulitis, and include discharge as a feature.

The afore mentioned ABPI is not indicated in patients with diabetes, as calcified vessels hinder an accurate result. As a substitute, the toe-brachial pressure index (TBPI) may be measured, as calcification of blood vessels in the toes is rarely encountered, (Teodorescu et al. 2004).

1.3.4 The Physiology of Wound Healing

Wound healing arises through the 'interaction of a complex series of phenomena that eventuates in the resurfacing, reconstitution and proportionate restoration of tensile strength of wounded skin', (Deodhar and Rana 1997). Disruption of this process results in chronic wounds, which are very slow to heal, or may not heal at all.

Ordinarily, there are four principal stages to the healing process; haemostasis (inhibition of blood loss by vasoconstriction and activation of coagulators), inflammation (influx of neutrophils and macrophages to eliminate bacteria and to supply growth factors for the formation of granulation tissue), proliferation (granulation tissue formation and epithelialisation) and remodelling, (MacKay and Miller 2003). Chronic wounds arise when the inflammatory or proliferative stages are interrupted due to hypoxia, infection, metabolic disorders (for

example, diabetes mellitus), malignancy and other chronic illnesses (Deodhar and Rana 1997), thus preventing the healing process from progressing.

Wound healing is a function of the tissues of the body, hence it is not viable to "heal an ulcer" per se; but it is feasible to enhance the wound healing process by excluding or reducing those factors by which it is impeded.

1.3.5 Current Treatment Methods

The management of lower limb ulceration involves 'correction of the cause and stimulation of healing', (Eaglstein and Falanga 1997) hence accurate discrimination of aetiology is essential to promote recuperation, as treatment methods vary.

Ischaemic ulcer healing involves improving the blood supply to the wound, whilst treatment of venous insufficiency entails assisting venous drainage and reducing oedema. In each situation enhancing vascular fluid flow is instigated, but the means by which this is achieved varies.

In ischaemic ulceration, conservative techniques such as elimination of risk factors, body positioning and exercise are primary considerations. Inclination of the bed, such that the patient is positioned in a feet down angle, would enable gravity to assist in augmenting blood flow to the lower limbs; and so as to encourage collateral vessel formation, regular, appropriate exercise should be undertaken, (Sarkar and Ballantyne 2000).

If rest pain and/or infection are present, surgery may be indicated. The principal operative procedures currently in place include endarterectomy, percutaneous transluminal angioplasty with optional stent insertion and/or bypass grafting; employed so as to remove an occlusion, enlarge the vessel lumen and circumvent the occluded vessel respectively.

Venous ulcer treatment involves reversal of venous hypertension and reduction of oedema. Elevation of the limb to a height above the heart will assist venous drainage; however, the foremost therapeutic technique used for patients with chronic venous insufficiency is compression.

The principle behind compression is to decrease the superficial venous pressure, and to reduce oedema by promoting the return of fluid to within the capillaries. Compression also enhances the functioning of the calf muscle pump, improving venous return, (Laing 1992).

Various compression techniques exist; the Unna boot is a non-elastic bandage which is suitable for the ambulatory patient. The bandage is impregnated with a paste containing, amongst other substances, zinc oxide, which assists in alleviating discomfort by soothing the skin, and hardens following application, resulting in the formation of a semi-rigid boot structure, (Eaglstein and Falanga 1997). The Unna boot exerts high pressures on the limb during calf muscle contraction, and slight pressure at rest. Elasticated bandages not only apply high pressures during exercise but also at rest, the most effective elasticated bandaging being a multilayered system. The 4-

layered graduated bandage incurs increased healing rates as compared with single layer elasticated bandages, (Laing 1992).

The necessary qualities in compression bandaging are to have sufficient pressure applied to the ankle, and decreasing graduated compression thereafter towards the knee, (Negus 1995), so as to proportionately counteract venous hydrostatic pressures, and encourage fluid drainage. Following ulcer healing, it is usually recommended to wear graduated compression stockings to prevent oedema and consequently ulcer recurrence.

Superficial and/or perforating vein ligation may be beneficial in the absence of deep venous incompetence, however, it has not been acknowledged whether ulcer healing rates are affected by the removal of these veins. Another surgical procedure which may be more readily accessible in the future, involves restoration of inefficient venous valves. Valvuloplasty or transplantation processes, have been demonstrated to be effective in pain relief, healing chronic ulceration and allowing the patient to walk again, (Laing 1992).

The foremost objectives in managing diabetic ulceration are to establish whether any infection prevails, indicating the need for thorough surgical debridement; whether any associated ischaemia may be revoked by revascularisation; and to protect any prominences, deformities of the feet which act as focal points for ulceration, (Jeffcoate and Harding 2003).

As demonstrated, the number of conservative treatment options for the management of chronic, non-healing leg ulcers is limited. For ischaemic ulcers, this implies controlled exercise and adaptation of risk factors, which are not always effective. Ischaemic and diabetic ulcers generally conclude in some form of surgery, which in itself has associated risks, such as the formation of an embolus or thrombus, the introduction of infection or the eventual loss of a limb, (Labropoulos et al. 1998). Following amputation, non-operative treatment options available to the patient are few, (Montori et al. 2002). Compression bandaging systems utilised for venous leg ulcers, although successful for some patients, are not in others, in whom compliance is an issue due to the unsightliness, discomfort and inconvenience of the technique, (Ginsberg et al. 1999).

The yearly expenditure for the treatment of lower limb ulcers is believed to approximate £400 million to the NHS in the United Kingdom, (Simon et al. 2004). With the aging population, and a high susceptibility for ulceration in the elderly, this expense is liable to increase.

Hence, an alternative conservative treatment method which may enhance the wound healing process, reducing the incidence of surgical procedures amongst ischaemic and diabetic limbs, whilst simultaneously incurring good patient compliance is advocated.

A common feature amongst those ulcer aetiologies mentioned is an inefficient vascular flow, and the subsequent need for flow restoration to promote ulcer

healing. A treatment method which has incurred great research interest and promising results in its ability to enhance vascular fluid flow, and hence wound healing, is intermittent pneumatic compression.

1.4 Intermittent Pneumatic Compression (IPC)

Intermittent pneumatic compression and its application to vascular pathologies is not a new concept. It is currently utilised for the prophylaxis of deep venous thrombosis, and has been demonstrated to have beneficial results in the treatment of lower extremity arterial disease, venous ulcer healing and the reduction of oedema (whether arising due to lymph or venous pathologies), (Chen et al. 2001).

Various degrees of pressure are transmitted to the underlying subcutaneous tissue, muscle and blood vessels during the 'cyclic mechanical compression of the limb', (Sayegh 1987), resulting in a range of physiological effects. The ability of intermittent pneumatic compression to assist in the management of vascular diseases, lies, not only in mechanical effects, which initiate alterations in the dynamics of blood flow, but also in its ability to stimulate the release of biochemical mechanisms of the circulation, (Chen et al. 2001).

Arterial compression, applied so as to occlude arterial blood flow, instigates ischaemia; and on release of the compression, a reactive hyperaemia ensues. A reactive hyperaemia occurs following the release of a complete obstruction to the blood flow. During the period of inhibited blood flow, arterioles dilate, possibly due to similar mechanisms as those proposed for the hyperaemia induced by venous compression; and on release of the obstruction, an increase in flow arises.

Venous compression enhances the function of the muscle pumps, increasing venous return and hence venous flow velocity, preventing blood stasis and

consequently reducing venous hypertension. Oedema diminishes as a consequence of an increased interstitial pressure, which favours the return of accrued extravascular fluid into the capillary circulation.

Venous compression has also been demonstrated to produce an increase in arterial blood flow, (Collens and Wilensky 1936b), which was originally believed to arise as compensation for the 'blood flow debt' consequent on compression, (Lewis and Grant 1925); however, the precise physiology behind this hyperaemia is not entirely understood, although many conjectures exist.

Intermittent pneumatic compression was primarily considered in the 1930's by Collens and Wilensky. Following on from the work of Lewis and Grant upon reactive hyperaemia, Collens and Wilensky developed a device to 'produce alternating periods of venous congestion and release of congestion', so as to beneficially implement the observation, that release of a venous obstruction is associated with active vasodilation of the arteries, and a consequent increase in arterial flow by as much as 600%, (Collens and Wilensky 1936b). It was proposed that loss of vascular tone and hence vasodilation appeared due to an accumulation of metabolites in the blood vessels during venous congestion, and the degree of the resulting hyperaemia was directly proportional to the length of congestion, (Lewis and Grant 1925).

A further theory suggested an increase in the arterio-venous (A-V) pressure gradient; whereby the difference between arterial and venous blood pressures

is believed to increase, due to the decrease in venous pressure brought about by compression, (van Bemmelen et al. 2000). Increased blood flow is considered to ensue, due to an increase in the effective perfusion pressure. However, since a hyperaemia was still obtained in patients with arterial obstruction, a subsequent conjecture involved a decrease in peripheral vascular resistance, (Kumar and Walker 2002). This was believed to transpire due to the release of relaxing factors by endothelial cells, consequent on increased shear forces on the endothelial lining of the vessel. Morgan et al, (1991) supported the hypothesis that nitric oxide is released in the microcirculation due to pressure changes in the venous circulation, leading to vasodilation and a resulting hyperaemia. In view of the fact that the half life of physiological nitric oxide has more recently been discovered to be in the range of a few seconds, and that hyperaemias vastly in excess of this time scale are observed; this theory is questioned by some, who propose the release of endothelium derived prostacyclin, which has a longer half life, but similarly leads to vasodilation, (Morris and Woodcock 2004).

Additional hypotheses include suspension of the venoarteriolar reflex, and a myogenic mechanism. The venoarteriolar response to an increase in venous pressure is a neural control, involving a sympathetic axon reflex, which instigates arteriolar vasoconstriction. Peripheral vascular resistance increases, preventing an increase in arterial blood flow. It has been suggested that the reduced venous pressure produced by compression, suppresses the venoarteriolar reflex; allowing arterioles to dilate, and enabling a hyperaemia to ensue, (Delis et al. 2001). The proposed myogenic mechanism is a

vascular response to alterations in intravascular pressures. Arteriolar smooth muscle is believed to respond directly to the increased distension arising due to raised intravascular pressure by constricting; and conversely, a loss in vascular tone and hence dilation occurring in response to a decrease in intravascular pressure. However, the precise mechanism responsible for these changes in the vasculature has not been elucidated.

In summary, venous compression has been demonstrated to produce an arterial hyperaemia; nonetheless, whether this hyperaemia arises as a consequence of an accrual of metabolites, alterations in the arterio-venous pressure gradient, due to the release of relaxing factors, subsequent to suspended neural controls, due to a myogenic mechanism, or possibly even as a result of a combination of these hypotheses, is yet to be clarified.

The consequences of IPC may be summarised as oedema reduction, enhanced vasodilation, increased blood flow, and in acute ischaemia, the use of IPC encourages the formation of collateral circulation, (Koch 1997).

In addition to these physiological benefits, IPC has been reported to have good patient compliance, (Kumar and Walker 2002). The importance of patient compliance was recognised by van Bemmelen et al, (2001), where it was noted that there was a 'direct correlation between compliance and clinical outcome'; optimal results being achieved in those patients using their device for longer time periods. Those factors which assist in achieving patient conformity include its non-invasiveness, the potential for use in the out-patient

or home care setting, with the possibility for treatment to be controlled by the patient, low complication rate and good treatment results; however, discomfort and the application timescale could contribute to inadequate use. As regards the expense, long term costs may be reduced as a consequence of fewer surgical interventions and hospitalisations, (Koch 1997).

The application of IPC to arterial and venous pathologies has been extensively researched, especially over recent years. A summary is included accordingly for the different aetiologies, with particular reference to the use of IPC in ulcer healing, up until the present.

1.4.1 IPC and its Application to Arterial Pathology

The use of intermittent compression was first applied to the treatment of peripheral arterial disease by Collens and Wilensky, (1936a). Using proximal compression at pressures approaching diastolic, a noticeable improvement in pain relief, walking ability, and ulcer healing was perceived. Further subjective results followed, demonstrating similar advantages. Recent years have seen a rise in more objective work; benefiting from the advent of non-invasive techniques such as Doppler ultrasonography, which could quantify any haemodynamical alterations. In 1983, Gardner and Fox demonstrated the venous foot pump, which on weight bearing, was shown to aid venous return, (Abu-Own et al. 1993). IPC applied to the foot was initially utilised to augment the return of blood to the heart; however, in 1991, Morgan et al investigated the effects of foot impulse compression on popliteal artery blood flow in healthy individuals, and also in patients with peripheral vascular disease. With

the subjects seated and the limb under observation in the dependant position, (so as to ensure venous filling), compression was found to increase the mean popliteal artery flow by 93% in healthy individuals and by 84% in patients; whilst in the supine position, compression did not have any significant effect, (Morgan et al. 1991).

Following on from the work of Morgan and colleagues, Abu-Own et al, (1993) demonstrated that IPC of the foot imparted altered microcirculatory function in patients with peripheral occlusive arterial disease and claudication. Significant increases in laser Doppler flux and transcutaneous oxygen tension ($tcpO_2$) were obtained on dependency, indicating enhanced skin blood flow and skin perfusion, due to compression induced vasodilation, (Abu-Own et al. 1993). Intermittent calf compression was subsequently discovered to increase popliteal artery blood flow in limbs with arterial insufficiency, (van Bemmelen et al. 1994); as also did the ensuing combination of foot and calf compression, (Eze et al. 1996; Labropoulos et al. 1998). Delis et al, (2001) compared the acute effects on popliteal artery blood flow, following calf, thigh and combined calf and thigh compression. Although thigh compression was found to be the least effective of the three techniques, producing an increase in popliteal artery volume flow of 114% in normal individuals and 57% in claudicants; Delis' study demonstrated that IPC of the thigh was an alternative method of achieving enhanced arterial inflow to previous techniques involving calf and/or foot compression. Combined calf and thigh compression produced an increased volume flow of 424% in normal subjects, and 229% in claudicants; hence, it was postulated that only part of the mechanism generating

augmented blood flow may be activated during thigh compression, (Delis et al. 2001).

As previously mentioned, compression has been applied with the subject seated, as supine compression has generally been considered to produce inefficient results. However, Morris and Woodcock, (2002) correctly hypothesised that increases in arterial flow could be obtained using IPC without requiring dependency; achieving increases of 21% in healthy subjects, and 29% in subjects with peripheral arterial disease. The ability to apply compression to the supine subject also implies that thigh compression may be more readily employed.

The results obtained by Morris and Woodcock are very much lower than those produced by Delis et al. However, comparison between the studies is not justified, as the results obtained by the two groups represent different quantities. This problem is addressed by Morris and Woodcock (2002); it is noted that those figures attained by Delis et al, are only indicative of the change in volume flow 'at one instant' in the IPC cycle. Their measurements do not consider the net change in blood volume flow incurred over the entire IPC cycle, and hence falsely imply that the use of IPC increases blood flow by, for example 424%. The results produced by Delis et al could therefore be subject to incorrect interpretation. In the work carried out by Morris and Woodcock, the results obtained are extrapolated from the area under the curve during the IPC cycle, consequently indicating the percentage increase in flow acquired by IPC as compared with a pre-compression value.

As a consequence of the acute effects obtained following lower limb compression, it was proposed that compression therapy could have potential long term beneficial effects in the management of ischaemic limbs, with associated rest pain and ulceration.

Delis and colleagues, (2000) were amongst the first to examine the long term clinical, as well as haemodynamical effects of IPC in patients with claudication. Patients received foot compression daily for 4.5 months, resulting in an increase in claudication distance of greater than 100%, along with a 36% increase in arterial calf inflow. Their work also demonstrated maximum benefits during the first 3 months of therapy, and treatment gains were maintained at least 12 months following cessation of compression, (Delis et al. 2000). Van Bemmelen et al, (van Bemmelen et al. 2001) also investigated the clinical effects in patients with critical limb ischaemia following 3 months of combined foot and calf IPC. Using rapid, high pressure compression for an advised 4 hours a day, a 70% limb salvage occurrence was achieved at 2.5 years follow-up.

As regards compression specific to the treatment of ischaemic ulceration; little has been accomplished. Dillon, since the 1980's has investigated the use of the circulator boot in patients with peripheral vascular disease. The circulator boot is an 'end-diastolic pneumatic compression boot therapy', which has been demonstrated to augment arterial blood flow in the lower limbs, (Dillon 1997a). Even though the technique used differs from the IPC therapy considered here, the fundamental mechanisms resulting in enhanced blood

flow may be similar, (van Bemmelen et al. 1994). Dillon reported partial to full ulcer healing in patients with various ulcer aetiologies as a consequence of receiving circulator boot therapy, (Labropoulos et al. 2002). However, the foremost study demonstrating the advantages of IPC in nonhealing ischaemic ulcer treatment was performed by Montori et al, (2002). Their observational review of patients with critical limb ischaemia and active ulcers, using rapid, graduated, sequential compression of the calf for an advised 6 hours a day, revealed unexpectedly high rates of ulcer healing. Subsequently, it was implied that IPC may have disturbed the normal clinical progression of nonhealing wounds. Total wound healing and amputation prevention was achieved in approximately half (47%) of the patients observed, (Montori et al. 2002). Moses and Yoffe, (2002) also demonstrated complete wound healing in a patient with rest pain and leg ulcers, 3 weeks following commencement of IPC therapy.

From the evidence here presented, it would seem that IPC could be used clinically, as a treatment option for nonhealing ischaemic ulcers, although further long term clinical studies are implicated. However, even though the outcomes of these investigations were all positive, there was significant variance in the results obtained between different trials. This discrepancy could be attributed to the difference in assessment method, treatment regime and/or the disease itself. No disorder manifests in one person, in exactly the same way as the next person; consequently, the needs of one person differ from those of another; additionally, the diseases targeted in different trials may not have been the same.

1.4.2 IPC and its Application to Venous Pathology

Intermittent pneumatic compression has had a long history of use in the prophylaxis of deep venous thrombosis, due to its proven ability to reduce venous stasis. The high flow pulsatility produced by IPC is considered to drain the veins intermittently, consequently clearing the soleal sinuses, axial veins and valve sinuses, (Nicolaides et al. 1980) which act as focal points for thrombi formation. Following further research demonstrating that IPC was also capable of influencing fibrinolysis, tissue oxygenation, oedema and venous return, (Vowden 2001), ensuing work suggested that venous ulcer healing may profit from IPC therapy.

As with all ulcer aetiologies, the key to achieving complete healing is to improve the perfusion of nutrients to the tissues surrounding the ulcer. The prerequisite for venous ulcer healing in particular is a reduction in oedema. Pflug, (1975) correctly appreciated that oedema, of venous or lymphatic origin, should be conservatively targeted at the microcirulatory level; aiming to attain net absorption of interstitial fluid into the vasculature. Consequently, Hazarika and Wright, (1981) designed a compression technique which aimed to decrease intracapillary pressure, anticipating enhanced transcapillary fluid exchange and improved cell nutrition. In their study of 21 ulcer patients, receiving daily treatment for an average of 26.7 weeks, it was deduced that IPC had an advantageous effect on chronic leg ulcers. Although complete healing was not achieved, in each patient there was a 'definite subjective improvement'.

Subsequent investigations demonstrated the effect of combining IPC therapy with standard conservative treatments, in comparison to standard therapy alone. Pekanmaki et al, (1987) performed an open clinical trial on patients with persistent or recurrent post-thrombotic leg ulceration receiving IPC therapy. An IPC device subjecting the limb to sequential graded compression was demonstrated to decrease the mean ulcer healing time from 13 weeks, with conservative compression treatment, to 5 weeks when included in the regime. An increase in $tcpO_2$ of approximately 80% was also noted during a single treatment session in a small subgroup of patients from whom the measurement was extrapolated. The increased $tcpO_2$ is believed to be justification for augmented capillary perfusion due to a reduction in extravascular fluid. This was substantiated by a progressive diminution in leg circumference during each IPC session. A one year follow up indicated that a single ulcer had recurred in the 8 patients included in the study.

An objective analysis involving daily home use of sequential pneumatic compression therapy for the treatment of venous ulceration was performed by Coleridge Smith and colleagues, (1990). A 3 month comparative study examined the addition of IPC to the standard treatment of graduated compression stockings, in contrast with standard treatment alone. The IPC device was applied on top of the stocking. A significant difference in ulcer healing rates between the two groups was obtained; 2.1% of the ulcer area healing per week in the control group as compared with 19.8% of the ulcer area per week in the group receiving IPC therapy. At the end of the study period, complete healing had occurred in 11% of the control ulcers, whilst the

addition of IPC increased this figure to 48%. However, the reliability of these results is questioned by Vowden, (2001) due to the difference in the number of ulcers per patient between the two groups, (1.5 in the control group as compared with 1 in the IPC group), and no indication of the number of ulcers healed in the control group.

Mulder et al, (1990) conducted a similar trial in which sequential IPC was combined to standard Unna's boot therapy. The patients involved acted as their own control, having undertaken previous failed treatment with the Unna's boot. It was concluded that the improvement in ulcer healing attained was consequent on direct treatment of the underlying pathology, decreasing venous hypertension and blood pooling, and enhancing venous return. Additionally, it was suggested that the fibrinolytic effect of IPC may assist in reducing pericapillary fibrin cuffs, which are hypothesised to inhibit the perfusion of nutrients.

These trials seemed to demonstrate that the addition of IPC therapy to standard treatments improved ulcer healing rates. The results obtained when direct comparison was made between IPC and standard compression techniques in venous ulcer healing however, did not produce a significant variance in their efficacy. The work accomplished by Schuler and colleagues, (1996) which compared the use of IPC with the Unna boot, did not demonstrate a significant difference between the therapies; with healing rates of 76% and 64% obtained respectively. It was considered however, that the IPC device was as effective as the Unna boot, but did not include the

disadvantages associated with the boot. Similarly, Rowland (2000) concluded that there was no difference between the effectiveness of compression bandages and IPC in the healing of ulcers or the management of oedema, following a randomised cross-over study. 11 patients were included in the investigation, of which 3 ulcers had healed within 4 months, one of which was originally from the IPC group; whilst no additional ulcers had healed by 6 months. However, a questionnaire completed by the patients revealed that IPC incurred greater compliance than bandaging, due to its ease of use and comfort.

Ginsberg et al, (1999) also performed a randomised cross-over trial in patients with severe post-phlebitic syndrome; although their study differed slightly in that it involved a comparison between two different IPC treatments. A therapeutic pressure of 50mmHg was compared with a placebo pressure of 15mmHg. Treatment was assessed by questionnaire, and only considered to be successful if the patient concomitantly revealed that the therapeutic pressure was preferred, and intended to continue pump use, and the difference between the pressures was deemed at least slightly important. On these grounds, an 80% success rate was achieved, following a 2 month trial.

From those trials mentioned, even though the studies involved small patient cohorts and the studies undertaken varied in compression technique, length, assessment method and outcome, it would seem that there is evidence implicating IPC as an alternative treatment method for chronic non-healing venous ulcers. The comparisons undertaken between IPC devices and

standard conservative treatments did not seem to reveal any significant differences between their clinical outcomes; however, when IPC was combined with bandaging or compression stockings, a considerable improvement in the healing rate of venous ulceration was achieved. The implications of this suggest that whilst IPC therapy may produce acute transient alterations in blood flow and oedema, predominantly, other measures are required to maintain these changes long-term. Hence, compression bandages or stockings are worn either intermediately between IPC sessions, or continually with the IPC cuff placed on top. Other measures were also advised to assist compression therapy, such as limb elevation, and avoiding standing for long periods of time.

It is stated in the Cochrane review, (Mani et al. 2004) that there is no conclusive evidence for improved ulcer healing as a consequence of IPC, either in comparison with or when combined with standard compression techniques . Although there seems to be a beneficial effect, the size of the studies and their quality are not sufficient to provide conclusive evidence, and larger random controlled studies in both the inpatient and home settings are advocated.

1.4.3 IPC and its Application to Diabetic Ulceration

The application of IPC to diabetic ulceration, has never received due attention, in part owing to the complexity of factors involved. Leg ulceration in a diabetic patient may arise as a consequence of venous and/or arterial

insufficiency, and neuropathy may also be involved; although the majority of diabetic ulcers occur as a consequence of arterial disease. Some trials concerned with IPC and its influence on ischaemic limbs however, include patients with concomitant diabetes. In particular, the review conducted by Montori et al, (2002) on the use of IPC for non-healing ischaemic ulceration involved 107 patients, of whom 64% were diabetic. The study demonstrated that IPC significantly enhanced ulcer healing in diabetic patients; complete healing attained in 51% of those patients with diabetes.

Dillon, (1997b) considers the function of the Circulator Boot in treating peripheral neuropathic ulcers. A case report is described of a patient with poorly controlled diabetes, which had progressed into an infected ulcer, with amputation imminent. Antibiotic injections were administered in conjunction with the circulator boot, and the patient was eventually discharged ambulatory, having avoided amputation, to continue boot therapy as an outpatient. The circulator boot was believed to be effective in distributing the antibiotic, and in enhancing blood flow throughout the infected foot.

Dillon, (1997a) also investigated the effectiveness of the circulator boot in the treatment of foot and leg lesions associated with diabetes and peripheral arterial, venous and neuropathic disease. Relapse following treatment appeared to be more likely in diabetic patients than non-diabetics, although amputation rates amongst these two groups were very similar. Overall, the percentage of diabetic and non-diabetic lesions, found to heal was

comparable; however the significance of this comparison may be questionable due to the variety of wounds included in the study.

The inference which can be acquired from these studies is the implication that some diabetic ulcers may also benefit from compression treatment.

1.4.4 The Device

It has been established that compression therapy may have potential as a treatment method for chronic non-healing lower limb ulcers of varying aetiologies; but, what exactly does the technique of intermittent pneumatic compression entail? Great conjecture exists concerning the optimal compression regime, consequent on the varying hypotheses regarding the associated physiological response.

Intermittent pneumatic compression therapy involves the application of an air-tight cuff about the limb, which is connected to a pump, enabling inflation of the cuff to a preset pressure for a given time, and deflation to another set pressure, (Sayegh 1987); the cycle is then repeated for a fixed period. However, the type of cuff, the pressures used, and the inflation and deflation times vary between arterial and venous treatment regimes, and also from one author to the next.

Originally, intermittent pneumatic compression devices consisted of a single compartment which was applied to the calf, at pressures below diastolic. Multi-compartmental devices followed subsequently, which could enclose a

greater part of the limb and enable varying pressures to be applied to different aspects of the leg, (Koch 1997). The graduated sequential compression device was designed specifically for the enhancement of venous return. It has been postulated, but never proven, that the single compartment device occludes the proximal before the distal veins, and in doing so trapping a volume of blood distally. The mechanism of action of the graduated sequential device, which involves inflation of the most distal compartment first, followed by a proximally directed progressive inflation of the remaining compartments, ensures complete venous emptying, applying a 'milking' affect on the leg, and in doing so augmenting venous return.

With regards chronic venous insufficiency and venous leg ulcers, both single and multiple chamber devices have been demonstrated to have beneficial results. Hazarika and Wright, (1981) and Rowland, (2000) employed a single chamber device in their studies on venous ulcer healing. The Flowtron system (Huntleigh Healthcare, Luton, UK) utilised applies uniform compression to the calf at pressures ranging from 30 to 90 mmHg, with equal periods of inflation and deflation lasting 90 seconds each.

Salvian et al, (1988) compared the use of a single chamber compression device with two different sequential compression devices. The PAS pulsatile anti-embolism system (American Hamilton, Two Rivers, Wisconsin) is a single chamber device, utilised at a pressure of approximately 45mmHg, with a 15 second compression period and 60 second recovery period, and complete inflation is attained after 5 seconds. The Thrombogard (Gaymar Industries,

Orchard Park, NY) is a knee length sequential device with four chambers, each inflating to a pressure of 45mmHg; with an associated cycle of 16 seconds compression and 60 seconds deflation. A Kendall SCD sequential compression device (Kendall Healthcare products, Mansfield, MA) was also utilised at a similar pressure. This device has three chambers placed over the distal and proximal calf and the distal thigh, which are sequentially inflated for 11 seconds and deflated for 60 seconds. Various comparisons between the devices were made on normal and postphlebitic legs, in supine and sitting positions. Although each device produced a comparable increase in peak blood flow velocity, it was demonstrated that the mean velocity increase in femoral vein flow was greater for the PAS and the Kendall devices; similar results were obtained for normal subjects and postphlebitic patients, position not influencing the results. Salvian et al query the significance of the difference between the mean velocity flows, suggesting that it is the peak velocity flow which is of greatest importance in reducing blood stasis; however, the peak velocity measurement is indicative of one instant in the compression period, whilst the mean includes the entire compression period. Consequently, one would assume that the mean velocity flow is a more accurate representation of the efficacy of a compression device, and hence it could be suggested that sequential compression encompassing the entire limb is the optimal device for augmenting venous return. The Kendall SCD device has also been used by Coleridge Smith et al, (1990) and Mulder et al, (1990).

Another sequential compression device was implemented by Ginsberg et al, (1999), namely the Jobst extremity pump (Jobst, Inc., Toledo, Ohio). This device can be used at pressures ranging from 20 to 120 mmHg, although in the study by Ginsberg et al, a pressure of 50 mmHg was administered therapeutically. This system involves a long compression period of 190 seconds, approximately 60 seconds compression by each of three chambers, with a 50 second recovery period.

Sequential compression progressed to the application of graduated sequential compression. A full leg Kendall sequential gradient IPC system (Kendall Healthcare products, Mansfield, MA) was demonstrated by Schuler et al, (1996) to be as effective as standard Unna's boot therapy. The device applies graduated pressures at intervals of 2.5 seconds to the ankle, calf and thigh of 50, 45 and 40 mmHg respectively, and involves a cycle of 12 seconds compression with 60 seconds of relaxation.

Compression therapies used in the management of venous disease at present are generally either sequential devices or graduated sequential devices applied to the calf and/or the thigh, implemented at pressures below diastolic blood pressures in order to ascertain that arterial compression does not arise. The recovery period needs to be of adequate length to enable maximal venous refilling following compression, as it has been hypothesised that the greater the venous congestion, the greater the volume of the expelled blood, and hence the higher the increase in blood flow velocity, (Nicolaides et al. 1980). Consequently, there is a tendency to use a recovery period of

approximately 60 seconds duration. The compression period varies considerably amongst the different devices; the majority of those devices mentioned use a compression period of between 11 and 16 seconds, however, exceptions include the Flowtron pump and the Jobst extremity pump, implementing compression periods of 90 and 190 seconds respectively.

Consequent on the discovery that venous compression could also induce an arterial hyperaemia, systems devised to take advantage of this finding began to appear. Collens and Wilensky's original system for augmenting arterial blood flow by venous compression was applied to the thigh. The long cycle adopted was consequent on the hypothesis that an accrual of metabolites resulted in the observed hyperaemia. Long compression periods were aimed at producing maximal vasodilation, and hence maximal hyperaemia. Earlier devices also involved a slow inflation cycle, consistent with the belief that compression increased the arterio-venous pressure gradient, by squeezing blood from within the veins, (Morgan et al. 1991).

Following Gardner and Fox's discovery of the venous foot pump in 1983, a compression device was designed in order to imitate the normal haemodynamical response of ambulation. The AV Impulse system (Novamedix, Andover, Hampshire, UK) is a foot compression device with a single small chamber applied to the mid foot, which inflates very rapidly. Originally, this device was utilised for the prophylaxis of deep venous thrombosis, the rapid inflation generating immediate propulsion of venous

blood towards the heart and clearance of the valve sinuses, (Gardner and Fox 1992). Inflation is achieved within 0.4 seconds; consequently a short duration, high pressure compression of 3 seconds is adequate to empty the veins of the foot, within a 20 second cycle. In 1991, Morgan et al, demonstrated that the AV Impulse device also produced a popliteal artery hyperaemia. The cycle used was identical to that implemented for DVT prophylaxis, which comprised a pressure of the order of 130mmHg. The AV Impulse compression device was subsequently employed by others in their investigations on arterial haemodynamics, (Abu-Own et al. 1993; Delis et al. 2000).

The ArtAssist device (ACI Medical Inc, San Marcos, California) enables compression of greater proportions of the lower limb. Eze et al, (1996) and Labropoulos et al, (1998) utilised the ArtAssist for investigating the effect of compression of the foot and calf on popliteal artery blood flow. The device applies compression to the foot, ankle and calf using a 12cm chamber applied to the dorsum of the foot, and a 22cm chamber applied to the muscular area of the calf, (Labropoulos et al. 1998). Both compartments are inflated to a maximum pressure of 120mmHg; however, the foot is compressed approximately 1 second before the calf. Although cycles of 15 seconds (Labropoulos et al. 1998) and 30 seconds (Eze et al. 1996) have been utilised, a 20 second cycle seems to have been established as standard, with compression times of 3 or 4 seconds, (Labropoulos et al. 2002).

The Aircast ArterialFlow system (Aircast Inc, Summit, New Jersey) used by Montori et al, (2002) is a graduated, sequential compression device applied to

the calf. It is comprised of two chambers; the distal compartment inflating to a pressure of 95mmHg 0.3 seconds before inflation of the proximal compartment to 85mmHg. A similar cycle of 20 seconds with 2 seconds of compression is utilised.

The 3 devices mentioned are all applied with the treated limb in the dependant position. Even though the compression devices differ with respect to the area of the limb to which they are applied, the cycles used demonstrate some similarities. Compression regimes, utilised for the treatment of arterial disease, generally involve compression of the foot and/or the calf, and a typical cycle of 20 seconds duration, with a short period of 2-4 seconds compression. However, foot compression involves higher pressures than calf compression. The devices similarly inflate very rapidly, ordinarily within approximately 0.3 seconds.

Morris and Woodcock provided an alternative treatment regime which involved simultaneous calf and thigh compression in the supine position. The DVT-30 cuff was used with a Flowtron pump at a lower pressure of 60mmHg, to prevent arterial compression, but ensure complete venous emptying. A comparison between two different cycles was undertaken; a 60 second cycle with 10 seconds of compression, and a 120 second cycle with 60 seconds of compression. The cycles involved in this study are of a longer duration than those previously mentioned due to longer inflation times. It was demonstrated that similar duration hyperaemias were encountered with both cycles,

although higher velocities were achieved with the long cycle, (Morris and Woodcock 2004).

One of the benefits associated with venous compression concerns the compression pressure utilised. Venous compression employs a lower pressure than arterial compression, which implements pressures greater than systolic blood pressures so as to completely occlude the blood supply. Consequently venous compression is more comfortable for the patient, which assists in incurring good compliance. Arterial compression is not frequently used, due to the pain inflicted by these pressures, and the possibility of exacerbating ischaemia by the occlusion and hence diminution of the blood supply. This poses a further advantage for venous compression, as at no instant during the compression cycle is the blood supply depleted.

In summary, arterial flow enhancement is achieved by venous compression, at pressures below systolic; however, the exact pressure depends on which part of the limb is being compressed. Foot compression implements higher pressures than full limb compression, and cycle durations are also shorter with foot compression than when the entire limb is compressed. A frequently observed foot, or foot and calf compression cycle is 20 seconds in length, with compression duration of a few seconds. The compression garment generally implemented for arterial flow improvement is a single compartment device, applying uniform compression. Venous return augmentation utilises lower pressures to prevent arterial compression, and a sequential or graduated sequential compression device, with higher pressures applied in the most

distal chambers. The cycles employed in venous return enhancement are longer than those in arterial cycles, with recovery periods of approximately 60 seconds to ensure venous refilling. Inflation times vary for both systems; some systems implement rapid inflation, whilst others involve slow inflation, however; slow inflation is usually associated with calf and/or thigh compression, and rapid inflation devices involve compression of the foot. Generally, venous compression for arterial or venous flow augmentation has required the limb to be in the dependant position to allow complete venous refilling, however recent evidence implies that this is not essential, and supine compression is feasible. No substantial evidence exists regarding the duration of treatment sessions. In the review conducted by Vowden, (2001) concerned with IPC for the treatment of venous leg ulceration, it is suggested that a two hour session repeated twice daily is successful in outcome and in obtaining patient conformity; whilst Montori et al, (2002) suggest a minimum of six hours to be received daily for treatment of ischaemic ulceration.

It has been established that intermittent pneumatic compression is beneficial in the management of some vascular diseases; however, the remaining subject area which has failed to be mentioned so far, regards the methods by which the competence of compression systems has been evaluated.

1.5 Imaging Methods

The efficacy of compression devices has been assessed by varying subjective and objective measurements over the years. Subjective measurements generally involve patient judgement regarding any alterations in sensations, for example pain perception; the patient may be requested to grade their level of pain on a scale of 1 to 10. These clinical indications may provide an approximate guide as to the consequences of compression therapy; however, the reliability of these measurements is suspect as they depend upon the accuracy and perception of the individual. Comparison between individuals is therefore not validated as human perception varies from one person to the next.

Objective measurements entail a precise quantification of the physiological effects of compression. These measurements are dependant on the individual extrapolating the information; subsequently, if the same individual collects the results from all subjects involved in a trial, comparison of results may be justifiable.

Originally an objective assessment of compression therapy involved invasive techniques such as angiography; which comprised the introduction of a contrast medium via injection into the vasculature and the production of a series of digital x-ray images. The images could not only be used for diagnostic purposes, but also for demonstrating any alterations in the vasculature pre and post compression therapy. Only in recent years has a non-invasive objective measurement been viable, following the development

of techniques such as ultrasonography and photoplethysmography, which could relatively accurately quantify any haemodynamical alterations.

1.5.1 Medical ultrasound

Medical ultrasound enables structures within the body to be imaged and blood flow characteristics to be extrapolated. The interaction of ultrasound waves with boundaries or moving targets inside the body is used to produce a cross-sectional image of tissues and organs within the body, or to determine a velocity.

Ultrasound is a high frequency sound wave; a longitudinal wave which propagates through physical media (Martin and Ramnarine 2003). As a sound wave passes through a medium, particles oscillate backwards and forwards along the direction of wave propagation, the frequency of the wave corresponding to the frequency of particle oscillations. This results in regions of compression, or increased pressure, where particles have moved closer together, and regions of rarefaction, or decreased pressure, where particles have moved away from each other. In this way, the sound wave and its energy are conveyed through the medium without any overall movement of the medium itself.

Medical ultrasound implements sound waves at frequencies in the range of 1 to 15 MHz. Ultrasound waves are produced using an electromechanical transducer, which converts an electrical signal into an ultrasonic pulse using a piezoelectric crystal. A voltage transmitted across a piezoelectric material

causes it to expand or contract; conversely, if a piezoelectric material is compressed or expanded, a voltage may be generated, (Martin and Ramnarine 2003). Hence, transducers are also capable of converting the ultrasound echo back into an electrical signal.

As an ultrasound pulse travels through tissues and organs of the body, some of its energy may be reflected at an interface between two or more surfaces and scattered from small tissue irregularities. Reflection and scattering occur when the ultrasound wave encounters a change in acoustic impedance at tissue boundaries. The acoustic impedance (z) of a medium is a measure of the particles' response to a sound wave of a particular pressure, (Martin and Ramnarine 2003), and is given by the ratio of sound pressure (p) to particle velocity (v), or the product of the density of the medium (ρ) and the speed of sound (c) (see equation 4, where k is the stiffness of the medium).

$$z = \frac{p}{v} = \sqrt{\rho \cdot k} = \rho \cdot c$$

Equation 4

Most tissues of the body have similar acoustic impedances; however, exceptions include bone, which has a high acoustic impedance, making imaging structures beyond bone very difficult, as a large proportion of an ultrasound wave may be reflected at tissue-bone interfaces. A similar problem is encountered with air, which has a low acoustic impedance. In order to

minimise the occurrence of reflection between the skin surface and the transducer an ultrasound coupling gel is used, which eliminates the air gap.

The reflected and some of the scattered ultrasound signals are directed back towards the transducer. The time taken for the echo to be received back at the transducer and the amplitude of the echo is indicative of the distance the pulse has travelled and the intensity or brightness of the reflection. Consequently, the series of echoes received by the transducer contains sufficient information to produce a grey scale image of the structures within the body from which the ultrasound has been reflected. This image is known as a B-mode image or brightness mode image, in which each echo is presented as a point.

Real time B-mode imaging is used in most diagnostic ultrasound procedures to obtain anatomical images, and to observe the changes which occur in the image over time. Due to the high rate of image production, for example, 30 images per second, and the negligible delay between data acquisition and image display, it is possible to observe tissue motion, such as the beating of a foetal heart, (Martin 2003). Real time imaging also enables the sonographer to visualise and explore different aspects of structures within the body by altering the direction of the scan plane.

The M-mode or motion mode of ultrasound scanning enables measurements of tissue motion with time. As with B-mode imaging, ultrasound pulses are transmitted into the tissue and echoes are received back at the transducer.

The M-mode scanning technique involves a vertical brightness modulated display line, which moves slowly across the screen following each pulse-echo sequence. A horizontal line represents a stationary structure, whilst the vertical movement of echoes across the screen indicates a moving structure.

The Doppler effect makes it possible to use ultrasound for the detection of tissue and blood motion, (Hoskins 2003). First derived in 1845 by the Austrian physicist C.J. Doppler, the Doppler effect describes the change in the detected frequency when a source of sound moves relative to an observer. If a source of sound is moving towards an observer, the apparent frequency increases, where as a source of sound moving away from an observer produces a decrease in the apparent frequency. The same is also true if the source is stationary and the observer is in motion. The change in the observed frequency is known as the Doppler shift, and its magnitude is proportional to the velocity between the source of sound and its observer.

When an ultrasound beam is transmitted towards a blood vessel, it is scattered at a frequency which varies dependant on the movement of red blood cells. Doppler ultrasound systems therefore, measure the change in frequency of the ultrasound scattered from the moving blood, (Hoskins 2003), and this information may be used to determine the velocity of blood. The Doppler shift frequency (f_d) detected is given by the difference between the transmitted (f_t) and the received (f_r) frequencies, (equation 5).

$$f_d = f_r - f_t = \frac{2 f_t v_b \cos\theta}{c}$$

Equation 5

In equation 5, v_b represents the velocity of blood, c the velocity of ultrasound through tissue, whilst θ is the angle of insonation, or the angle between the direction of blood flow and the ultrasound path. The angle of insonation can vary as a consequence of variations in the orientation of the ultrasound probe or the blood vessel, (Hoskins 2003). In order to obtain the maximum Doppler shift frequency an angle of insonation of zero is required. Cosθ is a maximum when θ is equal to zero, and hence, the Doppler shift frequency is also a maximum when θ equals zero. This occurs when the blood vessel and the ultrasound beam are aligned, which is not always possible in practice. Providing the angle between the blood vessel and the ultrasound beam is less than 60°, a good signal is obtainable.

The multiple two in equation 5 arises as a consequence of the two Doppler shifts which occur between the transmission of the ultrasound beam and the detection of the echo back at the transducer. The first Doppler shift transpires when the ultrasound reaches the moving blood (stationary source and observer in motion), whilst the second arises when the scattered ultrasound is travelling back towards the receiving transducer (source in motion and stationary observer).

If the angle of insonation and the Doppler shift frequency are known, it is therefore possible to determine the velocity of blood flow, as given in equation 6.

$$v_b = \frac{c\, f_d}{2\, f_t \cos\theta}, \text{ where } c >> v_b$$

Equation 6

There are two differing Doppler ultrasound systems: continuous wave and pulsed wave. Continuous Doppler ultrasound systems transmit a continuous ultrasound wave. Separate piezoelectric elements are required within the transducer to transmit and receive the ultrasound signals; a continuously transmitting element and a continuously receiving element. The Doppler signal is obtained from the region in which the transmitted and received ultrasound beams overlap.

Pulsed wave Doppler ultrasound systems implement a single element which both transmits short pulses of ultrasound and receives the returning signal. A pulsed wave system can be utilised for the detection of signals from known depths. This is achieved using a range gate; the depth and length of which controlling the region from which the signal is obtained. The depth and length of the gate can be manually controlled.

There are a number of different Doppler ultrasound display modes, namely spectral Doppler, duplex ultrasound and colour flow imaging. Spectral Doppler provides information on the range of frequencies or velocities detected from a

single location within the blood vessel. The information is displayed in the form of a frequency shift (or velocity) – time plot, with the grayscale indicating the amplitude of each frequency shift (or velocity).

The amalgamation of B-mode scanning with spectral Doppler ultrasound enables a Doppler signal to be obtained from a known anatomical location, for example from the centre of a blood vessel, or distal to a stenosis. This Doppler display mode is known as duplex ultrasound. Colour flow imaging superimposes the Doppler signal on to a real time B-mode image. The Doppler signal is displayed as a two dimensional colour image, where the colour of each pixel is indicative of the amplitude and direction of the Doppler shift. Through the infiltration of colour to the grayscale B-mode image, blood flow patterns may be visualised. The fundamental colours implemented are red and blue for directions towards and away from the transducer, whilst a third colour, occasionally green, is utilised for the illustration of turbulent flow.

Colour duplex imaging combines duplex and colour flow imaging, enabling the simultaneous visualisation of blood flow within vessels and quantification of the velocity of flow from specific locations within the vasculature.

Doppler ultrasound scanning is frequently used to assess vascular diseases. Pathology may be identified from the Doppler frequency or velocity spectrum; by observing the presence and directions of blood flow in a colour duplex image, and from the basic B-mode image, which may demonstrate calcium hardening or plaque formation due to the greater reflectivity of calcium.

Ultrasound techniques may also be utilised to quantitatively assess alterations in blood flow arising as a consequence of compression, by comparing results extrapolated pre, during and post compression sessions.

The method by which arterial and venous blood velocity measurements may be extrapolated varies as a consequence of their differing flow characteristics. Arterial flow is influenced by the cardiac cycle, producing a pulsatile Doppler spectrum, enabling average velocities to be automatically calculated by the system over a specified number of cardiac cycles. Venous flow is not pulsatile to the extent of arterial flow. This is due to a combination of factors, including their distance from the heart, the compliance of the vein walls which allows absorption of pressure changes, and the further masking of cardiac pressure changes by respiratory pressure changes. Consequently, venous velocity measurement involves manual extrapolation of a value from the Doppler spectrum.

1.5.2 Laser Doppler Flowmetry

Laser Doppler flowmetry (LDF) has also been utilised in some studies to assess the affect of compression on skin blood perfusion. This technique similarly implements the Doppler effect, transmitting laser light through the skin, which is reflected and Doppler shifted by moving blood cells. The quantity of Doppler shifted laser light corresponds to the concentration of blood cells, whilst the mean frequency shift depicts the mean blood flow velocity, (Abu-Own et al. 1994). The laser flux value detected which corresponds to microvascular perfusion is the product of blood cell volume

and their mean velocity. However, this technique is difficult to calibrate, and therefore is used mainly to measure changes in flux.

1.5.3 Photoplethysmography

Photoplethysmography (PPG) is a technique which enables determination of any alterations in blood volume. This method involves the transmission of infra-red light within the skin, which is absorbed dependant on the volume of blood contained in a selected area of tissue. Hence, changes in blood volume can be deciphered from the quantity of light reflected. Venous and arterial blood volume changes may be detected. There are two types of PPG probe, reflection probes and transmission probes. The reflection probe contains an LED and a photodetector which lie side by side, enabling reflected light to be detected; whilst in a transmission probe the LED and the photodetector are opposite to one another, such that the tissue area under investigation is placed between the light source and the detector. Reflection probes may be utilised for the analysis of venous or arterial blood volume changes, however the transmission probe is particular to the analysis of the arterial side of the circulation. In general the probes are applied to distal areas, such as the digits for examination of the microcirculation. By observing the form of the volume curve over time, vascular abnormalities may become apparent. For example, rapid venous refilling times are indicators for the presence of venous insufficiency, whilst damping of the normal pulsatile arterial signal may signify arterial pathology. The use of PPG may be indicated for the analysis of the efficacy of compression devices, as any blood volume alterations incurred as a consequence could be verified.

1.5.4 Electrical Impedance

Electrical impedance measurements may also assess alterations in blood volume. The underlying principle of the technique involves detection of the distribution of electrical impedances throughout the cross-section of a conducting tissue, by placing electrodes on the surface of the medium, (Vonk Noordegraaf et al. 1997). Pairs of electrodes are placed on the skin surface, and a series of small currents are applied to a pair of consecutive electrodes. The current applied travels through the body along paths of least impedance, and potential difference measurements are obtained from the remaining pairs of electrodes. Blood volume fluctuations are determined as a result of the alterations in impedance arising due to alterations in blood vessel volumes.

1.5.5 Assessment of IPC

The efficacy of a compression device is generally assessed by monitoring any alterations in blood flow dynamics, whether this involves Doppler or duplex ultrasound techniques, PPG and/or electrical impedance measurements. Each of these methods is non-invasive, and does not incur any risks to the subject or the operator provided the instrument is used correctly. These techniques are implemented for the assessment of acute changes in blood flow dynamics incurred as a consequence of compression. Transcutaneous oxygen partial pressure ($tcpO_2$) measurements have been deemed by some to provide a reliable indication of the degree of ischaemia, demonstrating the disparity between oxygen supply and consumption; consequently, $tcpO_2$ measurements could be implemented to determine the degree of tissue oxygenation, and whether oxygen perfusion is improved by the use of IPC. In

a longer clinical trial, for example investigating the affect of compression on ulcer healing rates, additional measurements may be required in conjunction with quantitative analysis of blood flow dynamics, such as, measurement of ulcer area, walking distances, leg circumference, skin temperature and colour, etc.

1.6 Summary

Chronic non-healing leg ulcers are a considerable source of morbidity and a potential huge resource problem to the National Health Service. The presence of a painful, malodorous, unsightly leg ulcer is not only disconcerting and restrictive to the patient, but the current management and treatment of the ulcer is protracted and inconvenient, and may often conclude in surgery and/or amputation. Consequently, improved ulcer healing techniques are indicated which incur greater efficacy.

This review has examined the method of intermittent pneumatic compression and its application to vascular disorders. In the past, IPC has been utilised for the prophylaxis of DVT, for the reduction of oedema and improvement of venous return, and for the symptomatic reduction of peripheral arterial disease; however, IPC and its specific application to the healing of ulcers has not been researched adequately. Although the number of studies examining the application of IPC to the treatment of ulcers are limited, and their reliability is questioned, it is known that IPC has the ability to enhance vascular fluid flow, which essentially is the basis of initiating ulcer healing; consequently the assumption that IPC has potential as an adjuvant treatment method for the healing of chronic leg ulceration seems plausible.

Current treatments of venous ulceration can be labour intensive for the nursing staff, varying in efficacy dependant on the skill of the health care professional in application of compression bandaging, relying on patient

compliance for a treatment that can be uncomfortable, unsightly (especially for women) and inconvenient. Arterial and diabetic ulcer therapy tends to veer towards medication and surgery, which incur associated risks and complications. It would seem therefore that the advantages of IPC, namely, its non-invasive nature, and its ease of use with minimal associated risks, would be beneficial for patients with chronic non-healing leg ulcers if it is found through investigation to be efficient in enhancing the wound healing process by improving the circulation. However, prior to trials on patients suffering from ulcers of various aetiologies, there is a need to evaluate the acute effects of the proximal IPC system on the dynamics of blood flow, distally, at the wound site. This is the first element by which this research differs from previous studies. Are there any effects incurred by IPC of the thigh (and/or the calf) on blood flow proximal to the wound site?

It would seem that the use of IPC proximally, if demonstrated to be successful, would be more agreeable to the patient, as it would not interfere with the wound itself. The second innovative element of this research involves investigating the feasibility of a single compression regime which may concurrently enhance arterial inflow and venous outflow. Hence, ulcers of different aetiologies could benefit from the application of this device.

However, outcome of the research in differing ulcer type may vary due to the variance in aetiology, and these differences will need to be considered for short term and long term benefit.

Chapter 2: Equipment

2.1 Introduction

This chapter discusses the equipment used in the chapters which follow.

2.2 Ultrasound and Photoplethysmography (PPG).

The research involved investigating the effect of differing intermittent pneumatic compression techniques on distal blood flow in healthy volunteers and patients. Doppler ultrasound and Photoplethysmography were implemented in all parts of the research to assess the acute effects of compression on distal blood flow, whilst colour duplex imaging was also utilised for assessing the absence of, or degree of vascular pathology in healthy volunteers and patients.

2.2.1 Doppler Ultrasound Frequency Spectrum Analysis Systems.

Two different spectral Doppler ultrasound systems were used in this research, namely:

a. the SciMed QVL-120 Doppler frequency spectrum analysis system, and
b. DopStudio software suite.

Both systems were used to extract real time blood flow velocity information from the distal vasculature; the general principles behind which are described in chapter 1.

Figure 2.1 The SciMed QVL-120 Doppler frequency spectrum analysis system.

The QVL-120 system measures the range of frequencies detected from a single location within a blood vessel. Blood flow velocities are calculated automatically, by assuming that the angle of the probe is 45 degrees with respect to the direction of blood flow. The frequency (or velocity) spectrum is displayed with the time on the horizontal axis, and in this research, the vertical axis represented the velocity in centimetres per second (cm/s). Within the spectrum, the amplitude of the individual velocities was represented by the greyscale, whilst the maximum velocity envelope of the spectrum was also displayed. The maximum and mean velocity traces are used to calculate measurements such as the pulsatility index, resistance index, and the time average maximum (TAM) velocity which are displayed alongside the spectrum. The TAM blood flow velocity is determined from the average of the maximum velocity envelope for every three cardiac pulses. It was the TAM

blood flow velocity which was recorded for the arterial investigations in this study. Other parameters were recorded for the venous studies, such as the peak velocity and the duration of blood flow.

The DopStudio software suite enables Doppler signals to be obtained on a standard laptop by means of a 'pocket Doppler device', which is connected to the laptop via an industry standard sound card. The pocket Doppler device converts measured Doppler shifts into an audio output, which is processed to provide a real time spectral Doppler signal. As with the QVL-120 system, various measurements are calculated from this signal, such as the pulsatility index and the time average maximum (TAM) blood flow velocity. The TAM blood flow velocity is similarly used for arterial investigations.

The frequency of the transducer implemented depends upon the depth of the blood vessel to be investigated within the body. Ultrasound is attenuated as it passes through the tissues and organs of the body; the energy of the ultrasound beam decreasing due to reflection, scattering, refraction, absorption and beam divergence. Generally, the intensity of the scattered wave (the ultrasound power lost) increases very rapidly with frequency, thus, for structures deep within the body, a low frequency (high penetration) ultrasound transducer is necessary, whilst for structures closer to the skin surface, a higher frequency (lower penetration) ultrasound transducer is sufficient to gain the required information. In this research, a flat 8MHz continuous wave ultrasound transducer was used to locate and gain information from the dorsalis pedis artery and the posterior tibial vein, which

are relatively superficially located in the lower limb. Figure 2.2 demonstrates the positioning of the 8MHz flat transducer for locating a signal from the dorsalis pedis artery.

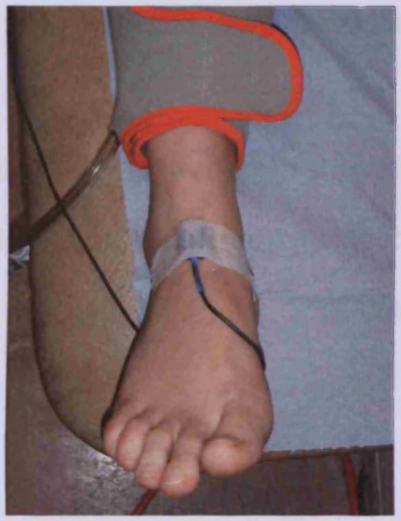


Figure 2.2 The flat 8MHz continuous wave transducer, positioned to locate a signal from the dorsalis pedis artery in a healthy volunteer, and held in place using micropore tape.

2.2.2 Colour Duplex Imaging

Colour duplex imaging was used to identify the presence and severity of vascular pathology in the patients who were to participate in the study. Colour duplex imaging combines duplex imaging with colour flow imaging, allowing the simultaneous visualisation of blood flow within the vessels and quantification of the velocity of flow from specific locations within the vasculature (see chapter 1.5.1).

Vascular pathology may be identified from colour duplex imaging though a variety of techniques. The basic B-mode image may demonstrate calcium hardening or plaque formation due to the greater reflectivity of calcium, whilst

the absence of and characteristics of blood flow in the colour flow image could indicate the presence and degree of a stenosis, a thrombus, or venous reflux due to venous valve incompetence. The dampening of the Doppler frequency or velocity spectrum is also an indicator for arterial disease.

The colour duplex imaging was performed by a clinical scientist within the department of medical physics at the University Hospital of Wales (UHW) and at West Wales General Hospital (WWGH). The colour duplex system used was the Toshiba Xario.

2.2.3 Venous Photoplethysmography (VPPG)

Venous photoplethysmography (VPPG) enables relative changes in microcirculatory blood volume to be measured. Infra red light is transmitted into the skin, which is absorbed dependant upon the volume of blood present in the selected area of tissue. Changes in blood volume are therefore determined from the amount of light reflected.

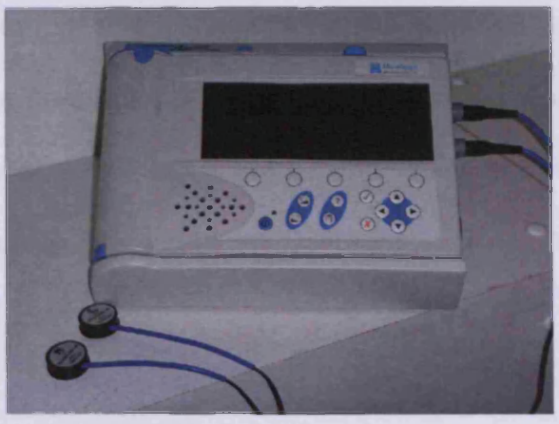


Figure 2.3 The Huntleigh Healthcare Vascular Assist (Huntleigh Healthcare, Luton, UK).

The Vascular Assist was used in this research to obtain PPG signals. The Vascular Assist is a portable vascular assessment system, which combines Doppler ultrasound, PPG and BP (blood pressure measurement). The dual channel PPG allows bilateral ABPI measurements, and screening for DVT's (deep vein thromboses) and venous insufficiency. In this research however, PPG was used to detect changes in distal microcirculatory blood volume as a consequence of venous empting and refilling due to intermittent compression.

2.2.4 Laser Doppler Flowmetry

Laser Doppler Flowmetry (LDF) measures blood cell perfusion in the microcirculation. The blood cell flux, or perfusion detected, represents the movement of blood cells through the microcirculation, and is the product of blood cell volume and their mean velocity.

The Oxford Array laser Doppler system was used in this research to examine the effects of compression on distal skin blood perfusion. This system measures real time blood cell perfusion at up to 12 different sites. Each of the probes was secured in a different place on the distal skin surface with micropore tape. The Laser Doppler signal, which is measured in units of BPU (blood perfusion units), is a relative units scale, therefore the results produced demonstrate the *changes* in skin blood perfusion.

2.3 Compression cuffs and Pumps.

In this section, the different compression cuffs and air pumps used in the research are described.

2.3.1 Compression cuffs

Initial investigations examined the action of four differing intermittent pneumatic compression cuffs, manufactured by Huntleigh Healthcare, Luton, UK.

- The *Huntleigh DVT 30 cuff*

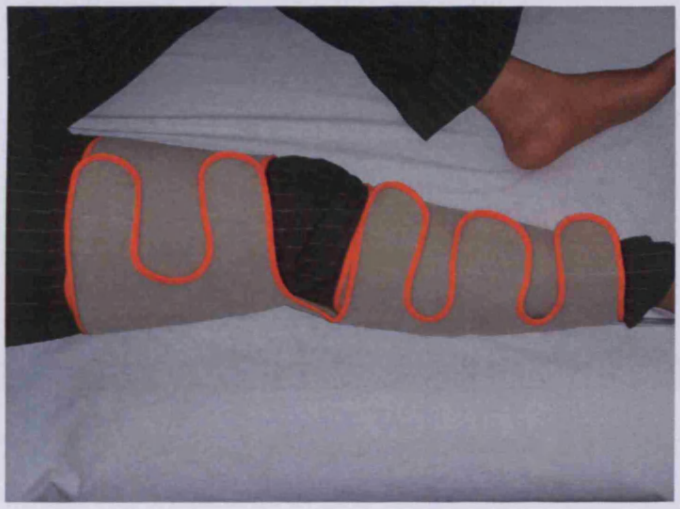


Figure 2.4 The Huntleigh DVT 30 compression cuff.

The Huntleigh DVT 30 cuff is a uniform whole leg compression garment. It consists of two chambers, one for the calf and one for the lower thigh. The cuff is positioned around the limb with the chambers sitting at the back of the leg and secured in place using the Velcro straps. The chambers are

connected to a pump through a single plastic tube, enabling both to be inflated simultaneously. The Huntleigh DVT 30 cuff is primarily used with the Flowtron range of pumps for DVT prophylaxis, however in this research its use is being investigated for improving both the distal venous and arterial blood flows.

The following graph demonstrates the pressure time analysis for the Huntleigh DVT 30 cuff, connected to a Flowpac pump (Huntleigh Healthcare, Luton, UK), using a 60 second cycle and a pressure of 60mmHg.

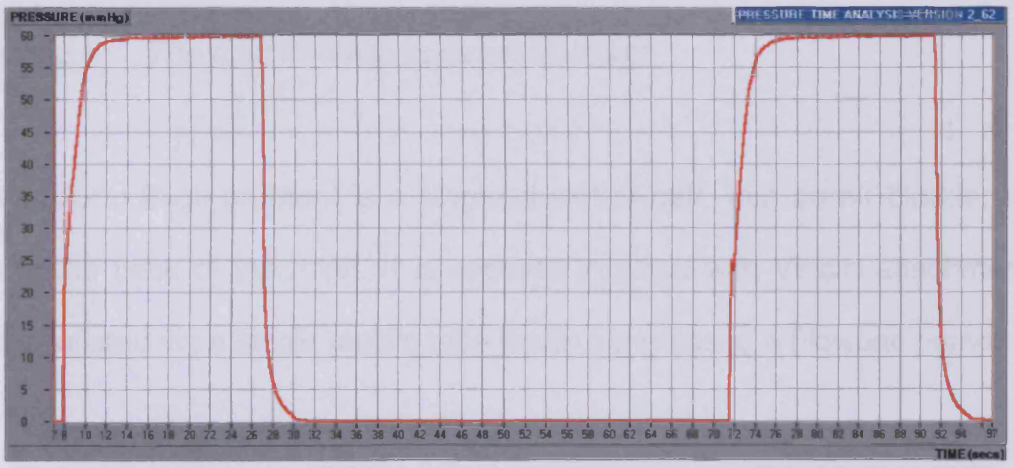


Figure 2.5 Pressure time analysis for the Huntleigh DVT 30 cuff.

As can be seen from figure 2.5, it takes approximately 3-4 seconds for the Huntleigh DVT 30 cuff to reach the required pressure.

- A *uniform thigh cuff*

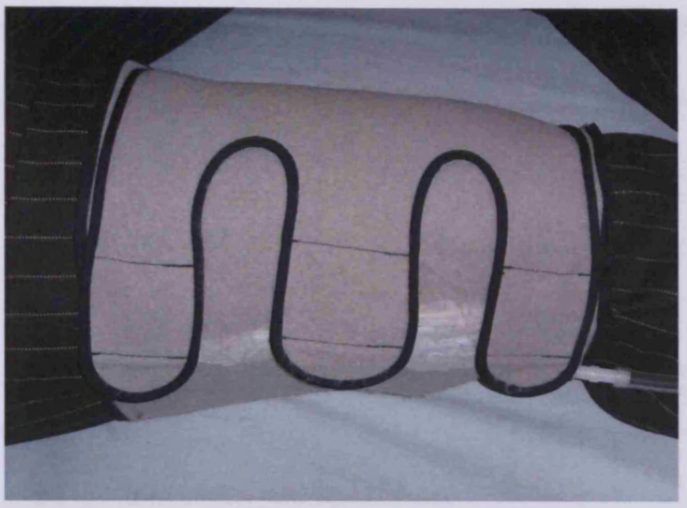


Figure 2.6 The uniform thigh compression cuff.

The uniform thigh garment is a single chamber cuff, with an air bladder that sits at the back of the thigh. It is secured in place with Velcro attachments, and is inflated via a single plastic tube which connects to a Flowpac pump.

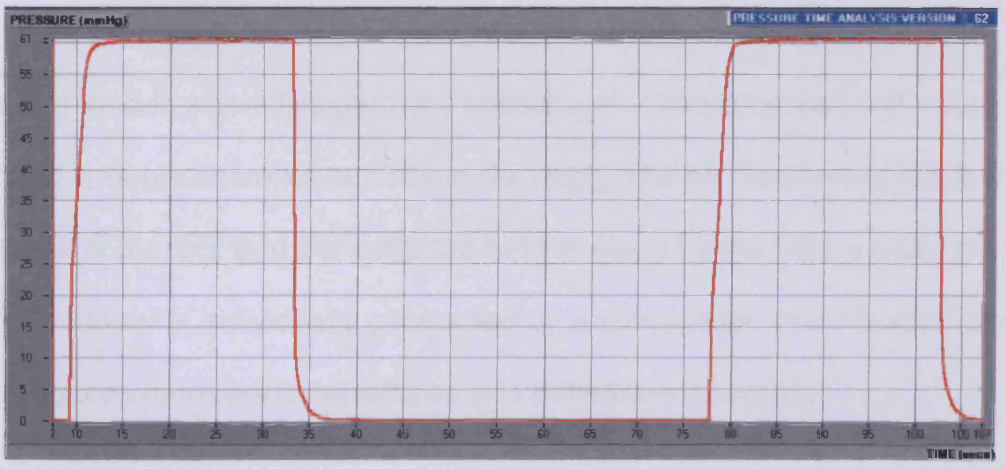


Figure 2.7 Pressure time analysis for the uniform thigh cuff.

Figure 2.7 displays the pressure time analysis for the uniform thigh cuff, using a 60 second cycle and a pressure of 60mmHg. The uniform thigh cuff inflates more rapidly than the Huntleigh DVT 30 cuff, reaching 60mmHg within approximately 2 seconds. This is due to the smaller chamber size.

- A *3 chamber whole leg cuff*

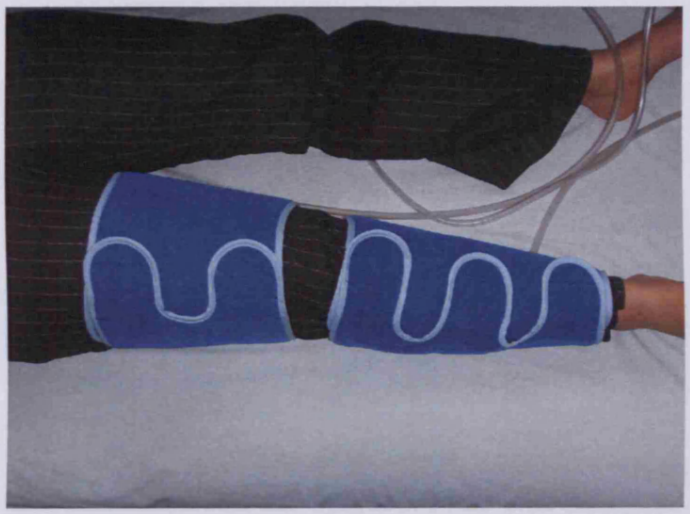


Figure 2.6 The 3-chamber whole leg compression cuff.

The 3-chamber whole leg garment consists of a two-chamber cuff about the calf and a single chamber cuff about the thigh. The air bladders similarly sit at the back of the leg, and the cuffs are held in place by the Velcro attachments. Each chamber is individually connected by a plastic tube to a Flowpac pump, allowing the chambers to be inflated and deflated sequentially.

- A *3 chamber thigh cuff*

Initially, it was proposed that the 3-chamber thigh cuff should comprise a large central chamber with two narrower chambers either side. It was intended for the narrow chambers to behave like venous valves preventing venous reflux. However, experimentation with different sized chambers did not reveal any benefits for having narrower chambers, therefore the 3-chamber thigh cuff consisted of three equally sized chambers. The chambers in this cuff were circumferential about the limb, therefore compression was also applied circumferentially. The garment was secured using Velcro tabs.

Figure 2.7 The 3-chamber thigh compression cuff.

Each chamber was connected by a plastic tube to either a Flowpac pump or to the adapted Flowtron AC300-R (Huntleigh Healthcare, Luton, UK).

Initially, the 3-chamber thigh cuff was as demonstrated in figure 2.7, being made of knitted nylon laminated to polyurethane film; however, after experiments had started, it was noticed that the cuff was slipping down the leg. A new cuff was manufactured using a non-slip fabric.

2.3.2 Intermittent Pneumatic Compression Pumps

Two different air pumps, manufactured by Huntleigh Healthcare were used in the studies; the Flowpac pump and the Flowtron AC300-R.

- *The Flowpac pump*

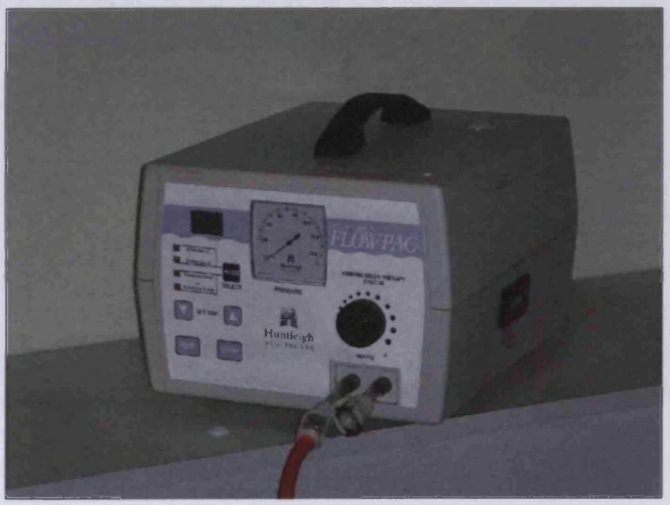


Figure 2.8 The Huntleigh Healthcare Flowpac pump.

The Huntleigh Healthcare Flowpac pump is routinely used with zip-up circumferential leg or arm cuffs, to treat venous ulcers and oedema. The

Flowpac can operate at pressures in the range 20 – 160 mmHg. The pressure is set by the user, and displayed on a gauge which has an accuracy of ± 5mmHg. The cycle times can be varied between 5 and 95 seconds in increments of 5 seconds; and the sequence can be set to run continuously or for a specified treatment time.

A single Flowpac pump was used with the Huntleigh DVT 30 and the uniform thigh cuff, whilst three Flowpac's were used with the 3-chamber compression cuffs.

- *The Flowtron AC300-R*

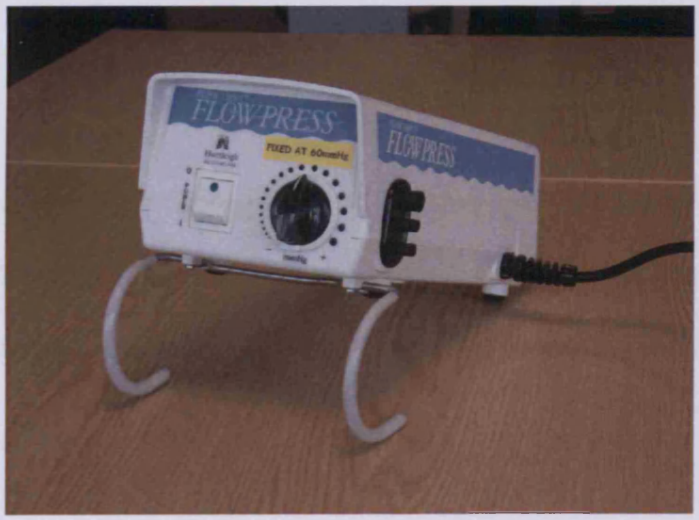


Figure 2.9 The Flowtron Flowpress AC300-R. An adapted Huntleigh Healthcare Flowtron Flowpress AC300 pump.

The Flowtron Flowpress AC300-R is a modified version of the Huntleigh Healthcare Flowtron Flowpress AC300 pump. The existing AC300 has been

manufactured by Huntleigh Healthcare for more than 15 years, and has been used for enhancing vascular and lymphatic flow in limbs.

The existing AC300 cycle comprised a 120 second sequential cycle followed by a rest period of 60 seconds. This cycle was adapted for the benefits of this research and as a consequence of the results of the preliminary investigations. The new operating cycle associated with the modified pump consisted of six consecutive 20 second sequential cycles followed by 120 seconds rest.

All 3 chambers of the 3-chamber thigh cuff are connected to the one pump, which has polarised connectors to ensure the chambers are connected in the correct sequence.

The Flowpress pump is compact and lightweight, allowing the patient to transport it with little difficulty. The pressure has been fixed at 60mmHg, so the patient only needs to start and stop the pump as and when required.

Chapter 3: Preliminary Investigations: Uniform Compression

3.1 Introduction

The aim of the preliminary investigations was to examine the distal haemodynamical effects of intermittent pneumatic compression on a healthy volunteer in order to develop an understanding of the physiological effects of compression and how they were affected by variations in cuff design, cycle duration and pressure. At the conclusion of the preliminary investigations, the optimal compression regime for enhancing the distal circulation in a healthy individual had been obtained.

3.2 Method

3.2.1 Variables

The variables examined for their effects on the distal circulation of a healthy volunteer were cuff design, pressure, inflation duration and deflation duration. Four differing cuff designs had been decided upon; a uniform whole leg cuff, a uniform thigh cuff, a 3-chamber whole leg cuff and a 3-chamber thigh cuff. The cuffs are described in detail in chapter 2.3. The two uniform compression garments were addressed primarily, in order to examine the effects of altering different aspects of the compression regime on distal blood flow, before applying the acquired information to the two sequential garments.

For each of the uniform compression garments, a series of investigations was conducted in order to examine the effects of pressure and cycle duration on

distal blood flow. The aim was to determine the optimal compression regime, which required individual investigation of the variables, pressure, inflation duration and deflation duration, for each differing compression garment.

A standard cycle encompassing a moderate pressure of 60mmHg, 15 seconds inflation and 45 seconds deflation was used throughout the investigations for those variables which were maintained constant. For example, whilst examining the effects of pressure on distal blood flow, a cycle of 15 seconds compression and 45 seconds deflation was maintained.

The investigated variables were to be examined at values between pre-determined ranges, based upon information acquired during the literature review. A moderate pressure range of 50 to 90 mmHg was to be studied. These pressures would compress the veins, improving venous return and inducing an arterial hyperaemia. This pressure range had also been chosen as it was considered to be more comfortable for the patient, ultimately aiding treatment compliance. Each investigation consisted of recording blood flow measurements before, during and after ten cycles of compression at pressures within this range, varied in increments of 10 mmHg.

Due to the size of the compression garments and hence the time taken for the cuff to completely inflate, the inflation duration was varied between 5 and 30 seconds, in increments of 5 seconds. Investigations progressed as with altering the pressure, recording distal blood flow measurements before, during and after a period encompassing ten cycles of compression.

The deflation period needed to be of adequate duration to enable complete venous refilling following the release of compression. Generally, complete venous refilling is attained within 30 to 40 seconds in people with no venous insufficiency (Morris et al. 2002), therefore, for investigative purposes, the deflation duration was varied between 15 and 60 seconds in increments of 15 seconds.

3.2.2 Data Acquisition

The preliminary investigations were conducted on a single healthy volunteer. The aim of these investigations was to understand the effects of compression, and the effects of altering different aspects of the compression sequence on normal healthy distal blood flow, for the purpose of optimising a compression regime to treat and manage patients with leg ulcers; and due to the number of experiments which were to be undertaken in order to achieve this and due to time restrictions, all investigations were carried out on a single volunteer. During each test, the volunteer was required to lie supine on a scanning couch, with their head on a pillow and their trousers removed. One of the IPC garments had been placed about the left lower limb of the volunteer, which was connected to a Huntleigh Flowpac pump. All investigations were carried out in a temperature controlled room (approximately 23 degrees Celsius).

Doppler ultrasound was used to locate the required blood vessels, and to observe blood flow during the studies. The QVL Doppler ultrasound system (see chapter 2) and an 8MHz flat transducer were used to locate the dorsalis pedis artery for the arterial studies, and the posterior tibial vein for the venous

studies. Once the required blood vessel had been located, the ultrasound transducer was secured in place using micropore tape. A blanket was then placed over both legs and feet of the volunteer to prevent cooling. Prior to the commencement of the study, a period of approximately 10 minutes was considered necessary to allow blood flow to stabilise.

Investigations were repeated for both the distal arterial and distal venous circulations. However, the measurements taken from the different blood vessels varied due to the differences between the arterial and venous blood flows.

The Doppler system calculates a time average maximum (TAM) blood flow velocity from the pulsatile arterial blood flow signal. The maximum velocity envelope of the Doppler spectrum is averaged for every three successive cardiac cycles, and displayed alongside the signal. In the arterial studies the TAM blood flow velocity is recorded from the display every 5 seconds throughout the test, and noted in a table by the investigator. Each arterial test is composed of a period of 180 seconds resting pre-compression, followed by 10 cycles of compression and then a further 180 seconds resting post compression.

Venous blood flow is not pulsatile to the extent of arterial blood flow. This is due to the distance of the veins from the heart, the compliance of the vein walls, and also due to the effects of respiratory pressure changes which mask any cardiac pressure fluctuations. Therefore, the TAM blood flow velocity is

not suitable for venous measurements. As an alternative, the peak velocity and the duration of venous blood flow were measured. Resting distal venous blood flow is not detectable by Doppler ultrasound due to the low velocities involved; only on release of compression is distal venous blood flow detected. Therefore, the peak velocity and duration of venous flow were measured following each deflation of the cuff. This was repeated for ten cycles of compression.

In some instances, contradictory results were obtained between the arterial and venous circulations, therefore further studies were conducted using photoplethysmography (PPG). PPG examines changes in microcirculatory blood volume. PPG sensors were placed on the sole of the left foot and lateral to the medial malleolus. Following the calibration of the PPG device, compression was started, and a blood volume signal was recorded. Each signal comprised a period of 600 seconds compression.

3.2.3 Data Analysis

Each arterial study was repeated six times. Results were normalised (see appendices) and then averaged together and plotted as a line graph in SPSS. An existing computer program, written in Turbo Pascal for the research of Morris and Woodcock, (2002) was also used to determine objectively the percentage change in blood flow as a consequence of compression. Each raw data set was entered into the program which calculated the percentage change in blood flow during compression as compared with a baseline

extrapolated from the resting period pre and post compression. The results obtained were averaged together, and a standard deviation was calculated. Venous results were repeated three times, providing 30 data values for each level of the variable investigated. The data were entered into SPSS, where mean values were determined, and error bar plots were constructed. One way ANOVA was also performed to determine whether there were any significant differences between different levels of the variables.

Where PPG was implemented, each study was repeated ten times, and the signals averaged together and plotted using Excel.

3.3 Results and Discussion

The results of the preliminary studies have been compiled in the order in which each garment was approached.

3.3.1 Huntleigh DVT 30

The initial objective was to discover whether compression produced any distal haemodynamical effects. From investigations with the Huntleigh DVT 30 cuff, which provides uniform compression to the calf and lower thigh, it can be concluded that there is both a distal arterial and venous blood flow response to IPC. The nature of the distal arterial response to compression comprises an increase in blood flow velocity following the release of compression, over and above the decrease in blood flow velocity arising during compression. The distal venous response is characterised by the presence of a short duration of accelerated venous flow following cuff deflation, indicative of a trapped volume of blood being released.

The following Doppler signals demonstrate the distal arterial and venous responses to the release of compression. Figure 3.1 displays resting distal arterial blood flow in a healthy volunteer; figure 3.2 is the distal arterial blood flow response obtained when compression is released, and figure 3.3 is the distal venous response to the release of compression.

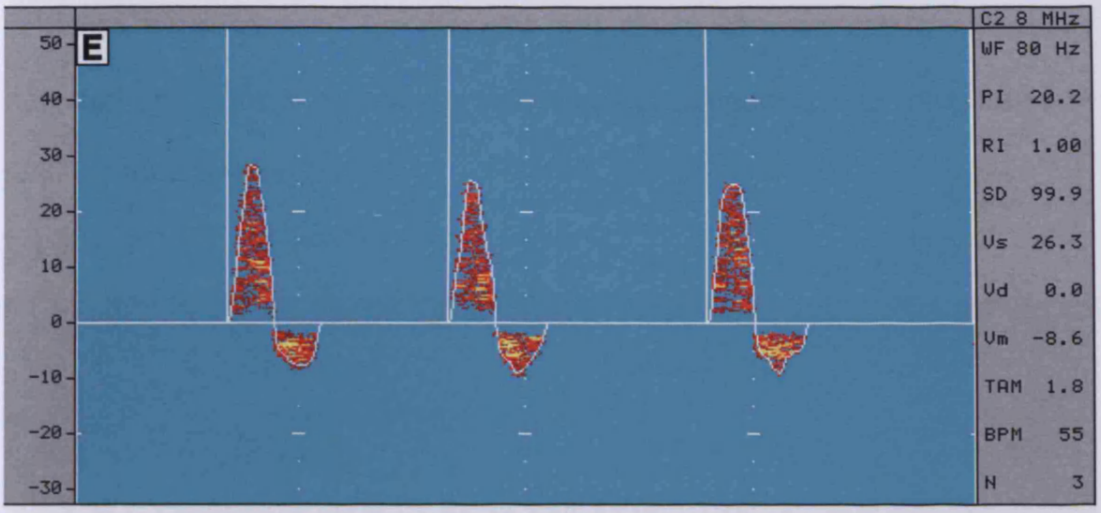


Figure 3.1 Resting distal arterial blood flow in a healthy volunteer.

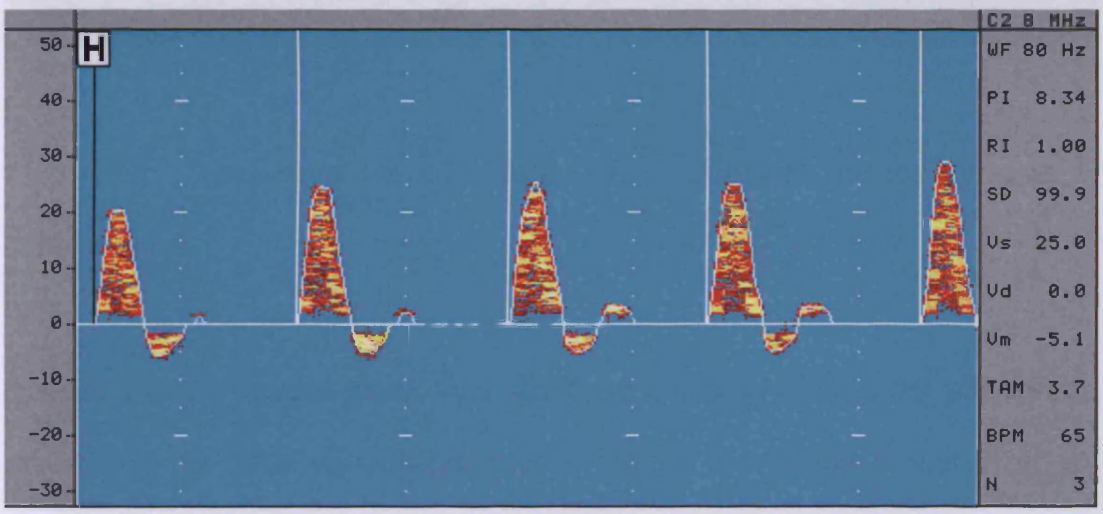


Figure 3.2 The distal arterial blood flow response obtained following the release of compression.

Figure 3.2 displays the hyperaemic response obtained distally, when compression is released. In figure 3.2 the signal has developed a third phase, as compared with the biphasic blood flow demonstrated in figure 3.1; and it

can also be seen from the quantity and colour of each individual velocity detected that blood flow is at a greater velocity in figure 3.2 as compared with resting blood flow in figure 3.1.

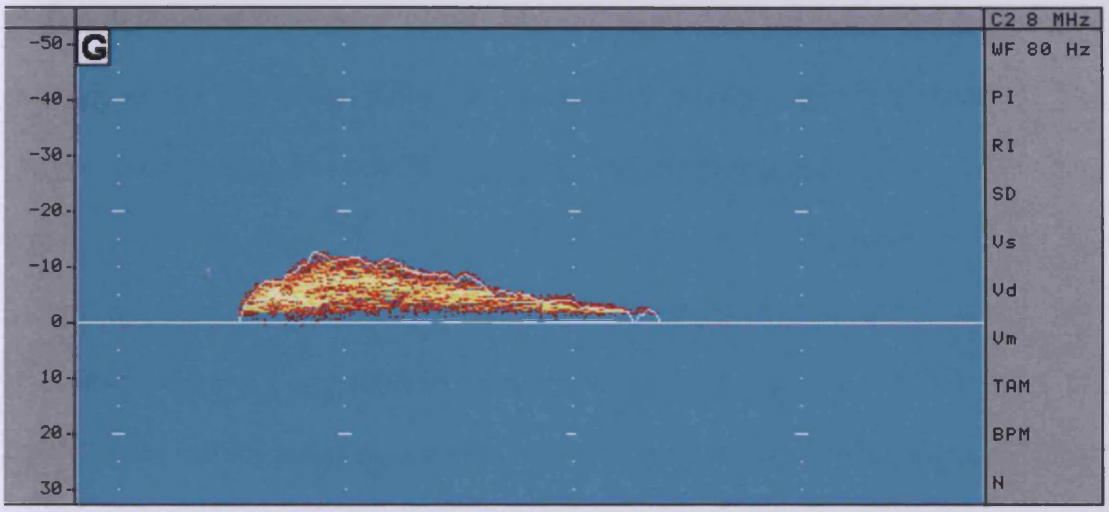


Figure 3.3 The distal venous blood flow response to the release of compression.

A resting distal venous signal has not been included as it is not possible to record resting distal venous blood flow due to the low velocities involved. Figure 3.3 demonstrates the distal venous response to the release of compression, a distally trapped volume of blood being released back towards the heart.

Investigations progressed into studies of the effect on this distal haemodynamic response, of altering various aspects of the regime. The effect of altering the pressure, inflation duration and deflation duration on distal arterial and venous blood flow was examined.

The graphs below (figures 3.4 – 3.8) represent the results obtained with the Huntleigh DVT 30 cuff for altering the pressure between 50 and 90 mmHg in increments of 10mmHg. The horizontal axis represents time in seconds, and the vertical axis represents the averaged normalised time averaged maximum (TAM) blood flow velocity in cm/s. The red lines indicate when compression is started, whilst the green lines are indicative of when the cuff deflates. The grey line represents the end of ten cycles of compression.

There appears to be a general trend amongst the graphs. Blood flow decreases during compression and increases following the deflation of the cuff. This is represented by a trough during compression (following a red line), and a peak following cuff deflation (after a green line). It is unknown precisely what causes the increase in arterial blood flow; however it appears to arise consequent upon changes induced in the venous circulation by compression.

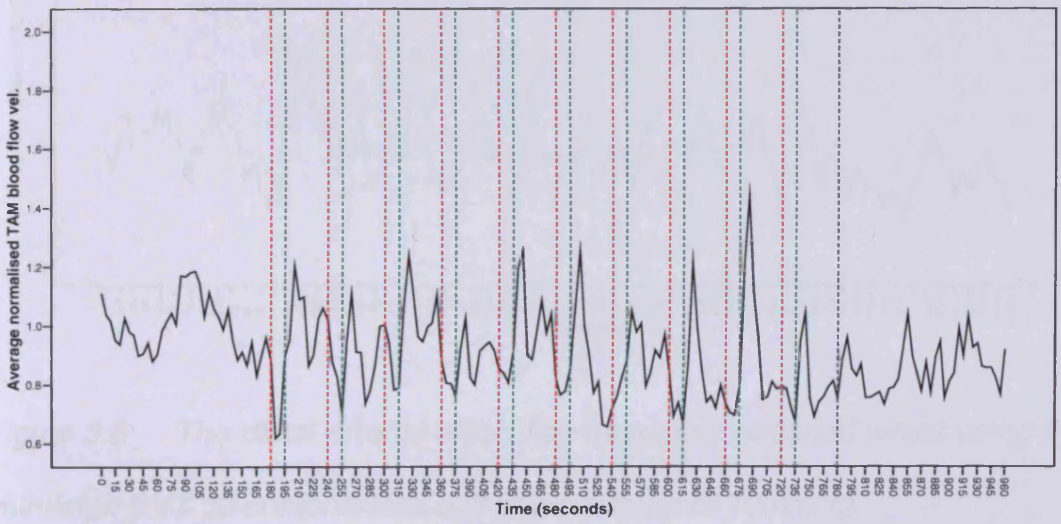


Figure 3.4 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff at a pressure of 50mmHg.

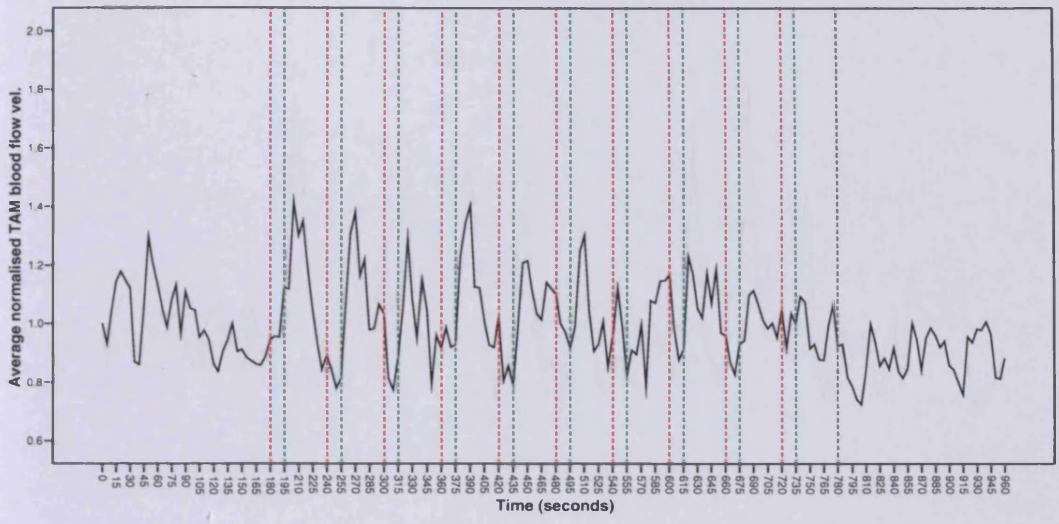


Figure 3.5 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff at a pressure of 60mmHg.

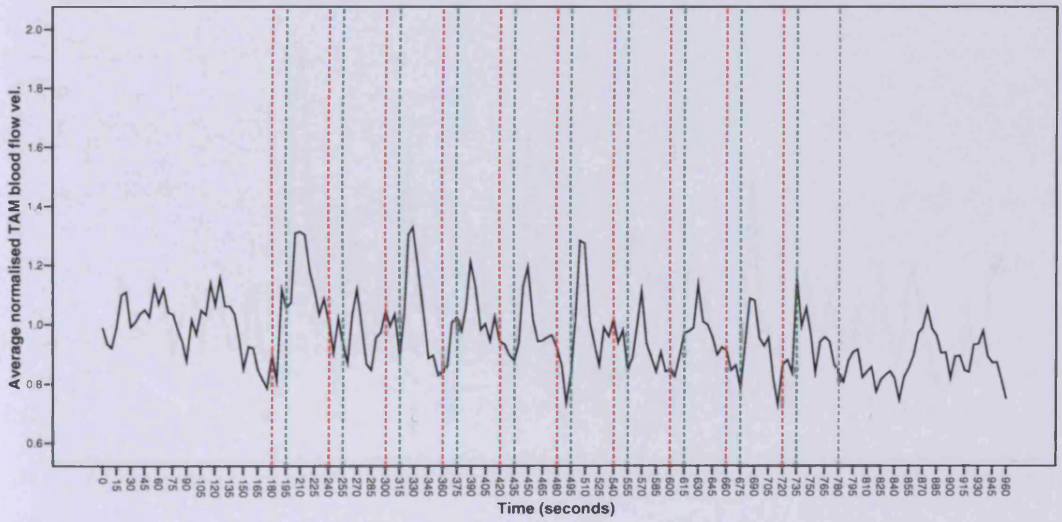


Figure 3.6 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff at a pressure of 70mmHg.

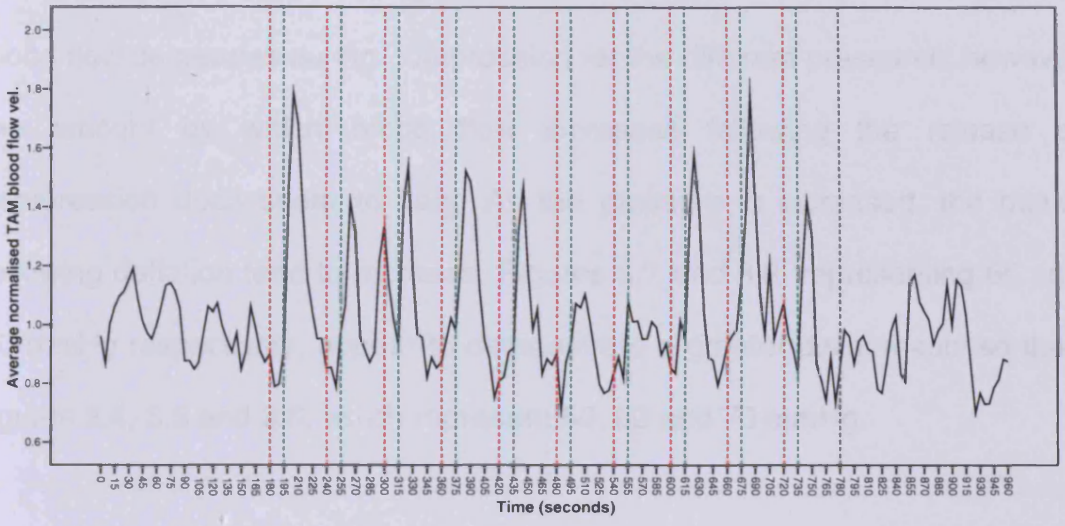


Figure 3.7 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff at a pressure of 80mmHg.

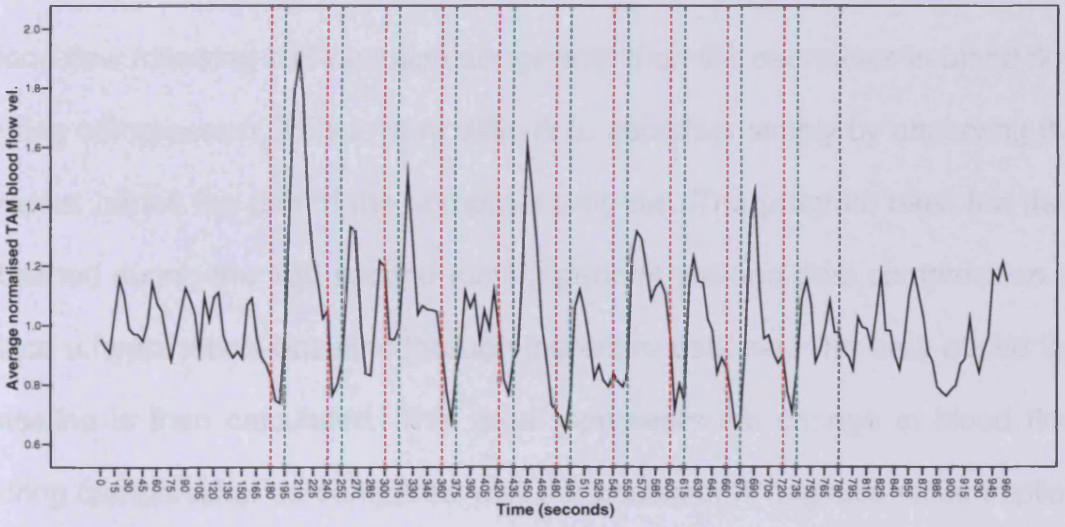


Figure 3.8 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff at a pressure of 90mmHg.

There does not seem to be a great difference between the amounts by which blood flow decreases during compression for the different pressures; however the amount by which blood flow increases following the release of compression does seem to vary. As the pressure is increased, the peaks following deflation tend to increase. Figures 3.7 and 3.8, representing 80 and 90 mmHg respectively, appear to demonstrate a greater distal response than figures 3.4, 3.5 and 3.6, which represent 50, 60 and 70 mmHg.

It is very difficult however, to decide conclusively whether one pressure setting is more advantageous than another. The aim of intermittent pneumatic compression (IPC) is to improve the circulation of blood. Therefore, from the graphs of the different pressure settings studied, it needs to be determined whether or not there is a net increase in blood flow; whether the increases in blood flow following cuff deflation are greater than the decreases in blood flow during compression. This is very difficult to ascertain simply by observing the graphs, hence the use of the computer program. The program uses the data obtained during the 180 second resting periods pre and post compression to place a hypothetical baseline through the entire data set. The area above the baseline is then calculated. This area represents the change in blood flow during compression as compared with the baseline. A negative value implies that the 'troughs' are greater than the 'peaks', whilst a positive value indicates that there is a net increase in blood flow over and above resting flow. The results obtained along with their standard deviations are given in Table 3.1.

Pressure (mmHg)	**50**	**60**	**70**	**80**	**90**
% change in blood flow	*-2.4*	*9.21*	*4.66*	*7.9*	*3.92*
% Standard deviation (2 d.p)	*5.31*	*7.43*	*5.88*	*11.78*	*8.09*

Table 3.1 The percentage change in blood flow arising during compression with the Huntleigh DVT 30 cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing pressures; and the associated standard deviations.

As can be seen from the results, pressures in the range 60 to 90 mmHg produce a net increase in blood flow, whilst 60mmHg produces the greatest increase in blood flow of 9.21%. The standard deviations are quite high in comparison with the results obtained for the mean percentage change in blood flow, however; this is to be expected when the results have only been repeated six times. Further repetitions were not possible due to the number of different variables being investigated and hence the number of tests which needed to be undertaken. The standard deviations are lower for 50, 60 and 70 mmHg, which coincides with the maximum percentage change in blood flow of 9.21% which was achieved for 60mmHg. It is assumed that 60mmHg will be above the diastolic blood pressures of most volunteers / patients.

Similar studies were conducted to investigate the effect of altering the inflation duration of compression on distal blood flow. A pressure of 60mmHg and a deflation duration of 45 seconds were maintained throughout the experiments,

whilst the inflation duration was varied between 5 and 30 seconds in increments of 5 seconds. Figures 3.9 – 3.14 demonstrate the results obtained.

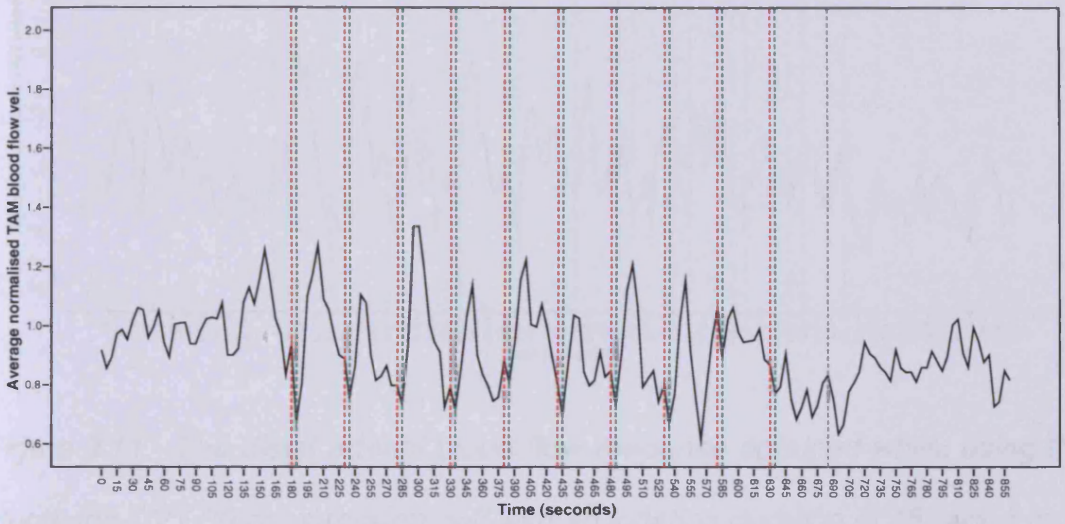


Figure 3.9 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 5 seconds.

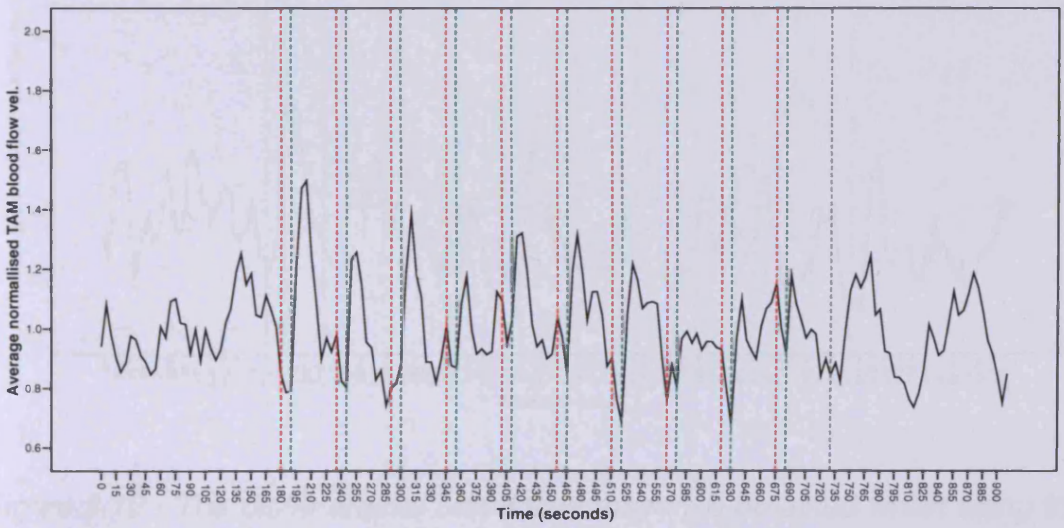


Figure 3.10 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 10 seconds.

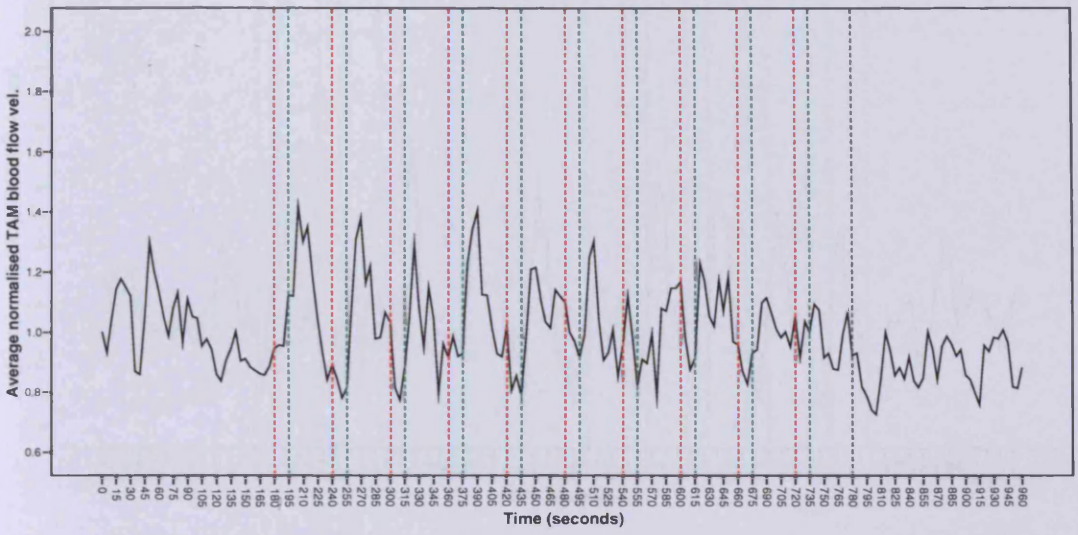


Figure 3.11 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 15 seconds.

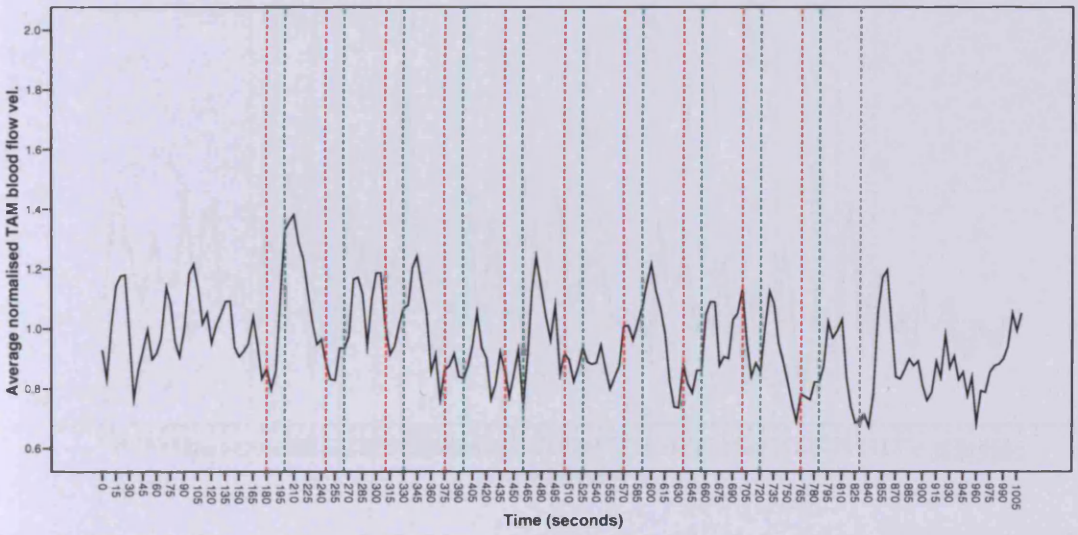


Figure 3.12 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 20 seconds.

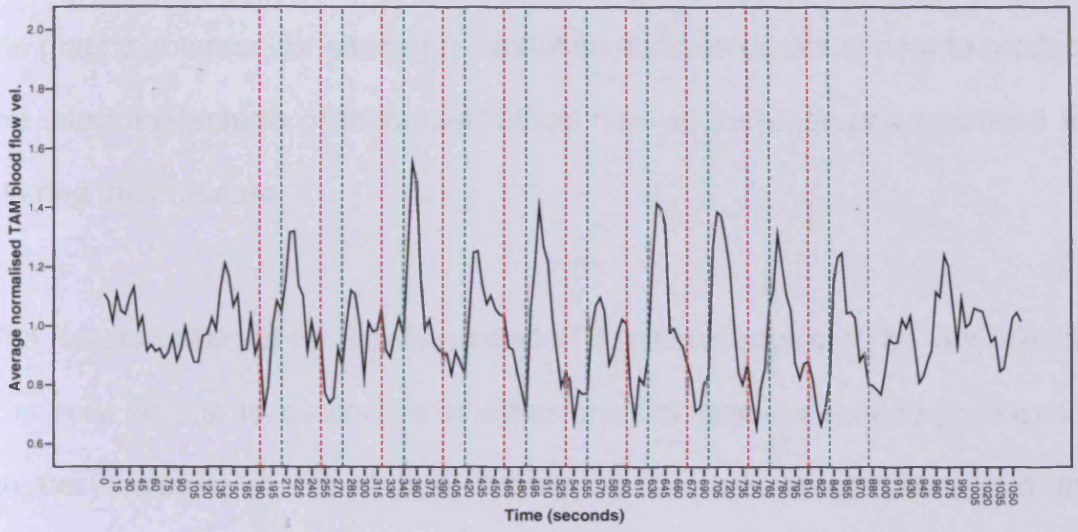


Figure 3.13 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 25 seconds.

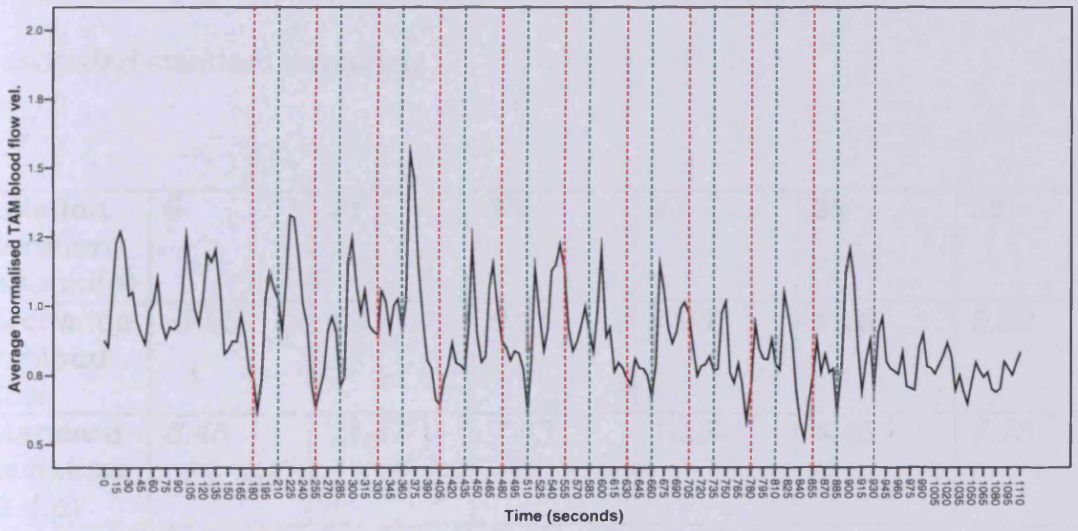


Figure 3.14 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with an inflation duration of 30 seconds.

Figures 3.9 – 3.14 demonstrate a similar trend to the results obtained for altering the pressure of compression. Blood flow decreases during

compression, and increases following the release of compression. However, the graphs obtained for altering the inflation duration do not appear to produce the same magnitude of increased blood flow as those graphs produced for altering the pressure.

The results obtained for differing inflation durations appear to be very similar; it is very difficult to determine whether one compression period produces a greater increase in blood flow. However, the results obtained from the computer program for calculating the percentage change in blood flow demonstrate that a compression period of 15 seconds produces the greatest net increase in blood flow during compression as compared with resting blood flow. Table 3.2 displays the percentage increase in blood flow during compression for each of the differing compression periods, and the associated standard deviations.

Inflation duration (seconds)	**5**	**10**	**15**	**20**	**25**	**30**
% change in blood flow	*-0.95*	*1.11*	*9.21*	*1.68*	*0.26*	*0.50*
Standard deviation (2 d.p)	*8.46*	*11.47*	*7.43*	*10.34*	*4.45*	*7.73*

Table 3.2 The percentage change in blood flow arising during compression with the Huntleigh DVT 30 cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing inflation durations; and the associated standard deviations.

The compression periods between 10 and 30 seconds all produced a net increase in blood flow; however, excluding 15 seconds, the increase was generally very small and the standard deviations are quite high.

An inflation duration of 15 seconds and a pressure of 60mmHg were maintained constant for investigations into the effect of varying the deflation duration on distal arterial blood flow. The period when the cuff was deflated was examined at 15, 30, 45 and 60 seconds duration. Figures 3.15 – 3.18 are the results obtained.

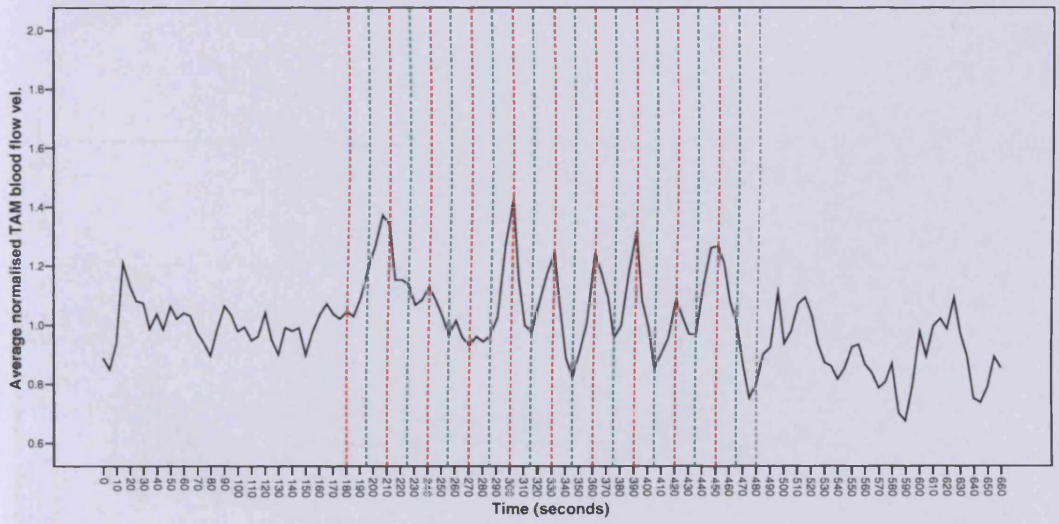


Figure 3.15 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with a deflation duration of 15 seconds.

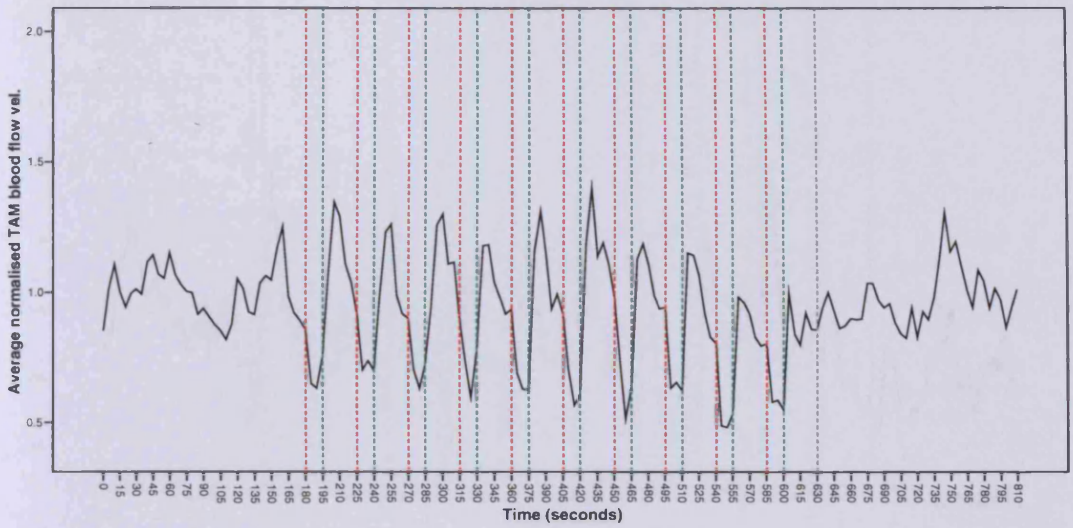


Figure 3.16 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with a deflation duration of 30 seconds.

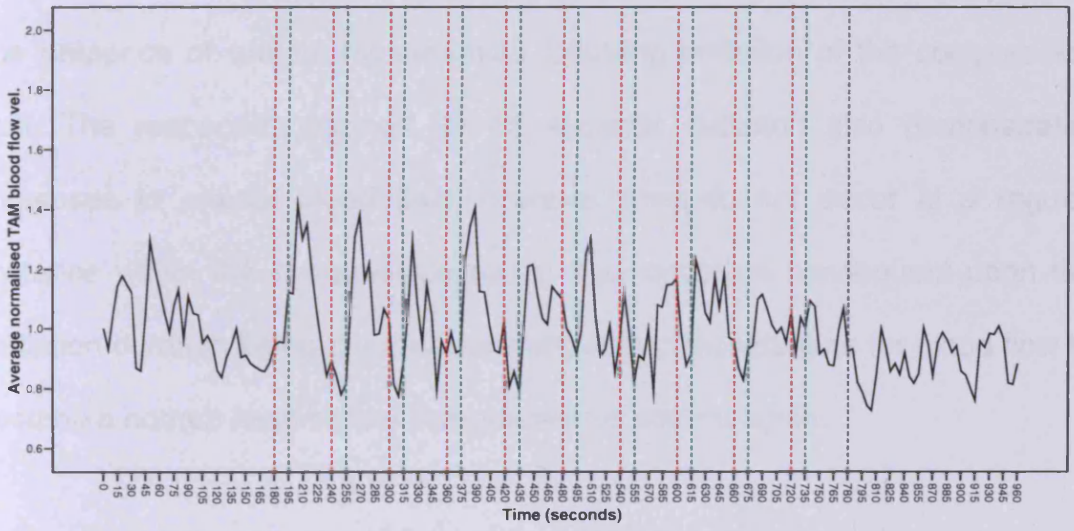


Figure 3.17 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with a deflation duration of 45 seconds.

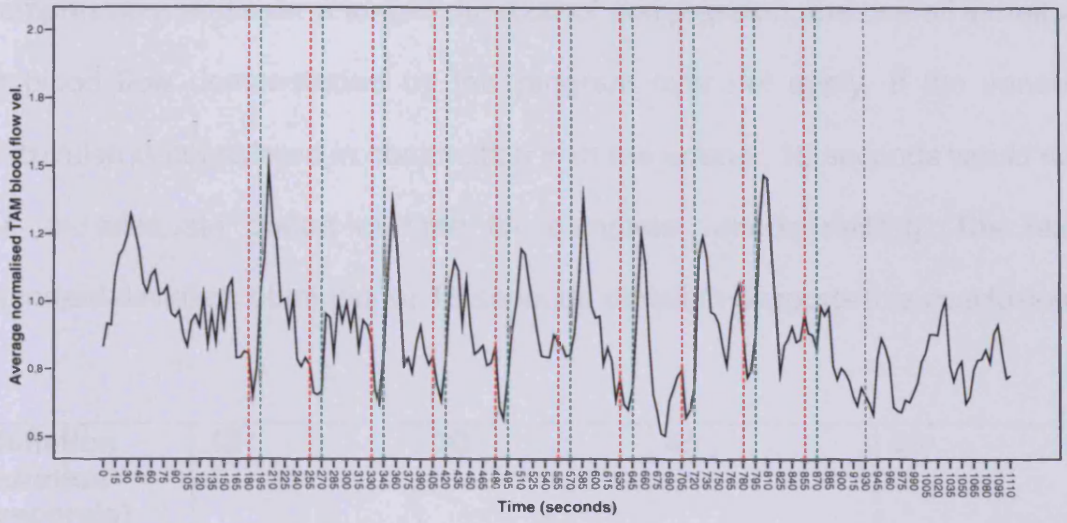


Figure 3.18 The distal arterial blood flow response obtained whilst using the Huntleigh DVT 30 compression cuff with a deflation duration of 60 seconds.

The graphs obtained for the longer deflation durations similarly demonstrate the presence of arterial hyperaemias following deflation of the compression cuff. The response obtained for 15 seconds deflation also demonstrates increases in arterial blood flow; however they do not occur at a regular instance within the compression cycle. This could be consequent upon the deflation duration being too short; not allowing adequate time for blood flow to resume a normal level before compression is started again.

The computer program results are demonstrated in table 3.3. Optimal results have been obtained for 15 and 45 seconds duration. Even though the greatest net increase in blood flow has been obtained for 15 seconds deflation, this is considered to be too short a duration to be used therapeutically. The distal arterial response to a short deflation period is not a regular decrease in blood flow during compression followed by a hyperaemia on release of

compression; and over a longer duration of compression, the overall increase in blood flow demonstrated by the program may not apply. If the venous circulation is considered in conjunction with the arterial, 15 seconds would not be an adequate period of time for complete venous refilling. The high standard deviation obtained for 15 seconds deflation supports this conclusion.

Deflation duration (seconds)	**15**	**30**	**45**	**60**
% change in blood flow	*12.22*	*-8.77*	*9.21*	*-0.16*
Standard deviation (2 d.p)	*11.51*	*9.37*	*7.43*	*4.26*

Table 3.3 The percentage change in blood flow arising during compression with the Huntleigh DVT 30 cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing deflation durations; and the associated standard deviations.

As can be seen from figure 3.16, for 30 seconds deflation, the decreases in blood flow during compression are quite large in comparison with the increases in blood flow following the release of compression. This explains the negative result, revealing an overall reduction in blood flow of 8.77%.

Therefore, it would seem that a deflation duration of 45 seconds would produce the optimal distal arterial blood flow response.

Similar studies were conducted to investigate the effects of pressure and cycle duration on the distal venous blood flow response.

Figures 3.19 and 3.20 are the results obtained for the effect on distal venous blood flow of altering the pressure. Figure 3.19 shows the effect of altering the pressure on the mean peak velocity of distal venous blood flow, while figure 3.20 represents the effect of altering the pressure on the duration of venous blood flow.

The peak velocity and the duration of venous blood flow were recorded following each deflation of the cuff. Each test encompassed 10 cycles of compression and each test was repeated 3 times. The results were averaged together and plotted as a graph using SPSS.

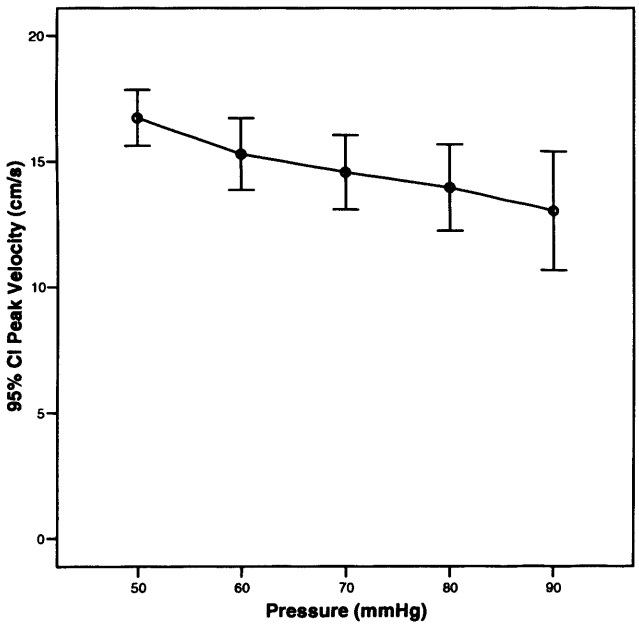


Figure 3.19 The mean peak venous blood flow velocity post compression obtained for pressures in the range 50 to 90 mmHg using the Huntleigh DVT 30 compression cuff.

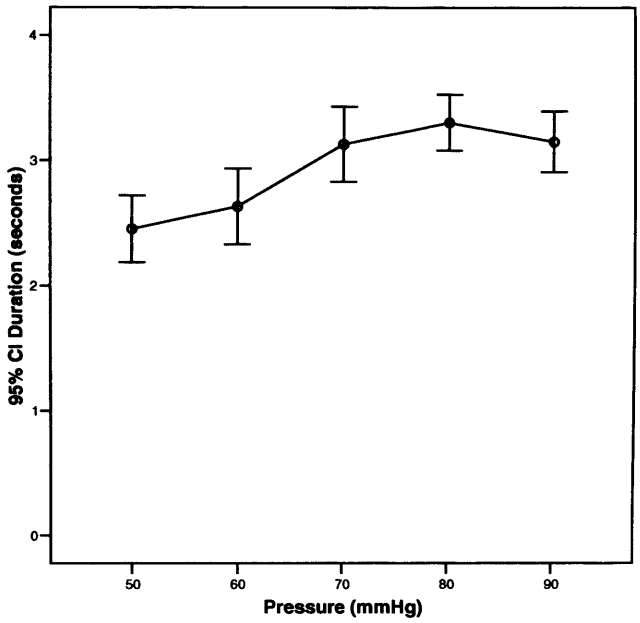


Figure 3.20 The mean duration of venous blood flow post compression for pressures in the range 50 to 90mmHg using the Huntleigh DVT 30 compression cuff.

Figures 3.19 and 3.20 demonstrate some interesting trends, as did the following figures for varying the inflation and deflation durations. However, it was discovered that the methods used were producing erroneous results.

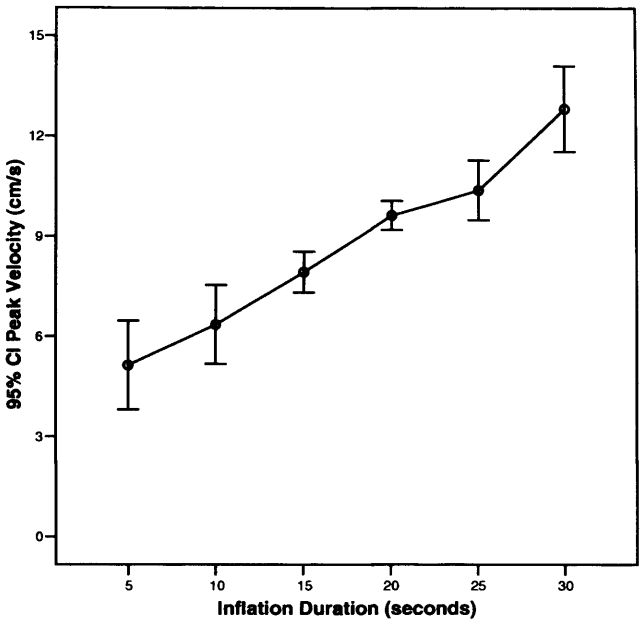


Figure 3.21 The mean peak venous blood flow velocity post compression for inflation durations in the range 5 to 30 seconds, using the Huntleigh DVT 30 compression cuff.

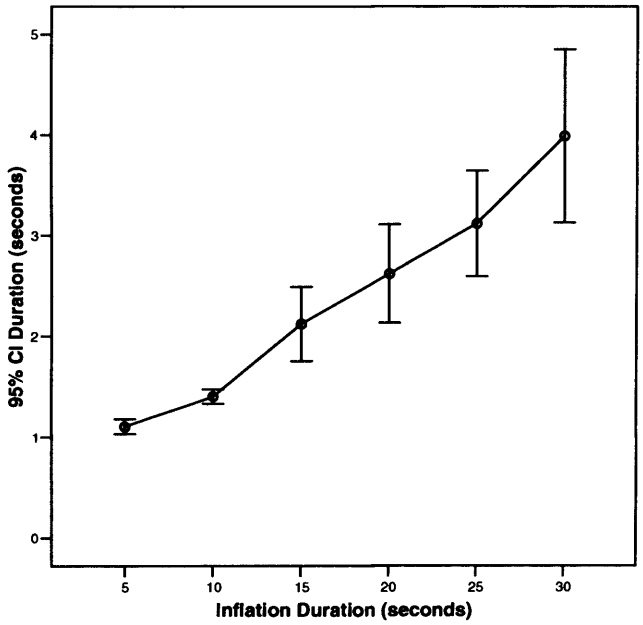


Figure 3.22 The mean duration of venous blood flow post compression for inflation durations in the range 5 to 30 seconds, using the Huntleigh DVT 30 compression cuff.

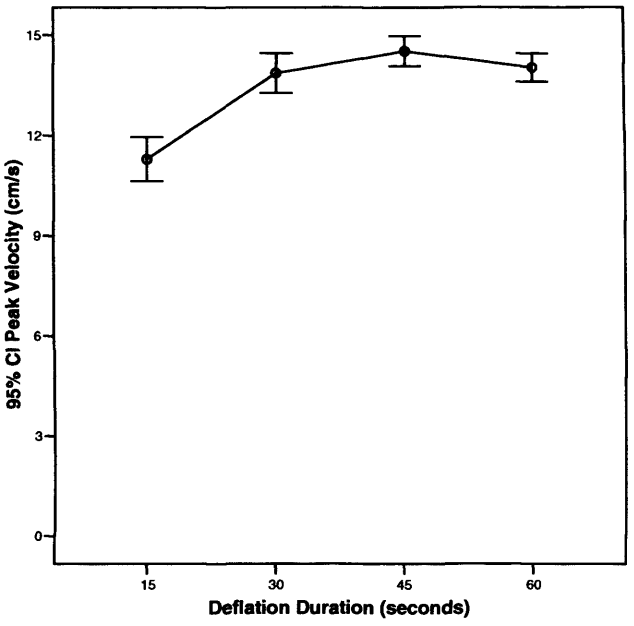


Figure 3.23 The mean peak venous blood flow velocity post compression for deflation durations in the range 15 to 60 seconds, using the Huntleigh DVT 30 compression cuff.

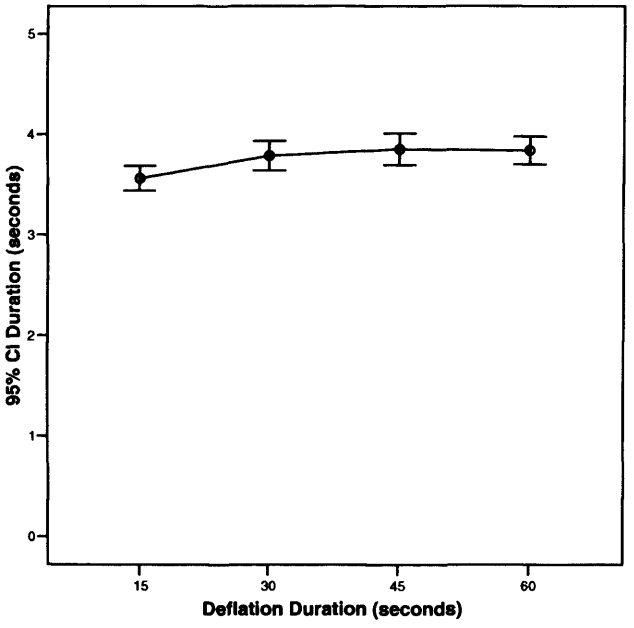


Figure 3.24 The mean duration of venous blood flow post compression for deflation durations in the range 15 to 60 seconds, using the Huntleigh DVT 30 compression cuff.

Each test was undertaken in such a way that the variable under investigation was increased (or decreased) systematically from one level of the variable to another. For example, a study examining the effect on venous blood flow of altering the pressure of compression would commence with recording 10 measurements at 50mmHg, and then progress to 10 measurements at 60mmHg, 70mmHg etc.., or, if starting at 90mmHg, the study would progress to 80mmHg, 70mmHg, and so forth. It was discovered however, that conducting the studies in this manner was producing erroneous results. Those measurements taken at the commencement of the study were not relative to those taken at the end of the study, due to the relaxation of blood flow over the time taken to complete the study. Therefore, results recorded for 50mmHg could not be compared with those recorded for 90mmHg. This was examined by conducting a test which maintained a constant pressure of 60mmHg, and a constant cycle of 15 seconds inflation with 45 seconds deflation. Every 10 minutes, three cycles of compression were initiated, and the peak venous velocity and the duration of venous flow were recorded following each deflation of the cuff. This was continued for 90 minutes. Each set of three results was averaged together and plotted as a graph. Figure 3.25 displays the average peak venous velocity obtained every 10 minutes. As can be seen, there is a definite decline in the average peak venous velocity with time.

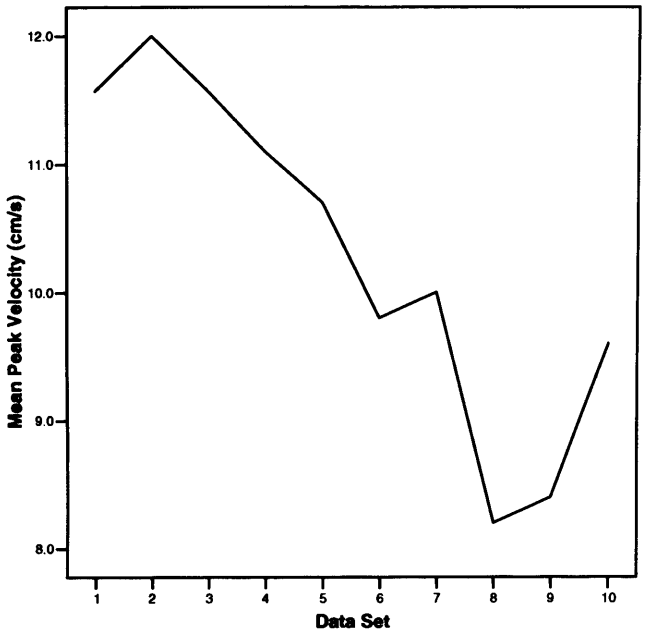


Figure 3.25 The results obtained using uniform thigh compression whilst testing for the relaxation of blood flow over time. A constant cycle of 60mmHg, 15 seconds inflation and 45 seconds deflation was maintained.

In order to correct for this anomaly all studies were repeated, however in this second set of investigations, the levels of the variable under investigation were randomised using a random number generator. For example, each investigation examining the effect of altering the pressure on distal venous flow involved a total of 50 measurements; 10 measurements for each pressure setting randomly ordered.

The results obtained for the randomised experiments appeared to be more consistent and differed substantially from those previously obtained.

Figures 3.26 and 3.27 are the results obtained for the effect on distal venous blood flow of altering the pressure.

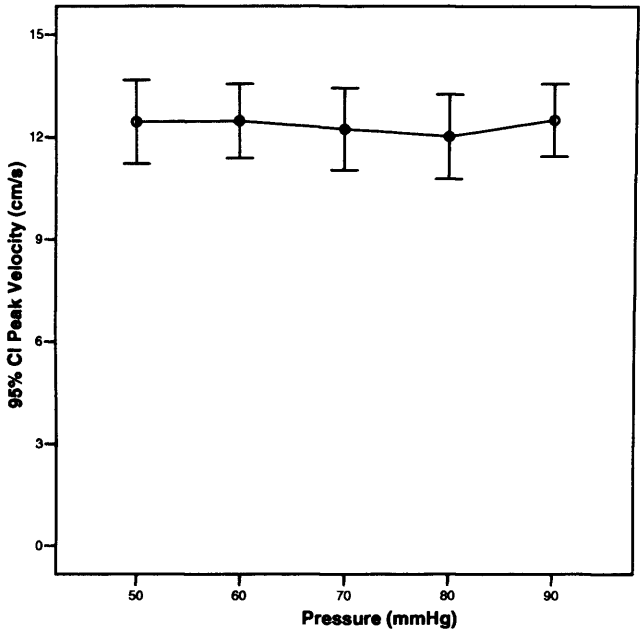


Figure 3.26 The mean peak venous blood flow velocity post compression for pressures in the range 50 to 90 mmHg, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

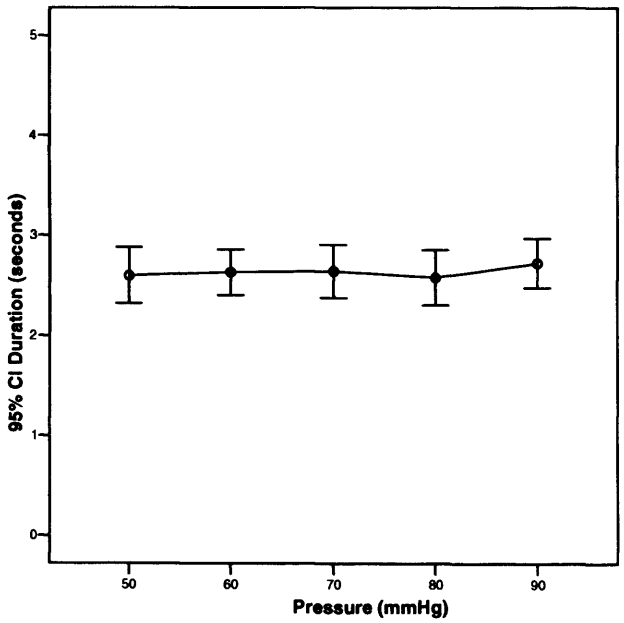


Figure 3.27 The mean duration of venous blood flow post compression for pressures in the range 50 to 90 mmHg, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

The error bars in figures 3.26 and 3.27 are indicative of the 95% confidence interval, which implies that 95% of the data lies within these limits.

As can be seen from figures 3.26 and 3.27, it would appear that varying the pressure of whole leg compression between the moderate pressure range of 50 to 90 mmHg does not impart an effect on the distal venous circulation; confirmed by the one way ANOVA ($p=0.970$, 0.943 for peak velocity and duration respectively).

Since the distal venous response is not affected by varying the pressure of compression, the optimal pressure can be deduced from the results of the arterial studies, which in this instance would imply a pressure of 60mmHg.

Figures 3.28 and 3.29 are the results obtained for altering the inflation duration of the Huntleigh DVT 30 cuff. It was revealed that the distal venous blood flow response increases for increasing inflation durations, as corroborated by p values of less than 0.005 for each variable using the one-way ANOVA.

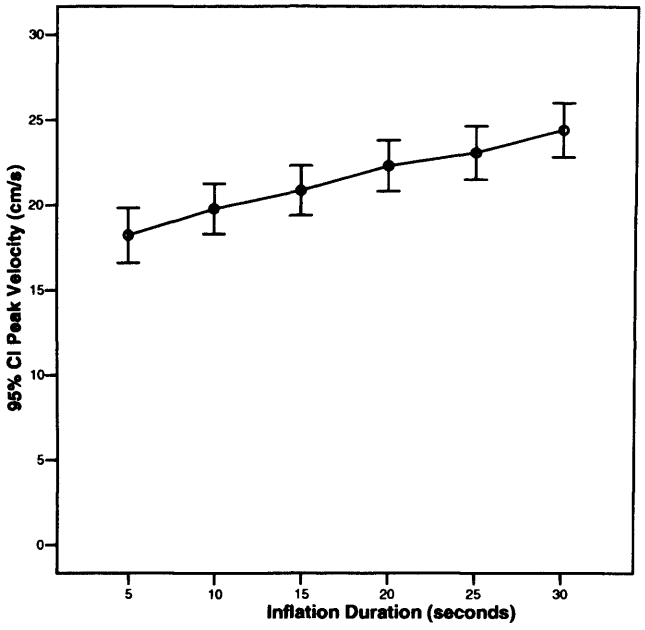


Figure 3.28 The mean peak venous blood flow velocity post compression for inflation durations in the range 5 to 30 seconds, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

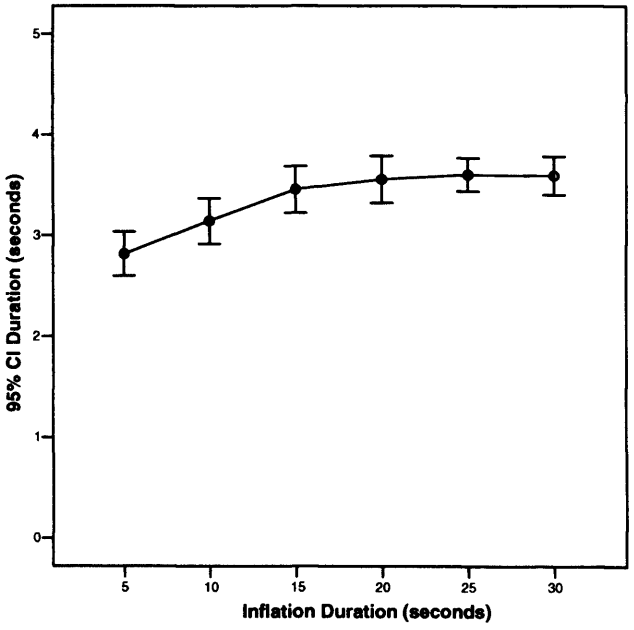


Figure 3.29 The mean duration of venous blood flow post compression for inflation durations in the range 5 to 30 seconds, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

These results seem to support the hypothesis that blood is trapped distally in the foot during compression, and is released when the cuff deflates. In order to further test this hypothesis, some investigations were repeated with a cuff inflated around the foot for the duration of the experiment, so as to empty the foot of blood and reduce the volume of blood trapped within the foot during compression of the limb. Intermittent compression of the leg was then carried out as previously, with similar measurements being recorded. If blood is trapped distally in the foot, the results should be reduced as compared with previous measurements.

Using the standard cycle of 60mmHg, 15 seconds compression and 45 seconds deflation, investigations were conducted to test the hypothesis that blood is trapped distally in the foot during compression. Two tests were conducted; the first involved the measurement of the peak velocity and duration of distal venous blood flow following 10 cycles of compression with the Huntleigh DVT 30 cuff, whilst the second test involved the addition of continuous foot compression to the proceedings of the first test. The foot cuff was inflated to a pressure of approximately 50mmHg. The results were entered into SPSS, where the mean was plotted, as demonstrated in figures 3.30 and 3.31.

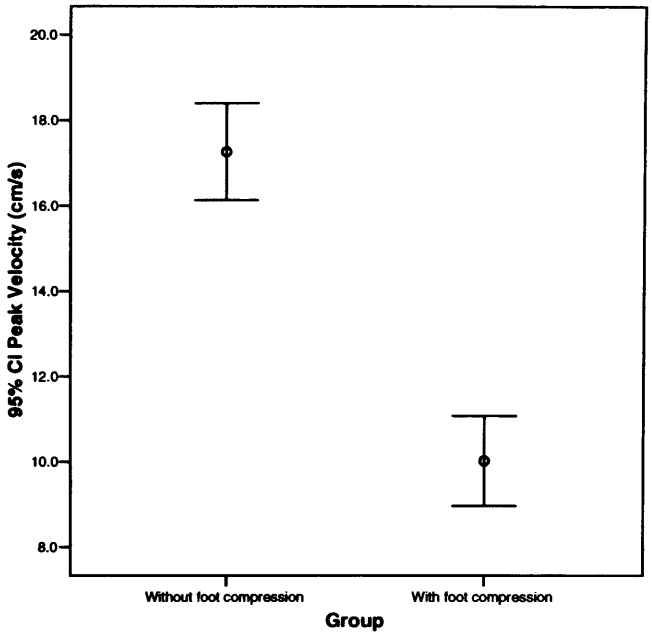


Figure 3.30 The mean peak venous blood flow velocity following 10 cycles of compression with the Huntleigh DVT 30 compression cuff, for tests without and with continuous foot compression.

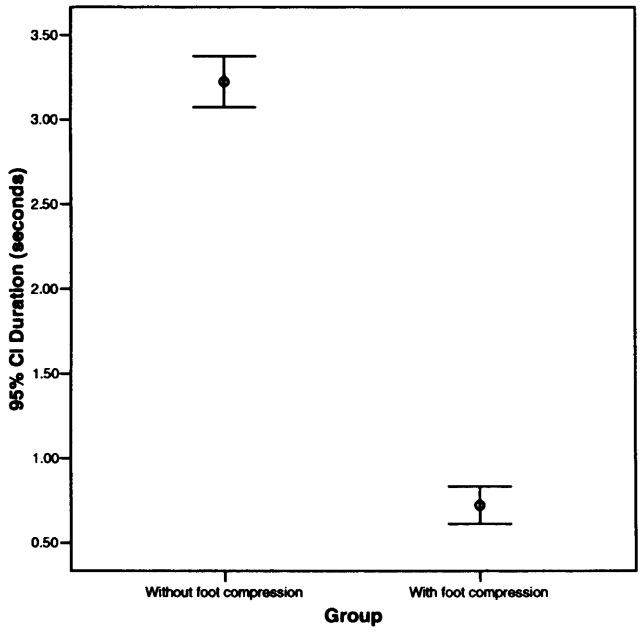


Figure 3.31 The mean duration of venous blood flow following 10 cycles of compression with the Huntleigh DVT 30 compression cuff, for tests without and with continuous foot compression.

As can be seen from figures 3.30 and 3.31, the peak velocity and duration of distal venous blood flow following the release of compression is greatly reduced when continuous compression is applied to the foot. This implies that blood is trapped distally during compression, which is released on deflation of the cuff.

From the results obtained for the effect of altering the inflation duration on distal venous blood flow, it would seem that the longer the duration of compression, the more blood accumulated in the foot, and consequently, the greater the peak velocity and the duration of blood flow. However, this increase in volume cannot continue indefinitely, due to the limited distensibility of the blood vessels within the foot. There must be a maximum compression duration above which no further increase in the volume of blood which may be contained within the foot can be obtained. To estimate the volume of blood flow post compression, and hence the volume of blood trapped within the foot, an approximation may be obtained by multiplying the duration of blood flow by the average maximum velocity of flow (TAM velocity). Figure 3.32 demonstrates the outcome of this calculation.

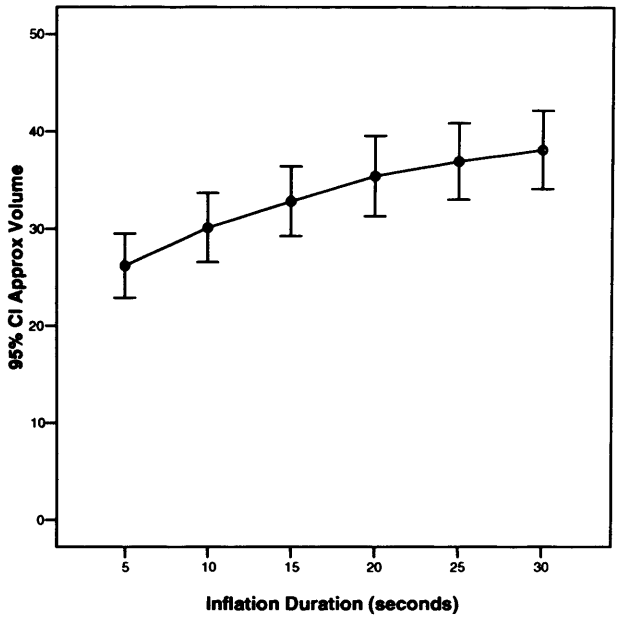


Figure 3.32 An approximation of the blood volume trapped within the foot for inflation durations within the range 5 to 30 seconds.

Figure 3.32 displays an increase in volume for increasing inflation durations. However, the slope of the graph does appear to be decreasing towards the higher inflation durations, indicating that the maximum volume which may be contained within the foot could have been attained at 30 seconds duration, or might only require a small increase in inflation duration to achieve.

The optimal distal venous blood flow response is attained using a long inflation period, however, as previously mentioned a 15 second inflation period produced optimal results in the arterial study. Therefore, PPG measurements were carried out in order to establish a compromise between the arterial and venous study results. The inflation durations 15, 20, 25 and 30 seconds were investigated, whilst maintaining a pressure of 60mmHg and a

deflation period of 45 seconds. 10 signals were obtained for each compression period which were averaged together. The graphs are displayed in the following pages, (figures 3.33 -3.36).

The graphs represent changes in microcirculatory blood volume; an increase in the signal represents a decrease in blood volume, whilst a decrease in the signal represents an increase in blood volume. As can be seen from the graphs, the shape of the signal is consistent for the different compression durations.

A large peak is obtained following cuff deflation. This peak represents a decrease in blood volume due to distally trapped blood being released. Blood volume then slowly starts to increase as the veins refill during the relaxation phase of the cycle, and continues to increase during compression.

There appears to be an overall decrease in blood volume over the first few cycles of compression, before reaching a constant level for the remainder of the signal. This is most noticeable for the 30 second compression period. This compression period also appears to produce the greatest decrease in blood volume within each cycle.

Figure 3.33

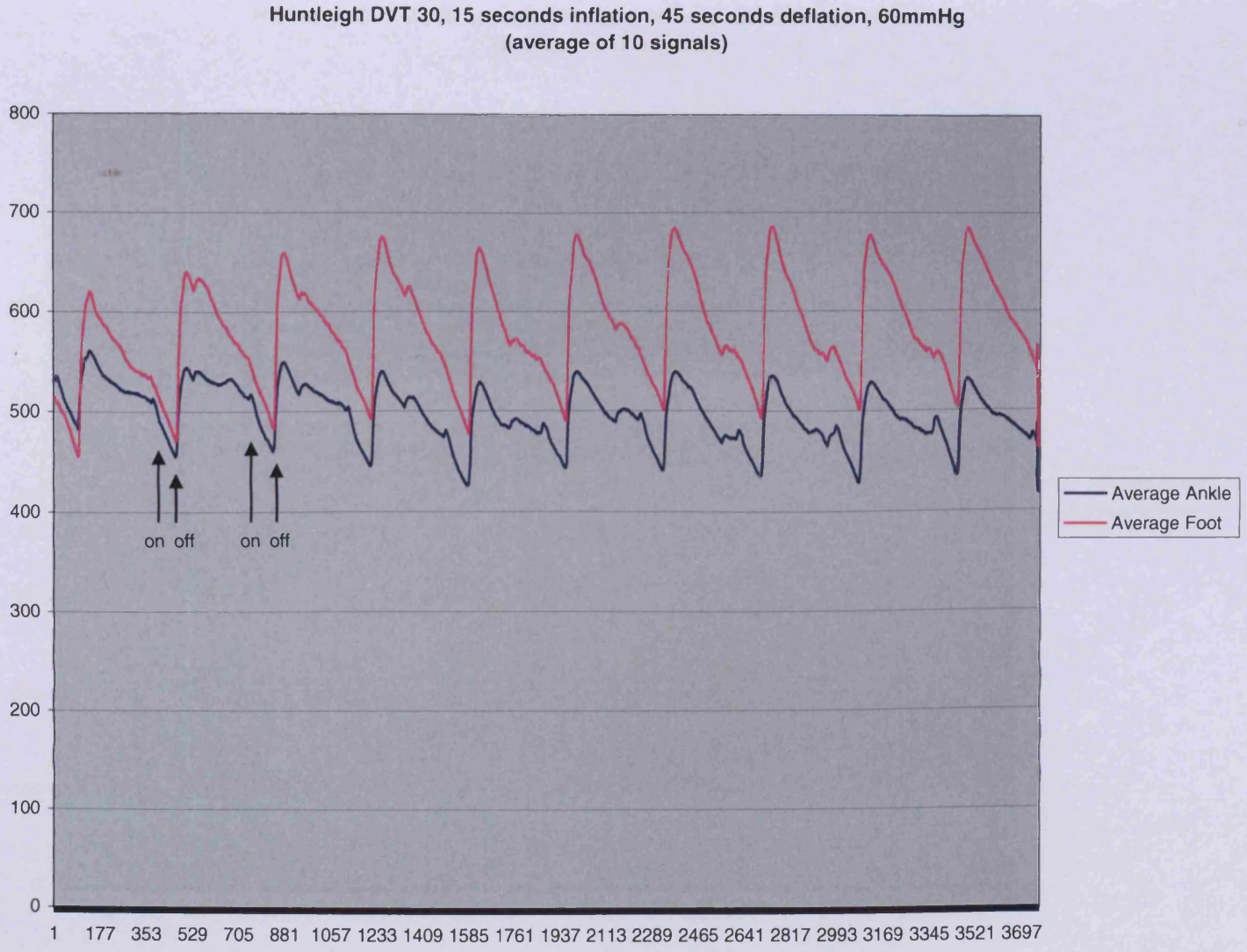

Huntleigh DVT 30, 15 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
800
700
600
500
400
300
200
100
0
on
off
on
off
1
177
353
529
705
881
1057
1233
1409
1585
1761
1937
2113
2289
2465
2641
2817
2993
3169
3345
3521
3697
Average Ankle
Average Foot

Figure 3.34

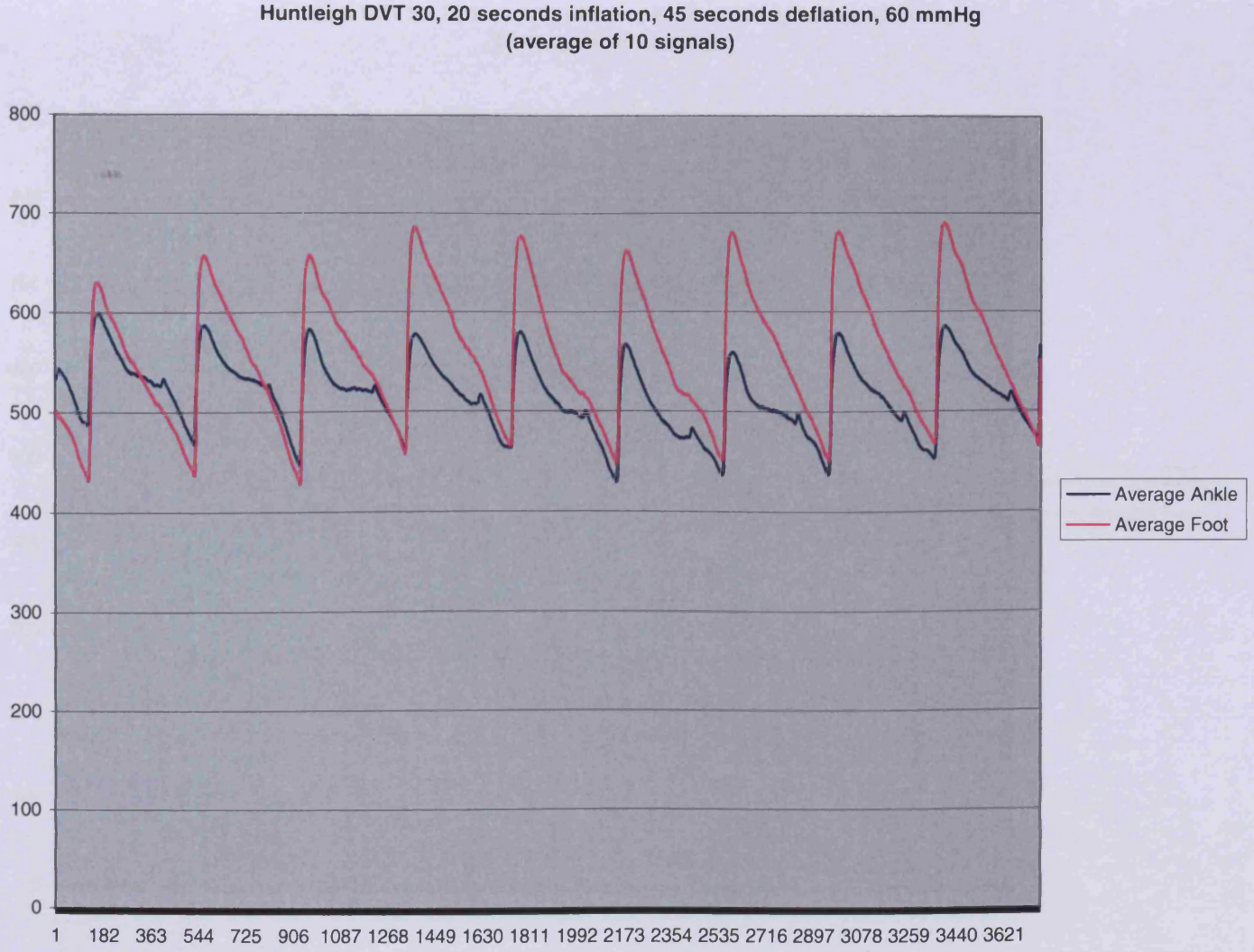

Huntleigh DVT 30, 20 seconds inflation, 45 seconds deflation, 60 mmHg
(average of 10 signals)
800
700
600
500
400
300
200
100
0
1
182
363
544
725
906
1087
1268
1449
1630
1811
1992
2173
2354
2535
2716
2897
3078
3259
3440
3621
Average Ankle
Average Foot

Figure 3.35

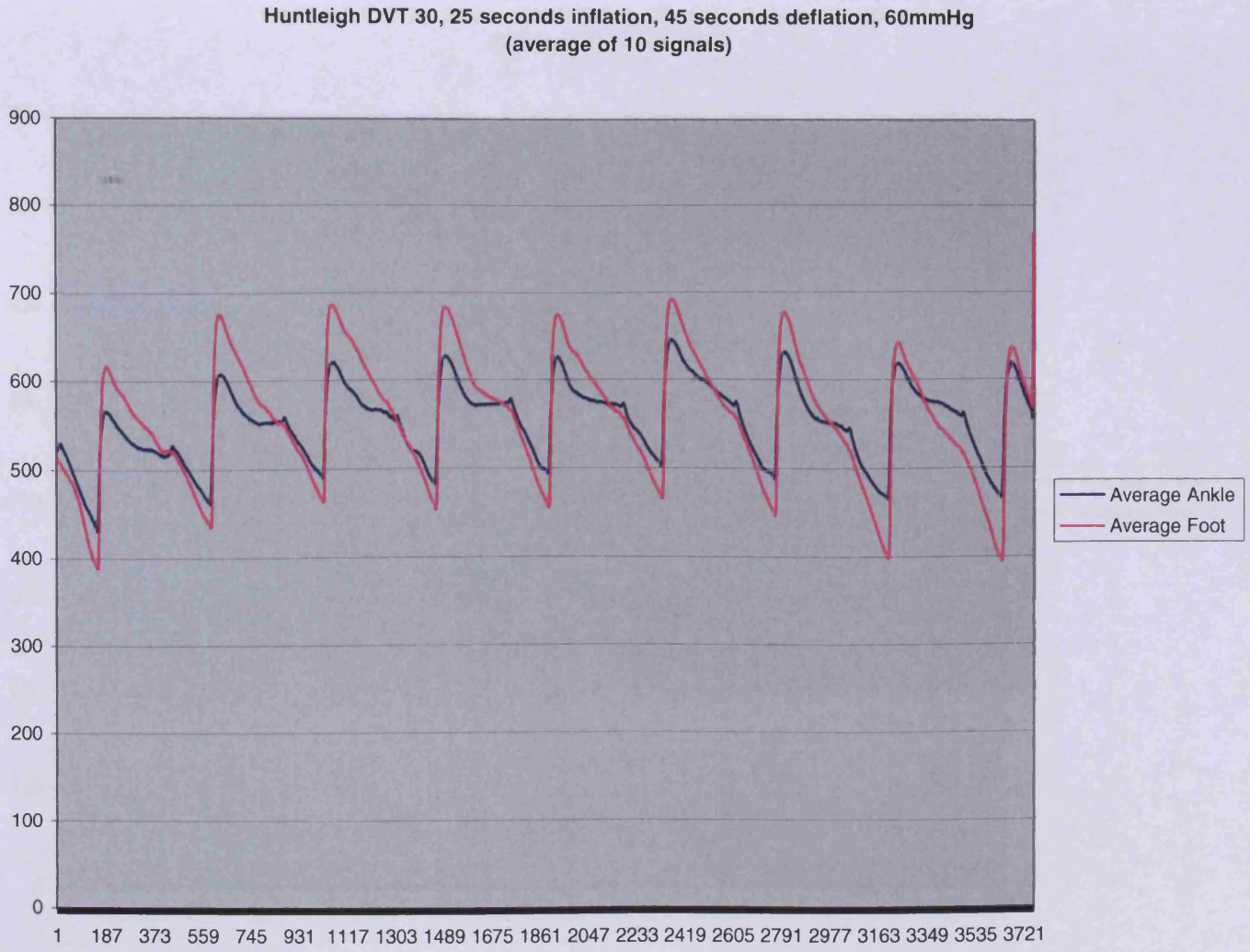
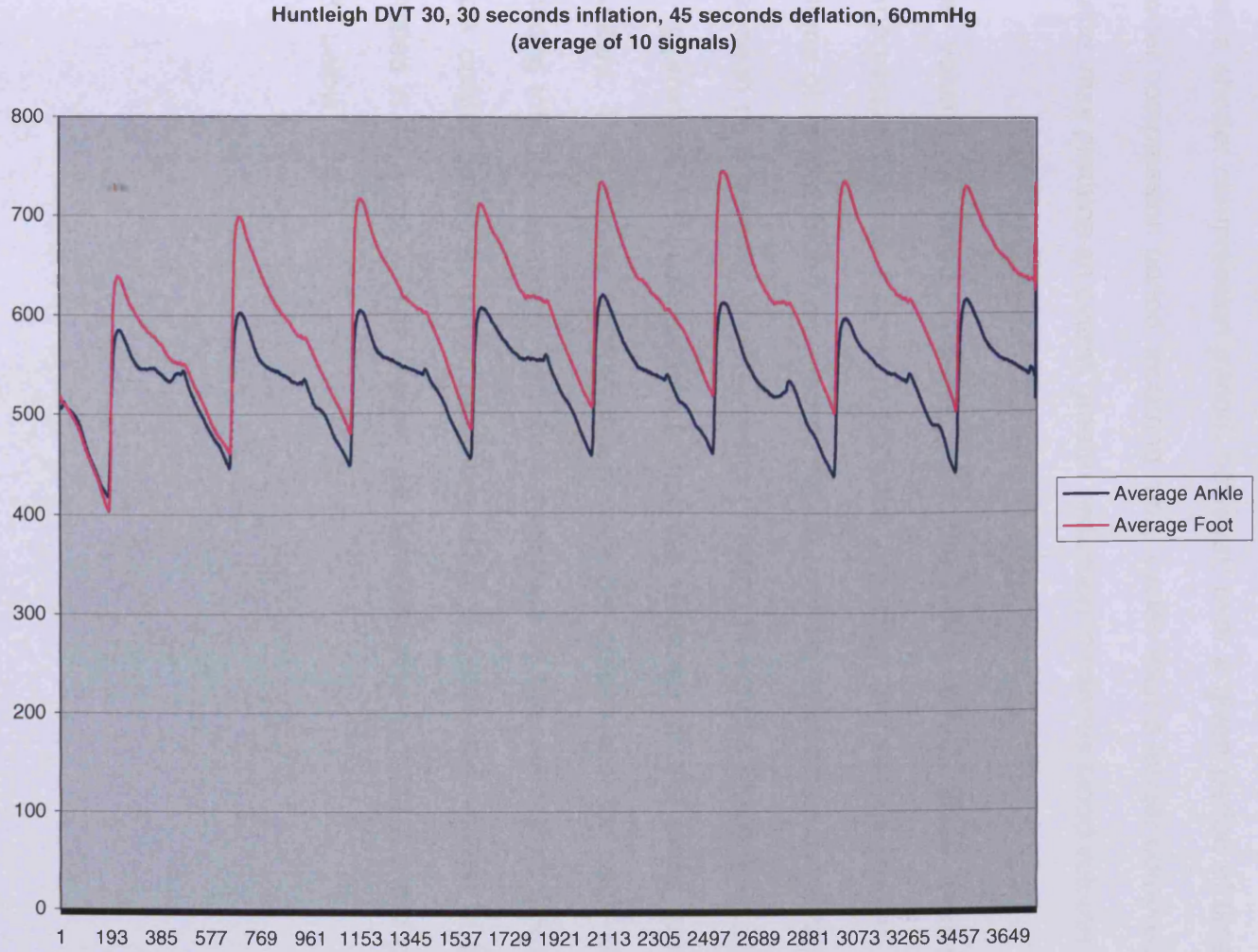

Huntleigh DVT 30, 25 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
900
800
700
600
500
400
300
200
100
0
1
187
373
559
745
931
1117
1303
1489
1675
1861
2047
2233
2419
2605
2791
2977
3163
3349
3535
3721
Average Ankle
Average Foot

Figure 3.36


Huntleigh DVT 30, 30 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
800
700
600
500
400
300
200
100
0
1 193 385 577 769 961 1153 1345 1537 1729 1921 2113 2305 2497 2689 2881 3073 3265 3457 3649
Average Ankle
Average Foot

However, a more objective analysis is required to determine which of the inflation durations produces the optimal results. The optimal compression period should produce the maximum venous emptying, in turn producing the maximum arterial supply. Therefore, in order to determine the optimal compression period, the volume of venous blood moved in a given time period needs to be determined for each differing cycle. The longer compression period may produce a greater reduction in venous blood volume per cycle than a shorter compression period, however, over a given period of time the shorter compression period, incurring more cycles than a longer compression period, may produce an overall greater reduction in venous blood volume.

The volume of blood emptied from the veins for a given period of compression, may be estimated from the results of the venous studies. The volume of venous blood emptied per cycle may be determined by multiplying the mean peak velocity and the mean duration of venous blood flow. This is an approximation which assumes that the diameter of the veins remains constant. This volume approximation may be determined for each of the differing inflation durations, and then multiplied by the number of times the cycle occurs during a 10 minute time period to obtain the volume of blood emptied in 10 minutes. The results are demonstrated in table 3.4 and graph 3.37 below.

Inflation duration (seconds)	Approx. volume per 10 minutes compression (3s.f.)
15	*720*
20	*732*
25	*712*
30	*701*

Table 3.4 The approximate volume emptied in 10 minutes of compression for different inflation durations.

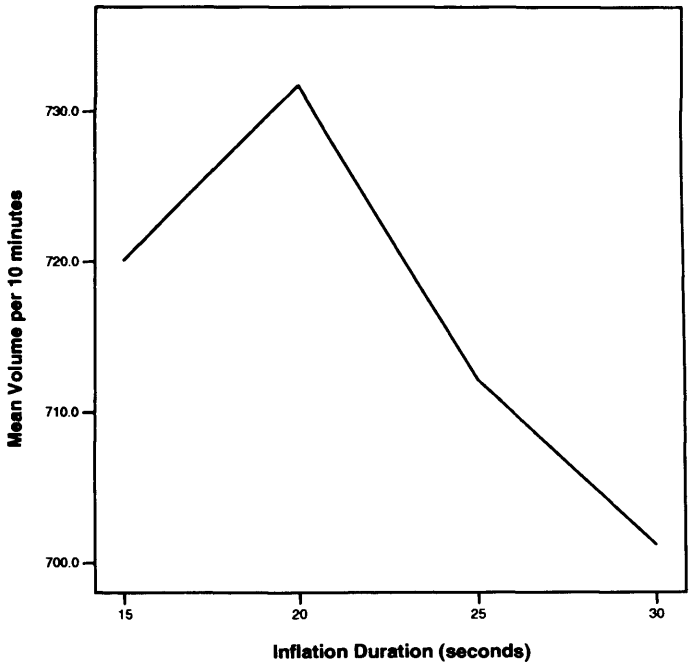


Figure 3.37 The approximate volume emptied during 10 minutes of compression for different inflation durations.

From the graph above it can be seen that the optimal inflation duration for whole leg compression is of 20 seconds duration.

Finally, the effect of altering the deflation duration on distal venous blood flow was investigated. Originally, as with the arterial study, investigations examined the deflation durations 15, 30, 45 and 60 seconds; however, it was

felt that smaller increments within the range 15 to 60 seconds were required in order to decipher an accurate representation of the effect incurred on distal venous blood flow. Therefore, the deflation duration was varied between 15 and 60 seconds, in increments of 5 seconds. A pressure of 60mmHg, and an inflation duration of 15 seconds were maintained throughout these studies. Each test comprised 5 measurements at each deflation setting, whilst each test was repeated 6 times. Figures 3.38 -3.40 display the results obtained.

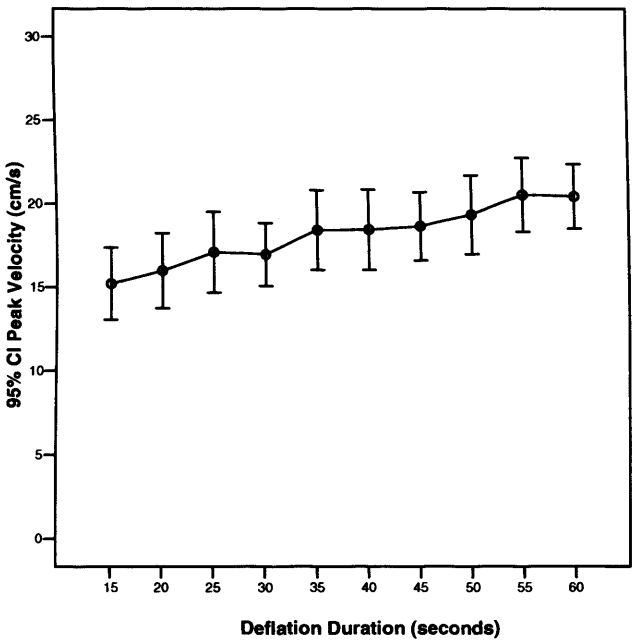


Figure 3.38 The mean peak venous blood flow velocity post compression for deflation durations in the range 15 to 60 seconds, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

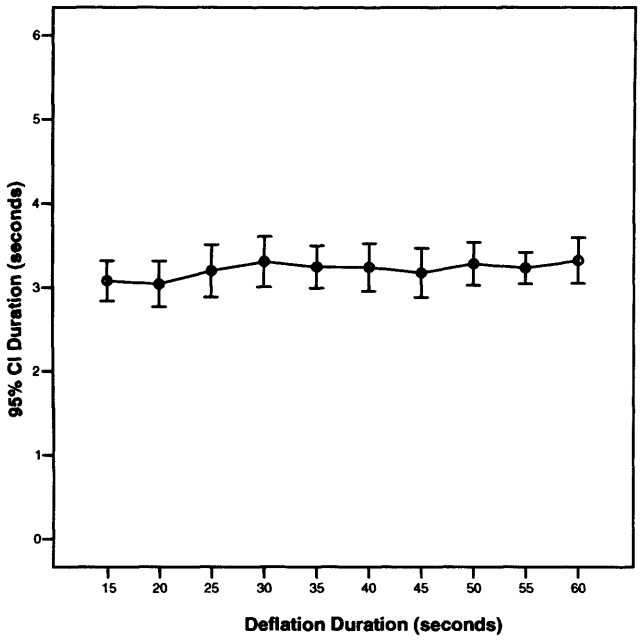


Figure 3.39 The mean duration of venous blood flow post compression for deflation durations in the range 15 to 60 seconds, using the Huntleigh DVT 30 compression cuff. These results were obtained using the randomised method.

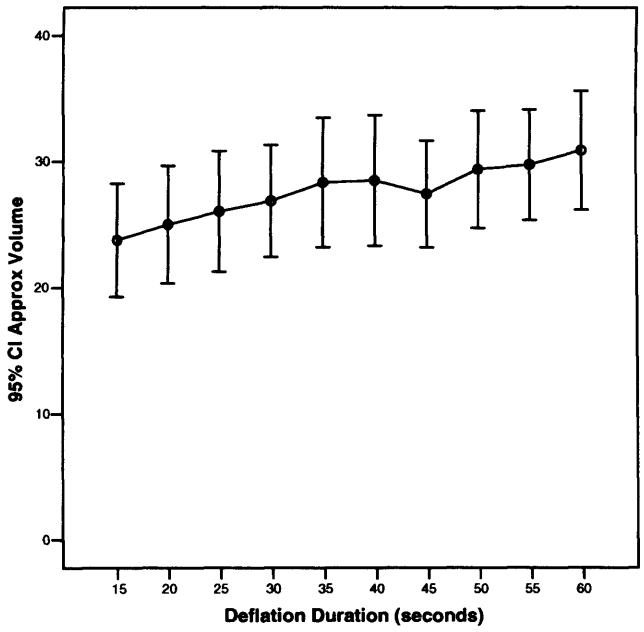


Figure 3.40 An approximation of the blood volume trapped within the foot for inflation durations within the range 5 to 30 seconds.

Upon increasing the deflation duration of the Huntleigh DVT 30 cuff between 15 and 60 seconds in increments of 5 seconds, an increase in the distal peak venous velocity and approximate venous volume was observed, as displayed in figures 3.38 and 3.40.

The one-way ANOVA revealed that there was a significant difference (p-value 0.005) between the peak velocities obtained for different levels of the deflation duration investigated; however, significant results were not achieved for the duration of venous flow and the approximate volume, (p-values 0.881 and 0.484 respectively).

Therefore, it would seem that a long deflation duration produces the optimal response in the distal venous circulation. In keeping with the results of the arterial studies, the optimal deflation duration for concurrently enhancing the distal arterial and venous blood flows is 45 seconds.

In addition to the studies performed using Doppler ultrasound and Photoplethysmography, a study was conducted implementing laser Doppler flowmetry (LDF), which measures tissue blood perfusion. A cycle of 15 seconds compression, 45 seconds deflation and 60mmHg was implemented, whilst the sensors were placed around the foot. The following graph (figure 3.41) demonstrates the tissue blood perfusion in the foot whilst compressing the leg with the Huntleigh DVT 30 cuff. The graph demonstrates distal tissue blood perfusion during 180 seconds without compression, followed by ten cycles of compression and a further 180 seconds without compression.

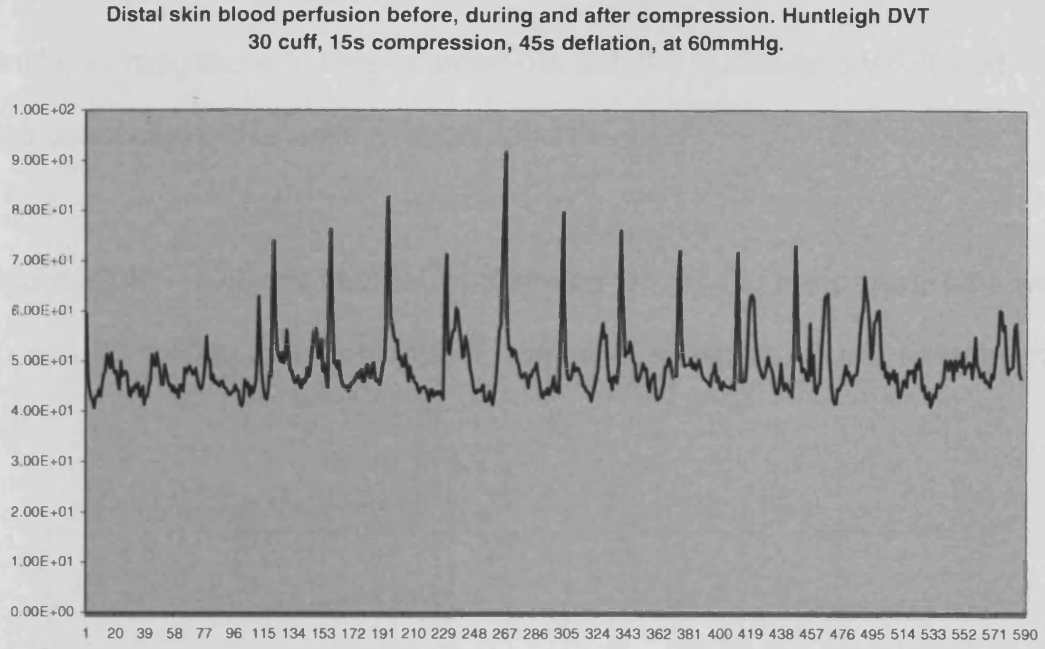


Figure 3.41 Distal skin blood perfusion in the foot of a healthy volunteer during compression with the Huntleigh DVT 30 compression cuff.

Figure 3.41 demonstrates that compression enhances the perfusion of blood in distal tissues.

3.3.1.1 Summary of Huntleigh DVT 30 findings

The investigations carried out have revealed that there is a distal haemodynamical response produced with the Huntleigh DVT 30 compression garment, and its associated optimal compression regime for concurrently enhancing the distal arterial and venous circulations has been found to involve a pressure of 60mmHg, and a cycle of 20 seconds compression and 45 seconds deflation.

3.3.2 Uniform Thigh Cuff

Similar investigations to those carried out with the Huntleigh DVT 30 cuff were also conducted with a uniform thigh cuff.

Figures 3.42 – 3.46 are the results obtained for varying the pressure between 50 and 90 mmHg in increments of 10mmHg, whilst using the uniform thigh cuff.

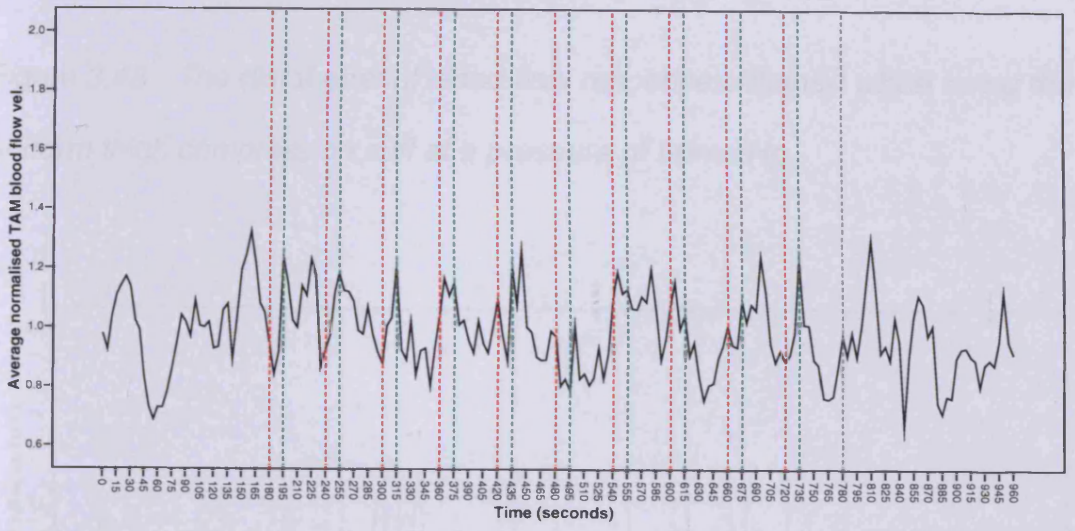


Figure 3.42 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a pressure of 50mmHg.

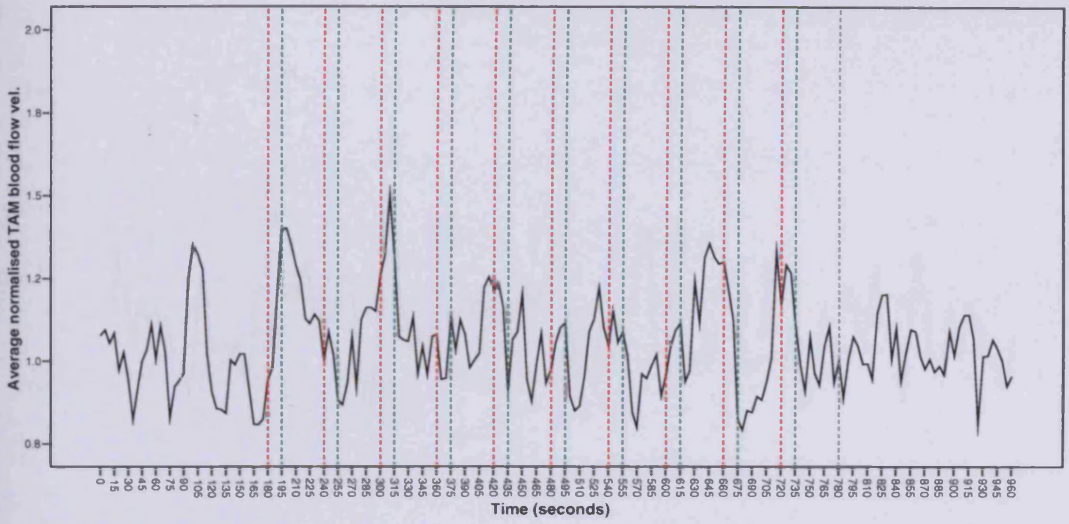


Figure 3.43 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a pressure of 60mmHg.

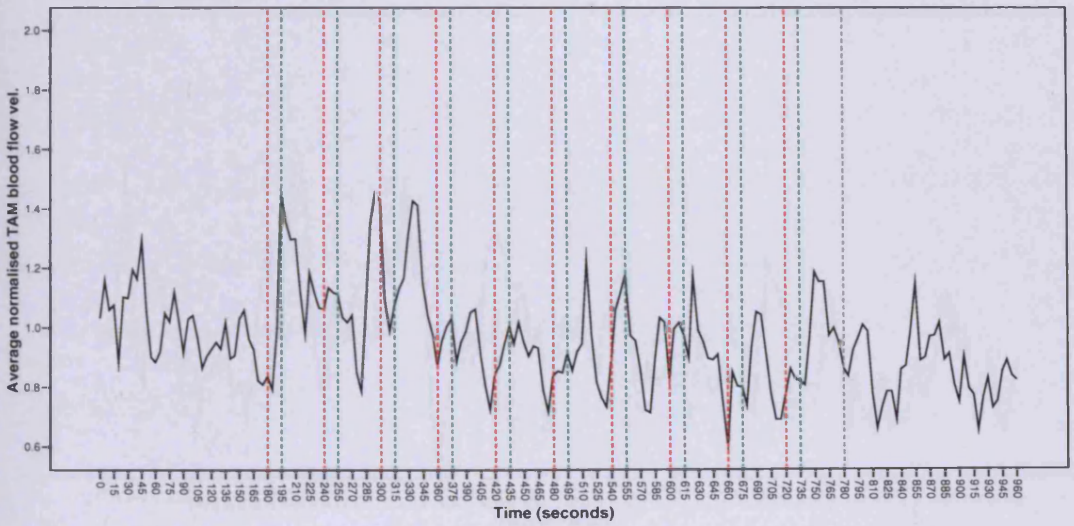


Figure 3.44 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a pressure of 70mmHg.

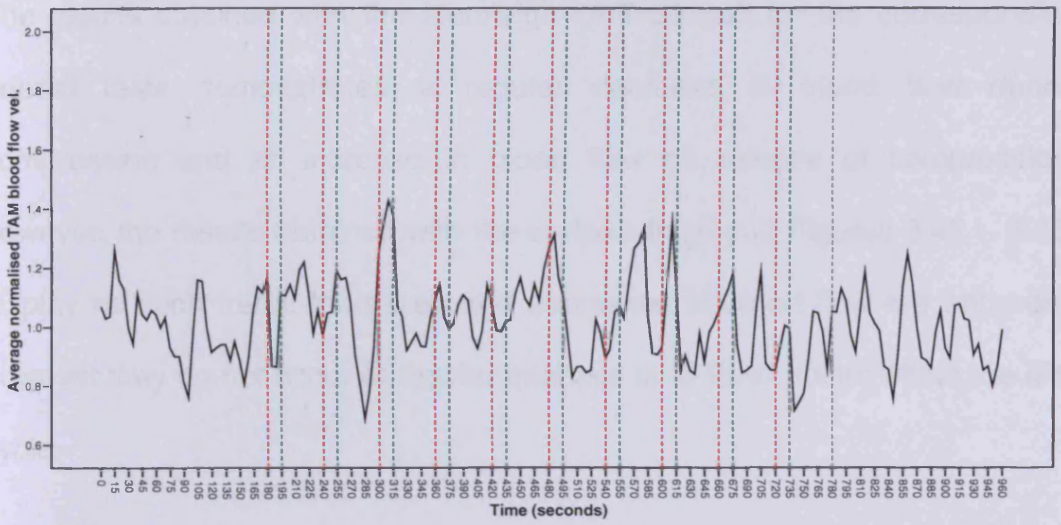


Figure 3.45 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a pressure of 80mmHg.

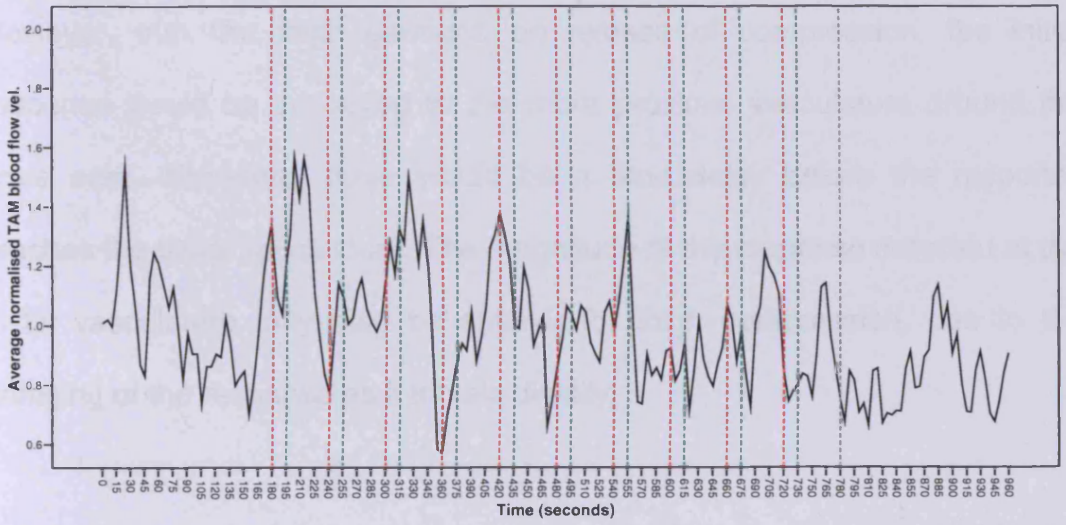


Figure 3.46 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a pressure of 90mmHg.

The results obtained with the Huntleigh DVT 30 cuff for the corresponding arterial tests demonstrated a regular decrease in blood flow during compression and an increase in blood flow on release of compression; however, the results obtained with the uniform thigh cuff (figures 3.42 – 3.46) display no such trend. Increases and decreases in blood flow are apparent; however they do not occur at regular intervals or at fixed points within the IPC cycle.

There are several possibilities which could explain the perceptible discrepancy between the distal response obtained for the whole leg garment and that obtained for the thigh garment. The whole leg garment imparted a direct effect on the distal circulation due to the extent of the leg receiving compression. However, with the thigh garment, on release of compression, the initial response would be conveyed to the more proximal vasculature around the knee area. Therefore, there would be a time delay before the response reaches the distal vasculature. The magnitude of the response detected at the distal vasculature may also be smaller for thigh compression, due to the damping of the response as it travels distally.

Due to these considerations, it is possible that the response imparted by the thigh garment is regular in the same way as the response obtained from the Huntleigh DVT 30 cuff; however by the time the thigh cuff response is conveyed to the distal circulation, it may involve a different timing, and therefore may not be as apparent from the graphs.

There does not appear to be a great difference between the graphs obtained for the different pressures, however, upon entering the data into the computer program for calculating the percentage change in blood flow during compression, it was revealed otherwise. The results of the program are given in table 3.5.

Pressure (mmHg)	**50**	**60**	**70**	**80**	**90**
% change in blood flow	*0.75*	*5.87*	*5.88*	*3.41*	*10.01*
Standard deviation (2 d.p)	*5.86*	*4.46*	*18.23*	*3.13*	*17.02*

Table 3.5 The percentage change in blood flow arising during compression with the uniform thigh cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing pressures; and the associated standard deviations.

A net increase in blood flow was obtained for each of the pressures implemented; it would seem however, that the optimal response has been obtained for a pressure in the 60/70 mmHg range, as 90mmHg is too high a pressure to be used comfortably. The result obtained for the standard deviation also supports an optimal pressure of 60mmHg.

Similar graphs were obtained for investigations examining the effect of altering the inflation duration on distal arterial blood flow. In these investigations, a

pressure of 60mmHg, and a deflation duration of 45 seconds were maintained constant throughout, whilst the inflation duration was increased from 5 to 30 seconds in increments of 5 seconds. The results are demonstrated in figures 3.47 – 3.52 below.

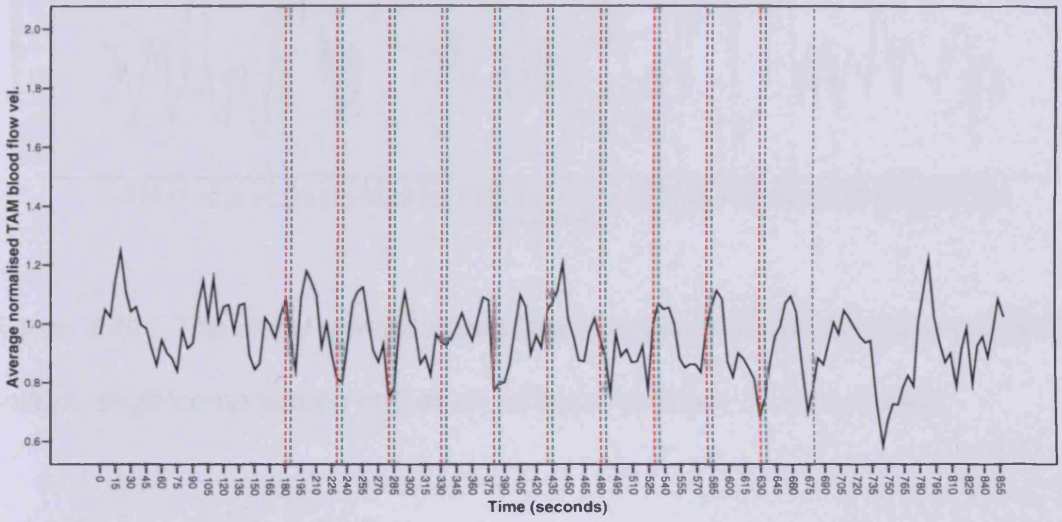


Figure 3.47 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 5 seconds.

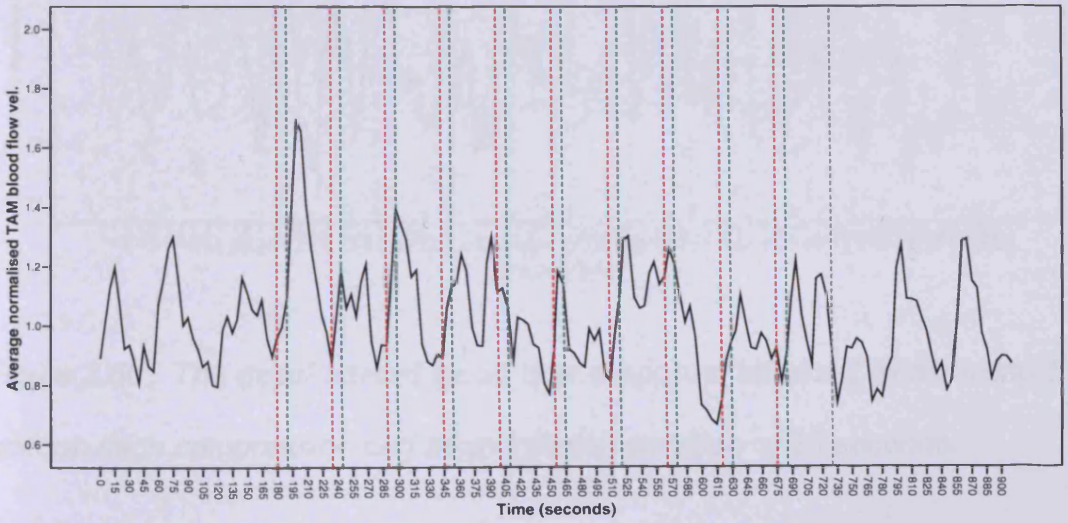


Figure 3.48 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 10 seconds.

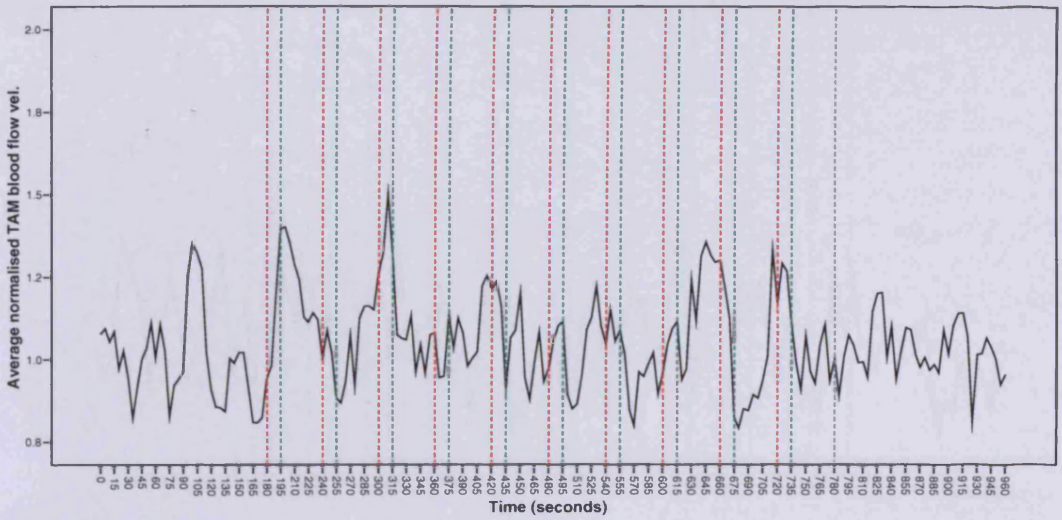


Figure 3.49 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 15 seconds.

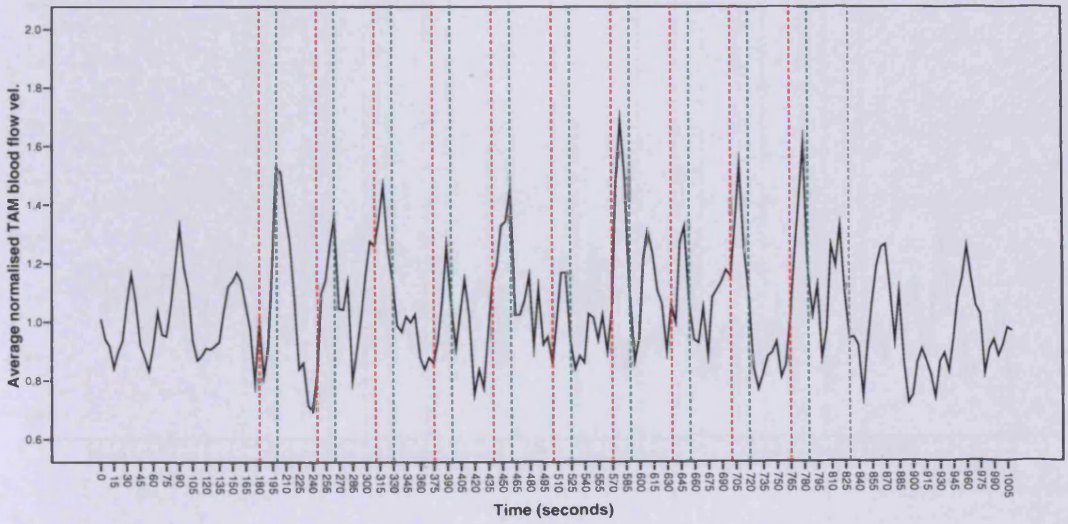


Figure 3.50 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 20 seconds.

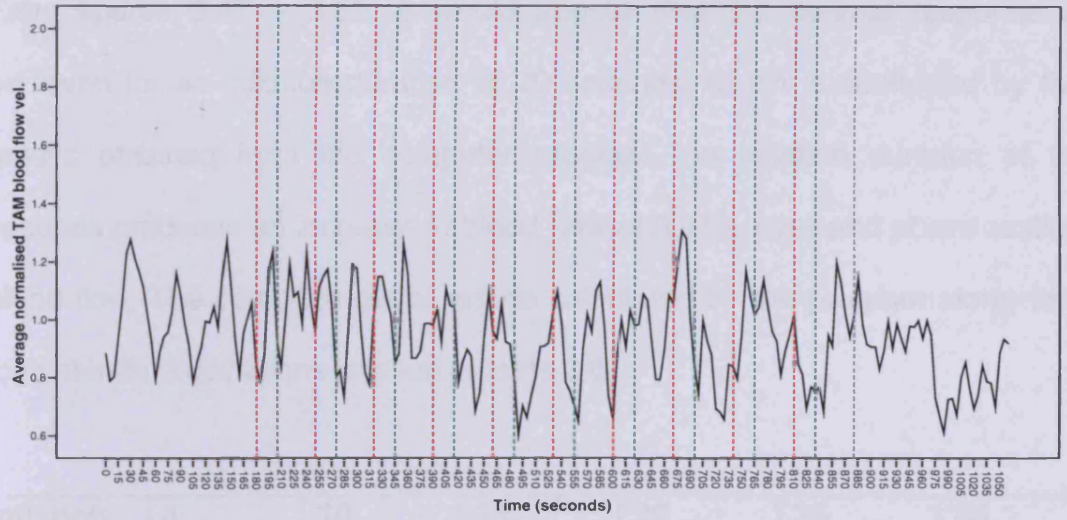


Figure 3.51 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 25 seconds.

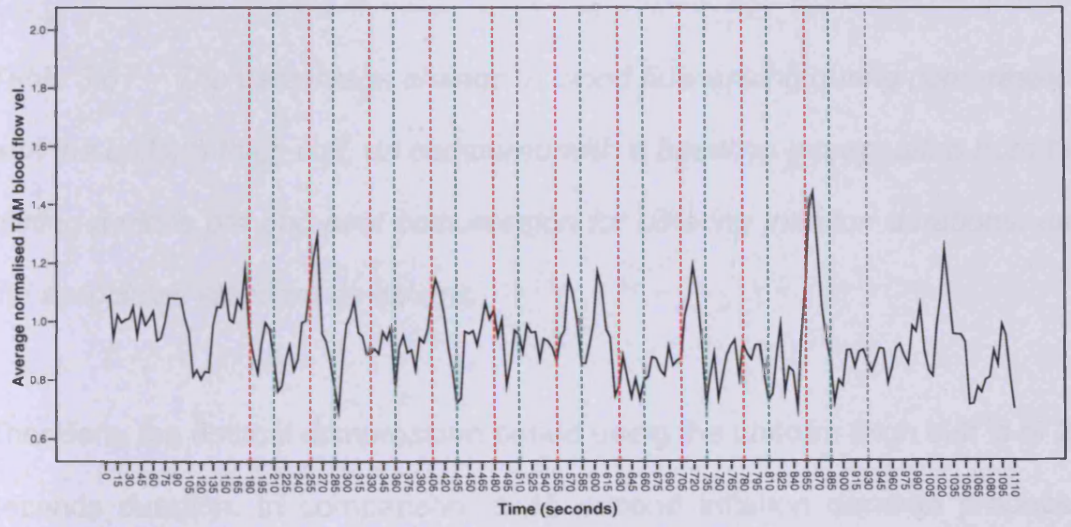


Figure 3.52 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at an inflation duration of 30 seconds.

From figures 3.47 – 3.52, it would appear that the optimal response is achieved for an inflation duration of 20 seconds, which is confirmed by the results obtained from the computer program. An inflation duration of 20 seconds produces an increase in blood flow of 9.81% over and above resting blood flow. The complete set of results calculated by the program along with their standard deviations is given in table 3.6.

Inflation duration (seconds)	**5**	**10**	**15**	**20**	**25**	**30**
% change in blood flow	*-1.27*	*6.44*	*5.87*	*9.81*	*2.51*	*-2.72*
Standard deviation (2 d.p)	*3.44*	*4.90*	*4.46*	*7.41*	*4.68*	*6.30*

Table 3.6 The percentage change in blood flow arising during compression with the uniform thigh cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing inflation durations; and the associated standard deviations.

Therefore, the optimal compression period using the uniform thigh cuff is of 20 seconds duration. In comparison, a 15 second inflation duration produced optimal results for the whole leg garment, giving rise to a 9.21% increase in blood flow during compression as compared with resting blood flow. Hence, a longer period of thigh compression is required to produce a similar increase in blood flow during compression as a shorter duration of whole leg compression.

The effect of altering the deflation duration on distal arterial blood flow was investigated through studies which maintained an inflation period of 15 seconds and a pressure of 60mmHg. The deflation duration was increased from 15 to 60 seconds in increments of 15 seconds. The graphs obtained did not reveal any great differences between the results obtained for the varying deflation periods, as demonstrated in figures 3.53 – 3.56.

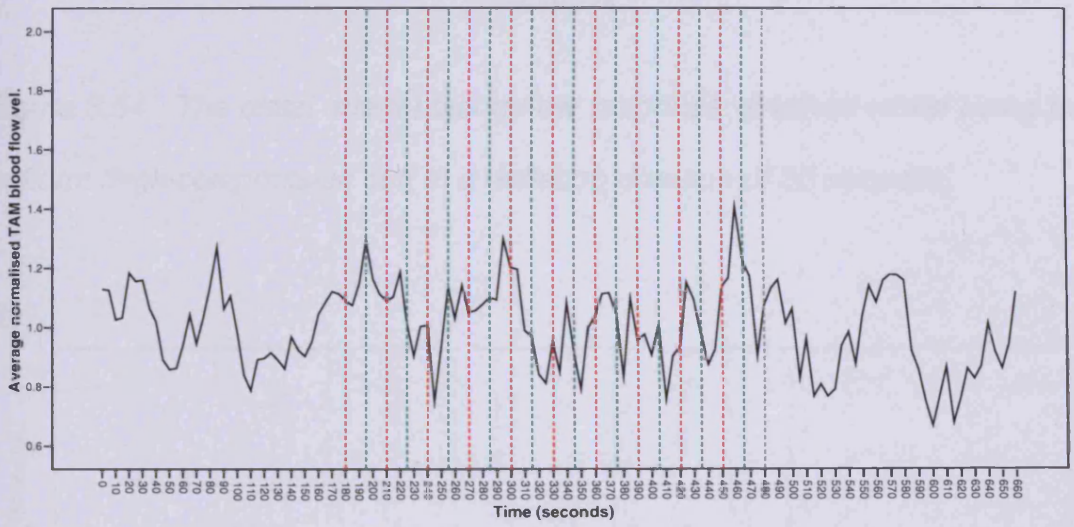


Figure 3.53 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a deflation duration of 15 seconds.

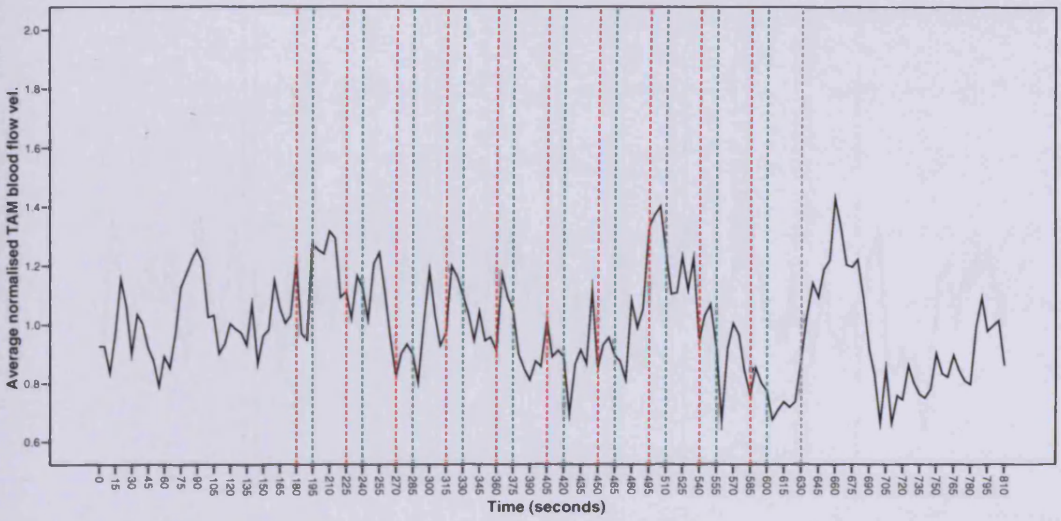


Figure 3.54 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a deflation duration of 30 seconds.

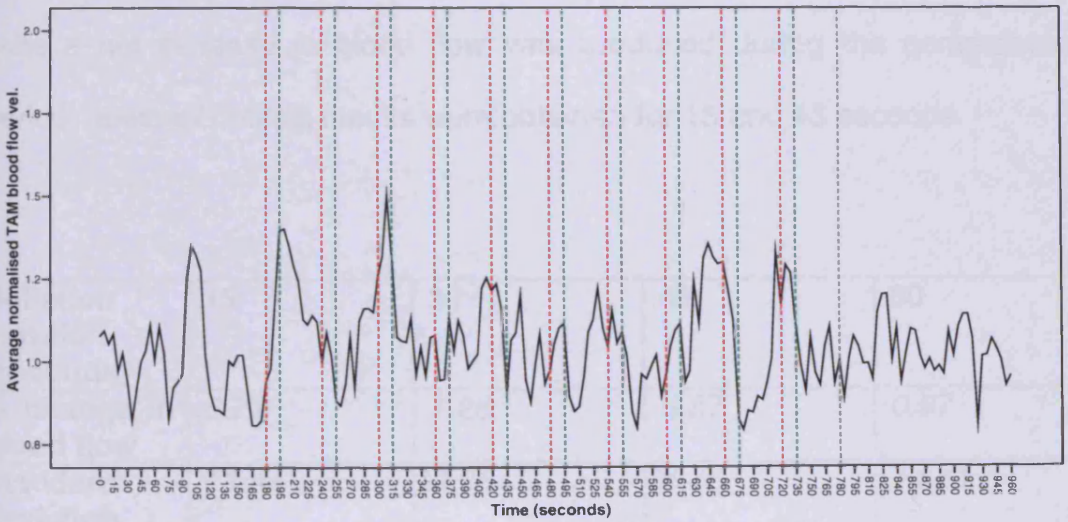


Figure 3.55 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a deflation duration of 45 seconds.

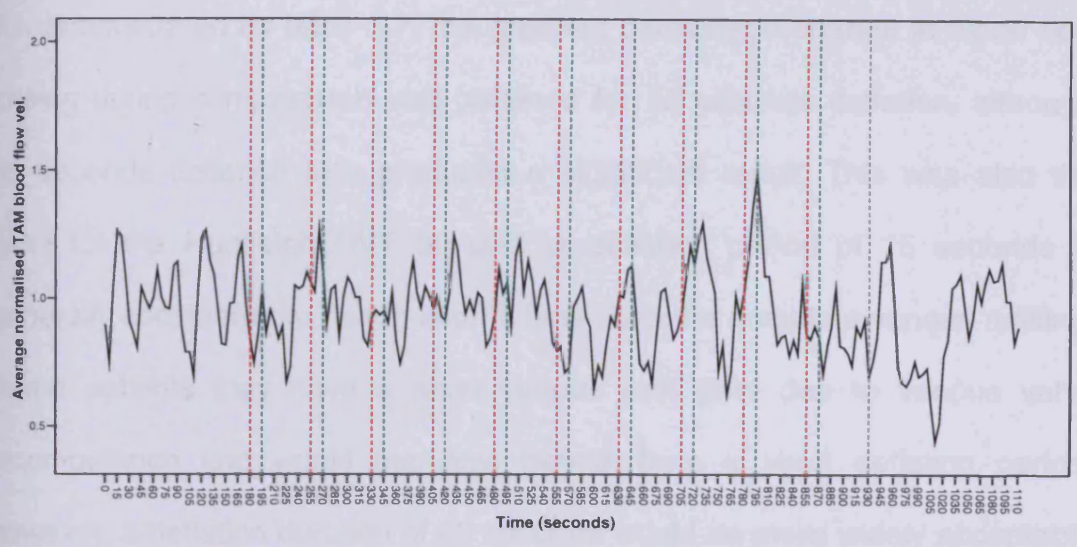


Figure 3.56 The distal arterial blood flow response obtained whilst using the uniform thigh compression cuff at a deflation duration of 60 seconds.

Results extrapolated from the computer program demonstrated that in each case a net increase in blood flow was produced during the compression period, however optimal results were obtained for 15 and 45 seconds.

Deflation duration (seconds)	**15**	**30**	**45**	**60**
% change in blood flow	*6.71*	*1.26*	*5.87*	*0.97*
Standard deviation (2 d.p)	*11.94*	*9.95*	*4.46*	*14.41*

Table 3.7 The percentage change in blood flow arising during compression with the uniform thigh cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for differing deflation durations; and the associated standard deviations.

As demonstrated by table 3.7, the greatest percentage change in blood flow arising during compression was obtained for 15 seconds deflation, although 45 seconds deflation also produced a significant result. This was also the case for the Huntleigh DVT 30 cuff. A deflation period of 15 seconds is generally considered to be too short a time scale for complete venous refilling. Some patients may have a short venous refill time due to venous valve incompetence and would therefore benefit from a short deflation period; however, a deflation duration of 45 seconds would be more widely acceptable allowing an adequate period for all differing venous refill times. A high standard deviation of 11.94% was obtained for 15 seconds, in comparison with the lower 4.46% which was obtained for 45 seconds; verifying the conclusion that 45 seconds deflation would be preferable.

Similar investigations were also conducted to examine the effect of thigh compression on distal venous blood flow. The effects of altering the pressure, the inflation duration and the deflation duration of thigh compression were examined on distal venous blood flow.

As with the Huntleigh DVT 30 cuff, the initial venous study results obtained for the uniform thigh cuff required repeating with randomised settings, in order to account for the effect of arterial relaxation over time. The following figures demonstrate the initial non-randomised results obtained with the uniform thigh compression cuff.

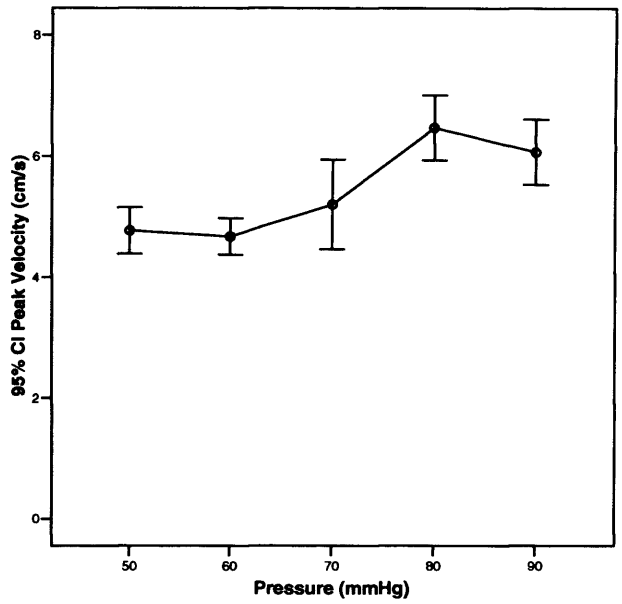


Figure 3.57 The mean peak venous blood flow velocity post compression obtained for pressures in the range 50 to 90 mmHg using the uniform thigh compression cuff.

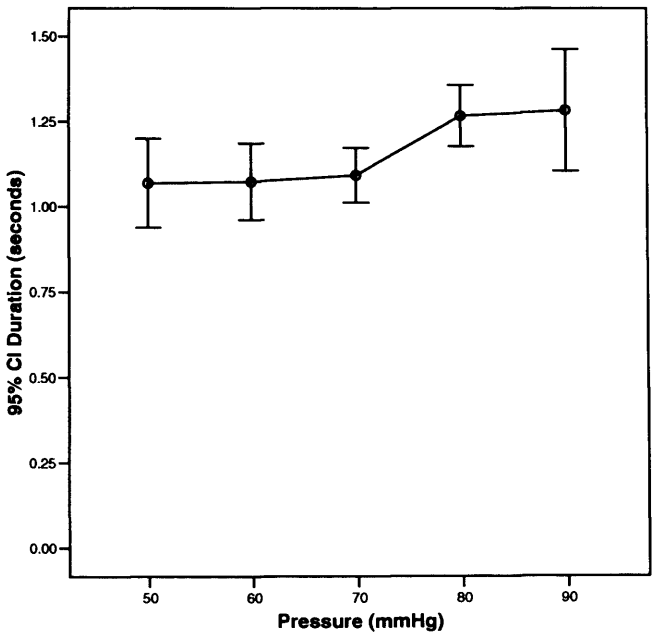


Figure 3.58 The mean duration of venous blood flow post compression for pressures in the range 50 to 90mmHg, using the uniform thigh compression cuff.

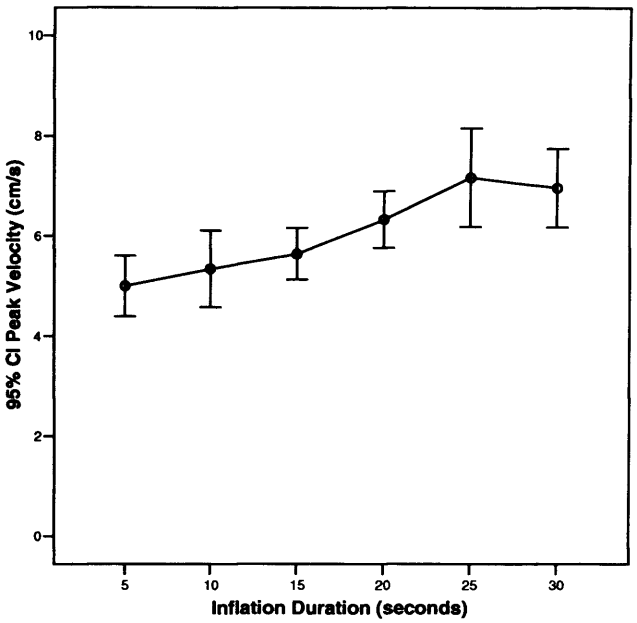


Figure 3.59 The mean peak venous blood flow velocity post compression obtained for inflation durations in the range 5 to 30 seconds, using the uniform thigh compression cuff.

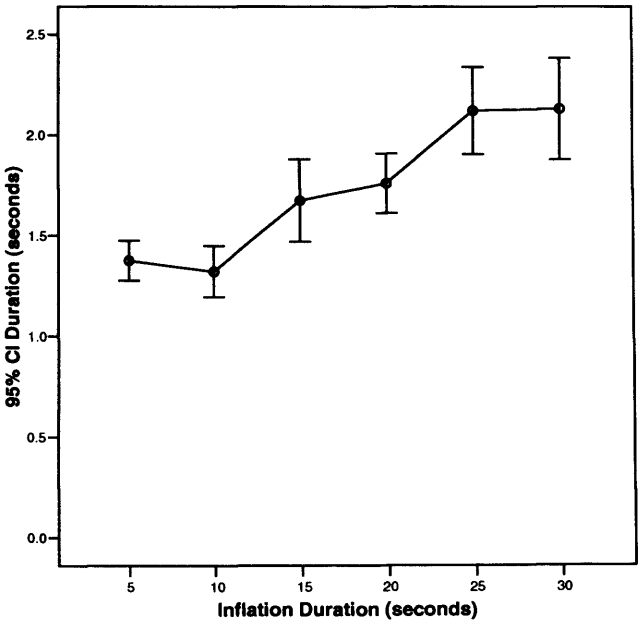


Figure 3.60 The mean duration of venous blood flow post compression for inflation durations in the range 5 to 30 seconds, using the uniform thigh compression cuff.

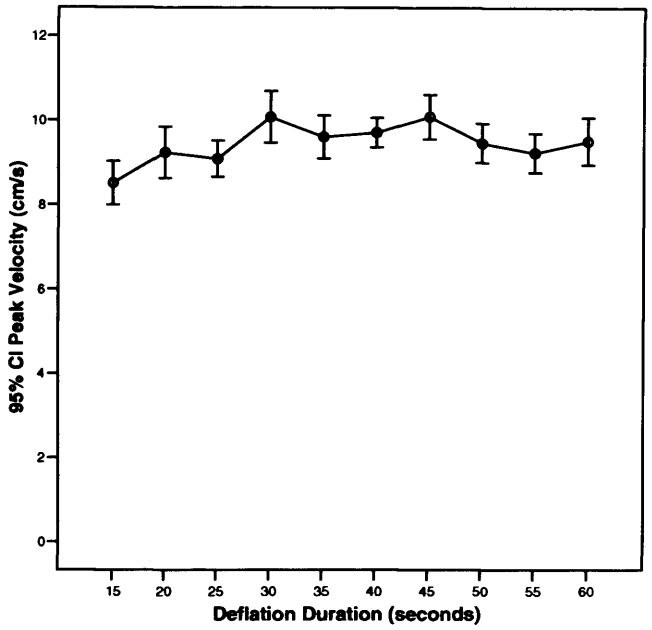


Figure 3.61 The mean peak venous blood flow velocity post compression obtained for deflation durations in the range 15 to 60 seconds, using the uniform thigh compression cuff.

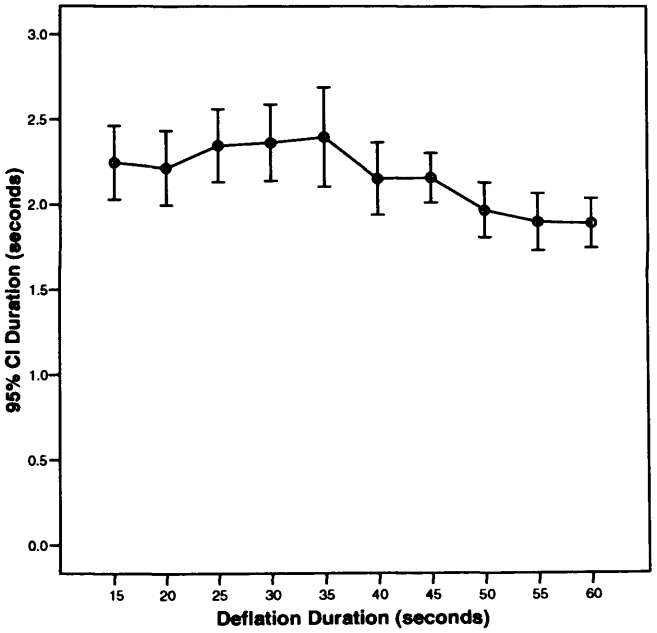


Figure 3.62 The mean duration of venous blood flow post compression for deflation durations in the range 15 to 60 seconds, using the uniform thigh compression cuff.

Therefore, the effects of altering the pressure, and cycle duration of uniform thigh compression on distal venous blood flow was re-examined using the randomised method as previously utilised for the Huntleigh DVT 30 cuff.

The results obtained from the randomised experiments were not in complete agreement with the results previously attained, as demonstrated below.

Figures 3.63 -3.65 are the results obtained for the effect of altering the pressure of compression on distal venous blood flow. A cycle of 15 seconds compression and 45 seconds deflation was maintained throughout, whilst the pressure settings ranged from 50 to 90 mmHg in increments of 10mmHg.

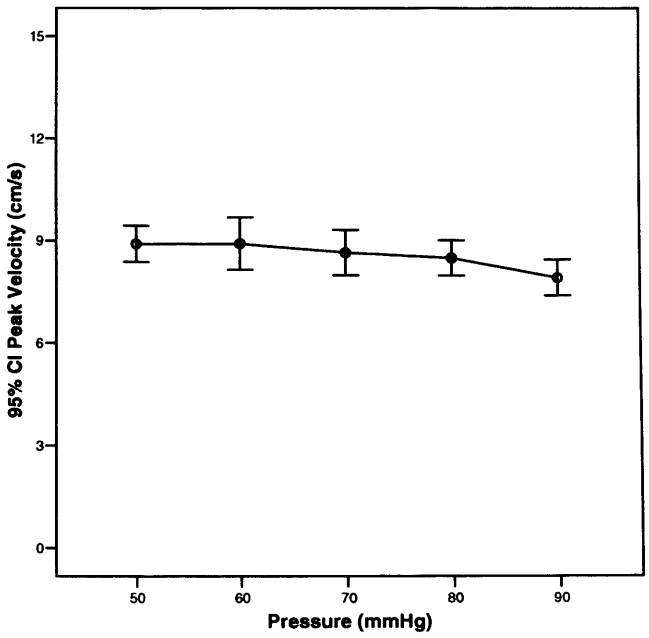


Figure 3.63 The mean peak venous blood flow velocity post compression for pressures in the range 50 to 90 mmHg, using the uniform thigh compression cuff. These results were obtained using the randomised method.

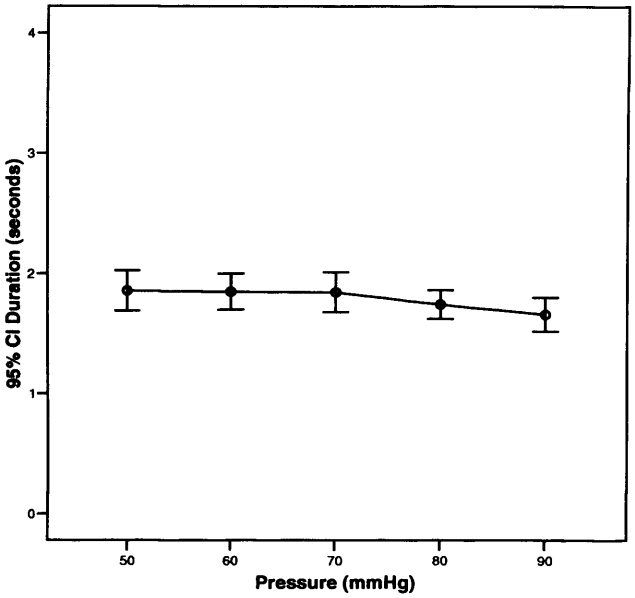


Figure 3.64 The duration of venous blood flow post compression for pressures in the range 50 to 90 mmHg, using the uniform thigh compression cuff. These results were obtained using the randomised method.

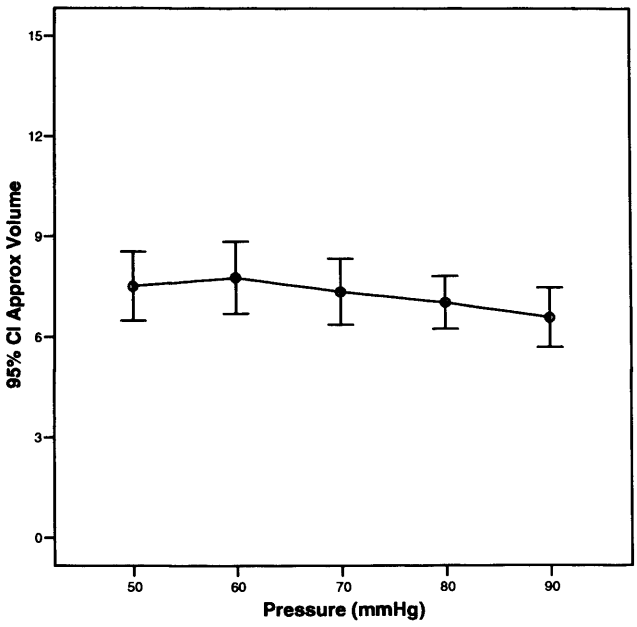


Figure 3.65 The approximate volume of venous blood flow post compression for pressures in the range 50 to 90 mmHg, using the uniform thigh compression cuff. These results were obtained using the randomised method.

These results display a similar trend to those obtained whilst using the Huntleigh DVT 30 cuff, although the magnitudes of the individual results are greater for the Huntleigh DVT 30 cuff. It would appear that varying the pressure of uniform thigh compression between the moderate pressure range of 50 to 90 mmHg does not impart an effect on the distal venous circulation. The one way ANOVA substantiated this finding, revealing that there were no significant differences between the different pressures examined; $p=0.124$ for peak velocity, $p=0.252$ for duration and $p=0.442$ for approximate volume. Since the pressure of compression does not affect the post compression distal venous blood flow response, the optimal pressure of thigh compression which may be used to concurrently enhance distal arterial and venous blood flow may be governed by the results obtained from the arterial studies.

The effect of altering the inflation duration of uniform thigh compression on distal venous blood flow produced the following results (figures 3.66 – 3.68). The pressure was maintained at 60 mmHg, and the deflation duration at 45 seconds. The inflation settings were randomised between 5 and 30 seconds in increments of 5 seconds, ensuring 10 measurements for each inflation setting within each test.

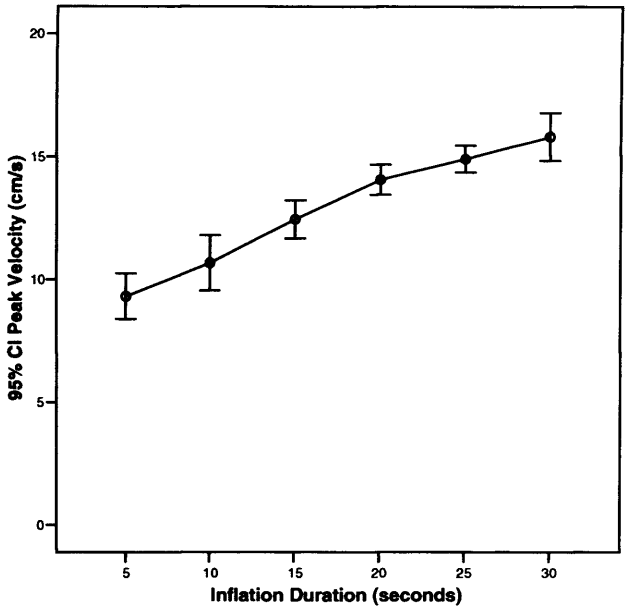


Figure 3.66 The mean peak venous blood flow velocity post compression for inflation durations in the range 5 to 30 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

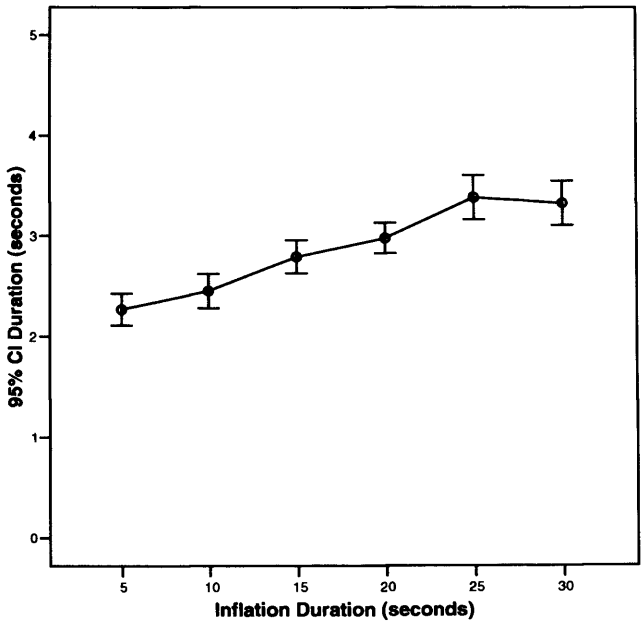


Figure 3.67 The duration of venous blood flow post compression for inflation durations in the range 5 to 30 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

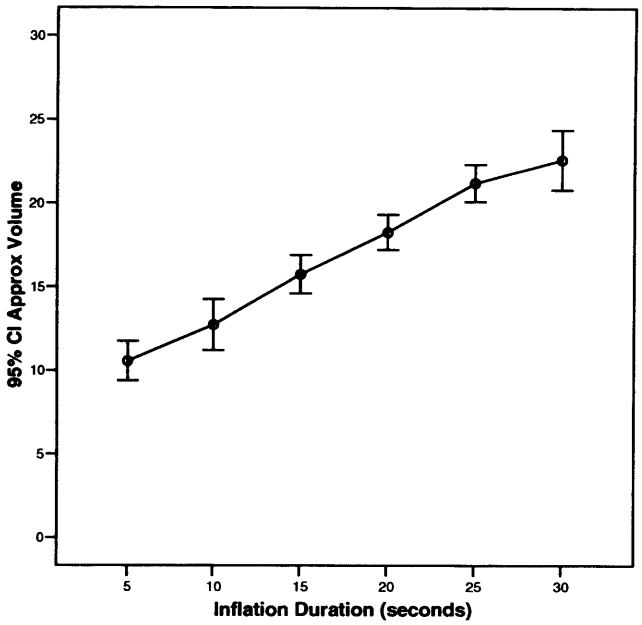


Figure 3.68 The approximate volume of venous blood flow post compression for inflation durations in the range 5 to 30 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

From these graphs, it can be seen that there is a clear trend; the longer the period of compression, the greater the distal venous response. This seems to be a reasonable result; the longer the period of compression, the greater the volume of blood trapped distally and hence the greater the peak velocity, duration and volume of venous blood flow released on deflation of the cuff. Therefore, to produce an optimal venous response, a long inflation duration is required. The one-way ANOVA confirmed this trend, revealing that there was a statistically significant difference between the varying compression periods; $p < .005$ for peak velocity, duration and approximate volume. Multiple comparisons with Tukey's HSD test demonstrated that there were significant differences between the majority of consecutive pairs of inflation periods;

therefore, each 5 second increase in compression period produced a statistically significant improvement in the distal venous response.

However, the results of the arterial study demonstrated beneficial results for 10 to 20 seconds compression, with a 20 second inflation duration producing the optimal response. It would seem that a compromise needs to be arrived at. In order to facilitate this decision, further investigations into the optimal compression period were undertaken with Photoplethysmography (PPG).

Using a pressure of 60mmHg, and a deflation period of 45 seconds, the compression periods 15, 20, 25 and 30 seconds were investigated. PPG sensors were placed on the sole of the foot and behind the medial malleolus, and a blanket was placed over both legs. Compression was commenced immediately following calibration of the PPG device, and was continued for a total duration of 10 minutes. This was repeated 10 times for each inflation period, and the signals were then averaged together. The results obtained are demonstrated in the following pages (figures 3.69 – 3.72).

The graphs represent changes in microcirculatory blood volume; an increase in the signal represents a decrease in blood volume, whilst a decrease in the signal represents an increase in blood volume. As can be seen from the graphs, the shape of the signal is consistent for the different compression durations

Figure 3.69

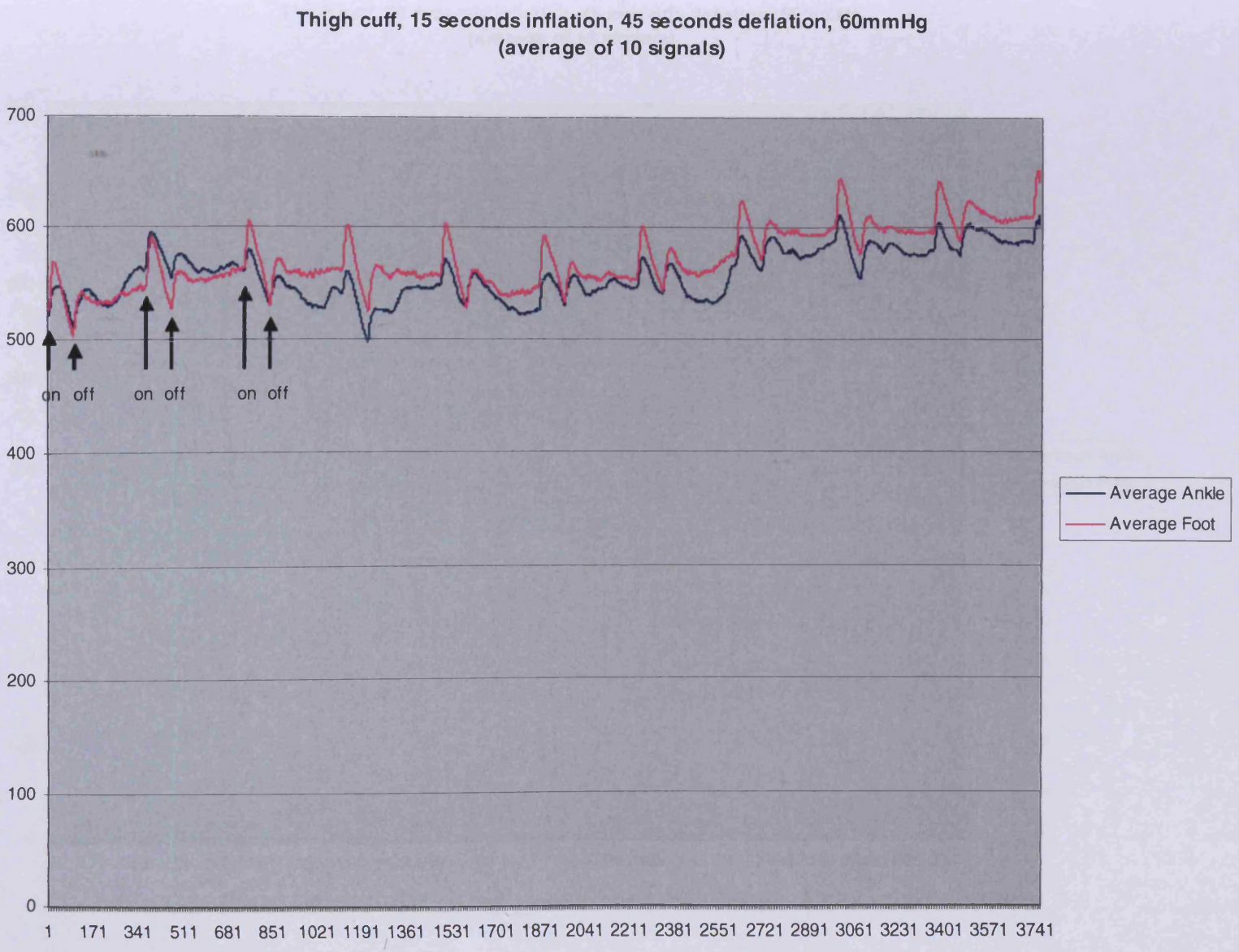

Thigh cuff, 15 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
700
600
500
400
300
200
100
0
on
off
on
off
on
off
1
171
341
511
681
851
1021
1191
1361
1531
1701
1871
2041
2211
2381
2551
2721
2891
3061
3231
3401
3571
3741
Average Ankle
Average Foot

Figure 3.70

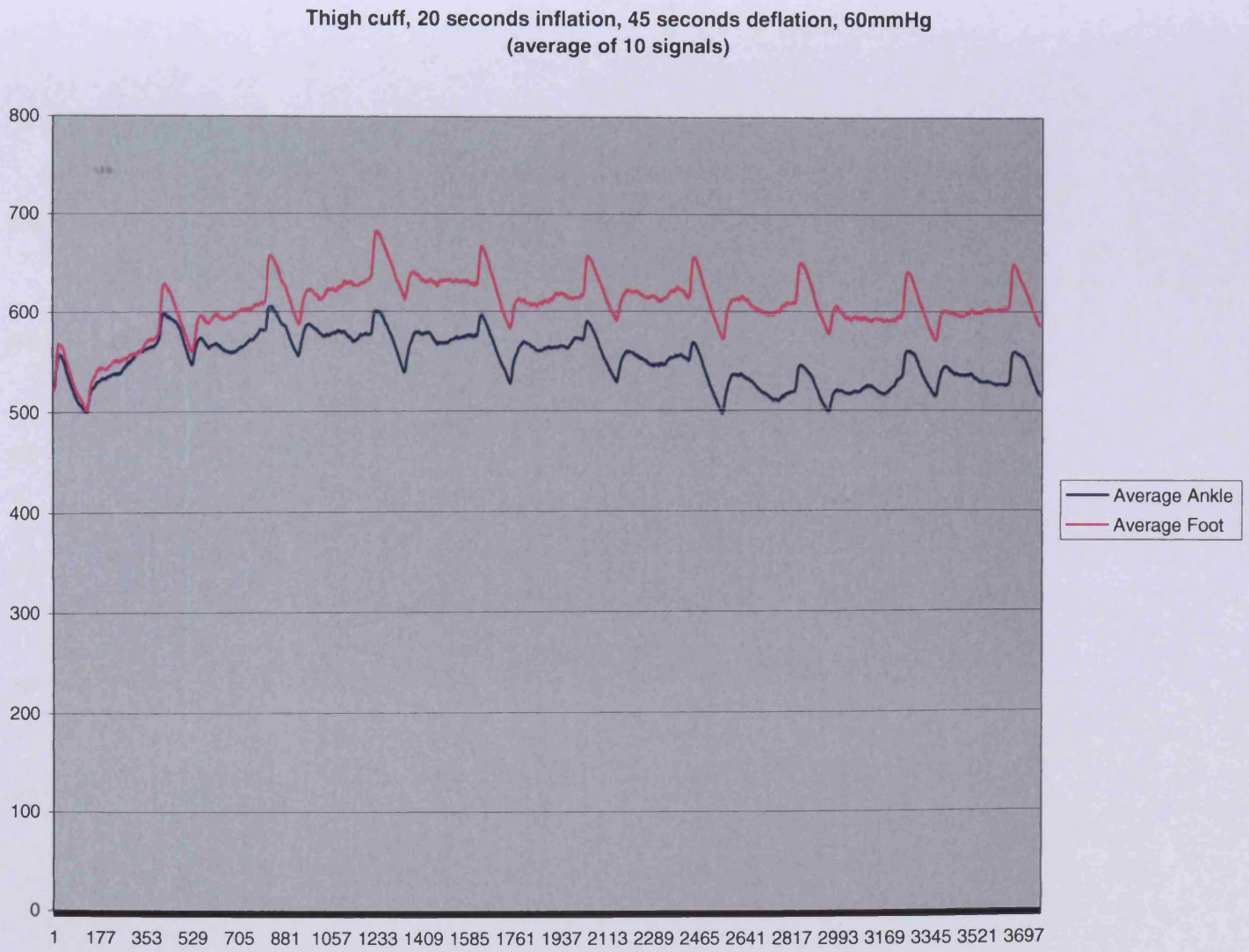

Thigh cuff, 20 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
800
700
600
500
400
300
200
100
0
1
177
353
529
705
881
1057
1233
1409
1585
1761
1937
2113
2289
2465
2641
2817
2993
3169
3345
3521
3697
Average Ankle
Average Foot

Figure 3.71

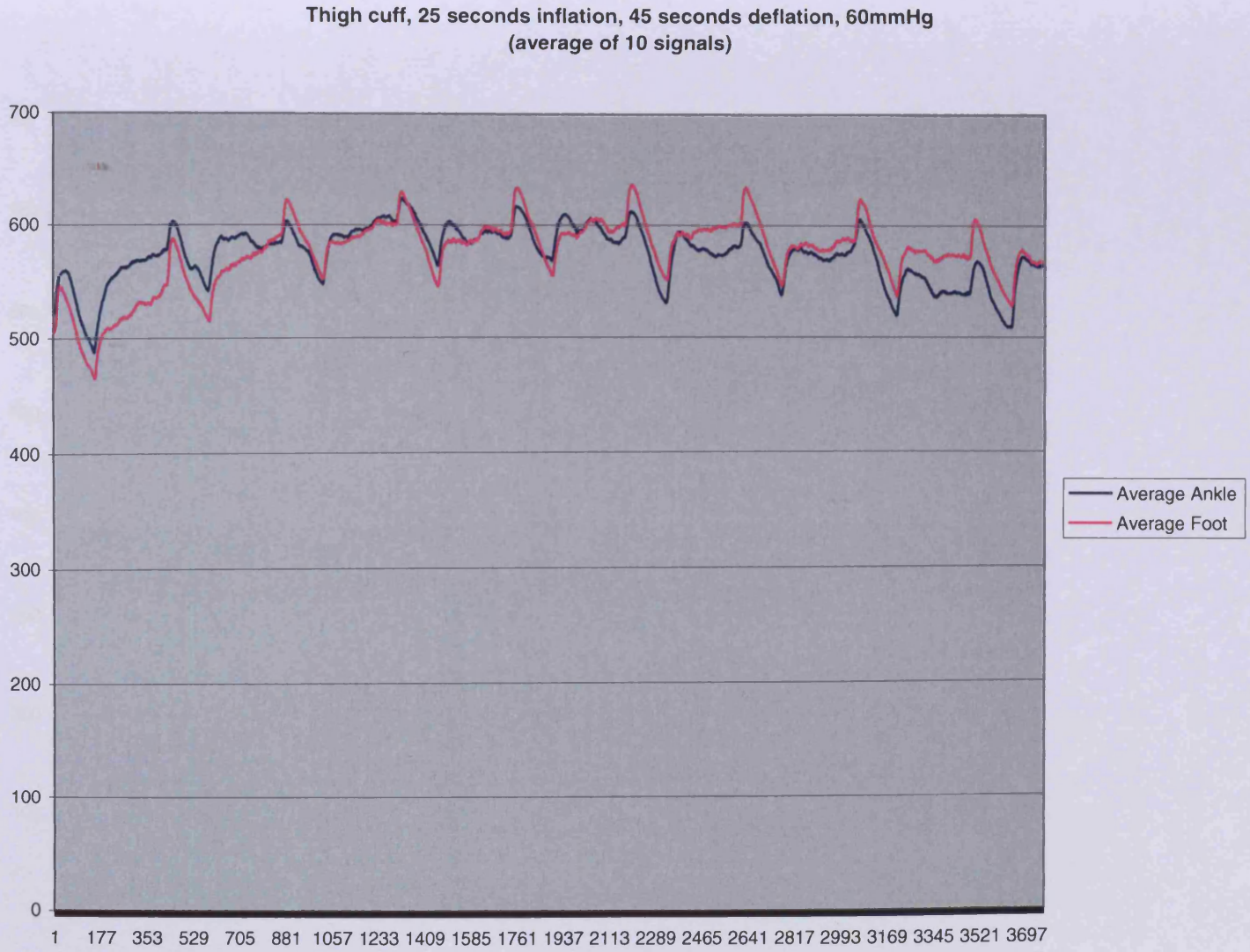
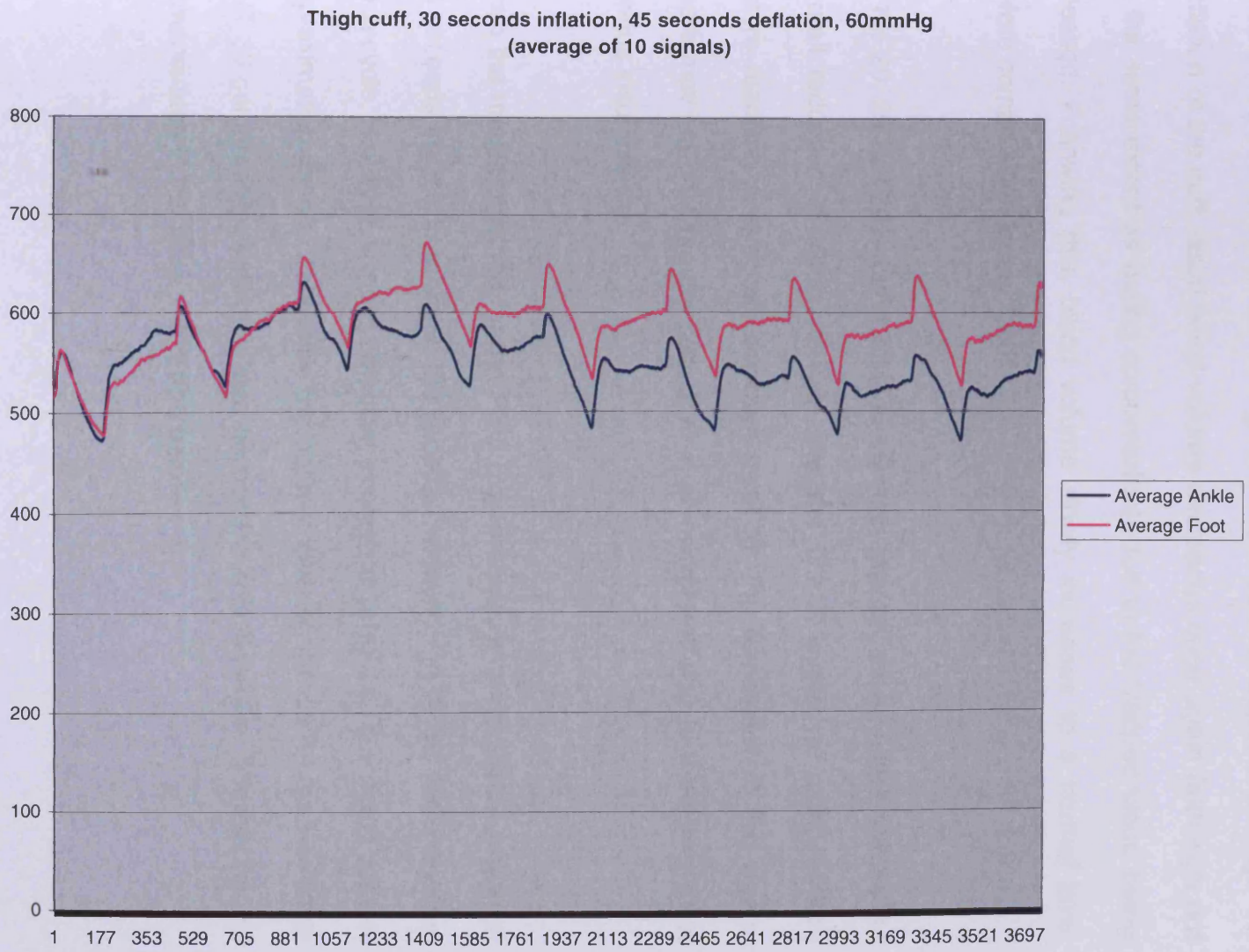

Thigh cuff, 25 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
700
600
500
400
300
200
100
0
1 177 353 529 705 881 1057 1233 1409 1585 1761 1937 2113 2289 2465 2641 2817 2993 3169 3345 3521 3697
Average Ankle
Average Foot

Figure 3.72


Thigh cuff, 30 seconds inflation, 45 seconds deflation, 60mmHg
(average of 10 signals)
800
700
600
500
400
300
200
100
0
1
177
353
529
705
881
1057
1233
1409
1585
1761
1937
2113
2289
2465
2641
2817
2993
3169
3345
3521
3697
Average Ankle
Average Foot

During compression (as indicated by the period between 'on' and 'off' in the graphs), there is a peak in the signal, indicative of an initial decrease followed by an increase in blood volume. When compression is started, there may initially be a suction effect, whereby blood is drawn up the venous circulation, therefore decreasing the distal blood volume. Once the veins are completely closed, blood volume starts to increase as blood is trapped distally. On deflation of the cuff, distal blood volume decreases once again (although not to the same extent as during compression), due to the trapped blood being released. Following this, blood volume slowly increases to a normal level before compression is resumed.

In the 20, 25 and 30 second inflation duration graphs, there appears to be an overall reduction in blood volume over the first 3 cycles of compression, before reaching a relatively constant level for the remainder of the signal. There may not be a greater reduction in blood volume due to the absence of venous insufficiency.

From the results obtained for the PPG experiments, a compression period of 30 seconds seems to produce the greatest reduction in blood volume within each cycle. However, a more objective analysis is required. The blood volume approximation used to determine the optimal inflation period for the Huntleigh DVT 30 compression cuff may also be used in this instance. The results are demonstrated in the table and graph below.

Inflation duration (seconds)	Approx. volume per 10 minutes compression (3s.f.)
15	*348*
20	*387*
25	*433*
30	*421*

Table 3.8 The approximate volume emptied in 10 minutes of compression for different inflation durations.

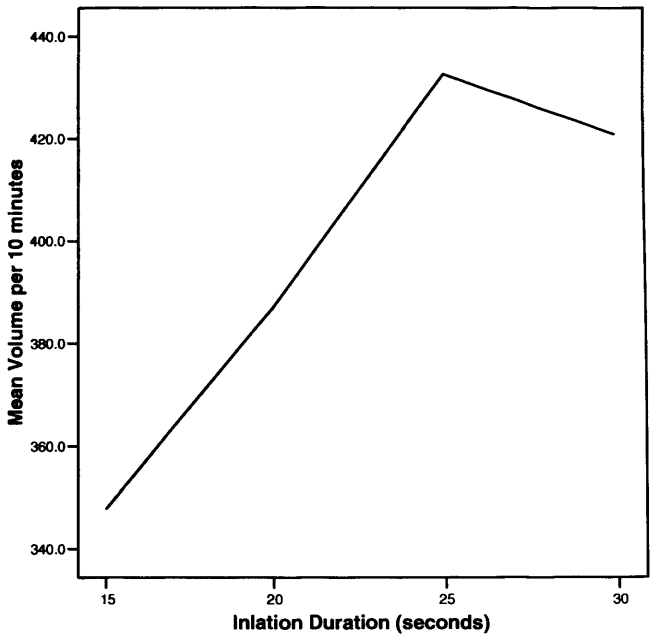


Figure 3.73 The approximate volume emptied during 10 minutes of compression for different inflation durations.

From graph 3.73 it can be seen that a compression period of 25 seconds produces the greatest reduction in venous blood volume over a 10 minute period. Therefore, it would seem that for thigh compression, the optimal inflation duration is of 25 seconds duration.

Finally, the effect of altering the deflation duration on distal venous blood flow was investigated. As with the study for whole leg compression, the deflation duration was varied between 15 and 60 seconds in increments of 5 seconds, whilst the pressure was maintained at 60mmHg and the inflation duration at 15 seconds.

The results obtained from investigations which examined the effect of altering the deflation duration of uniform thigh compression on distal venous blood flow, demonstrated a different trend to that which was observed with the Huntleigh DVT 30 cuff. Upon increasing the deflation duration of the Huntleigh DVT 30 cuff, an increase in the distal peak venous velocity and approximate venous volume was observed, however, whilst using uniform thigh compression, varying the duration of deflation did not have an effect on the distal venous response. Figures 3.74 – 3.76 demonstrate the results obtained.

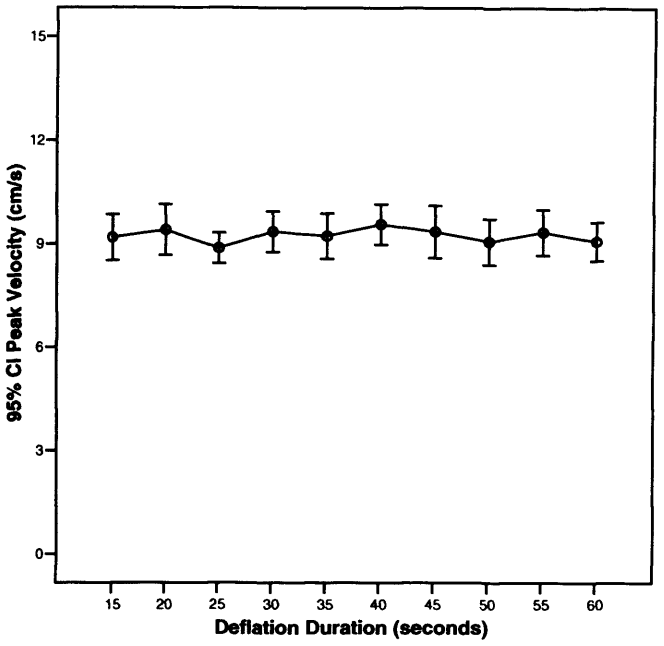


Figure 3.74 The mean peak venous blood flow velocity post compression for deflation durations in the range 15 to 60 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

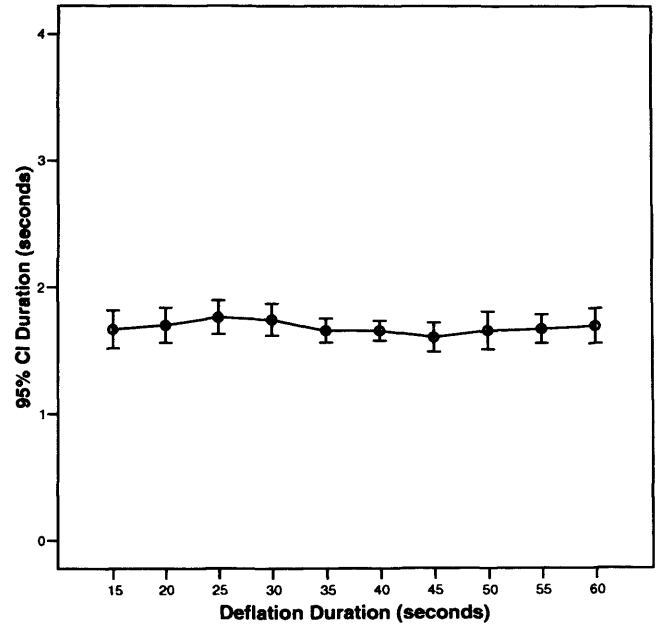


Figure 3.75 The mean duration of venous blood flow post compression for deflation durations in the range 15 to 60 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

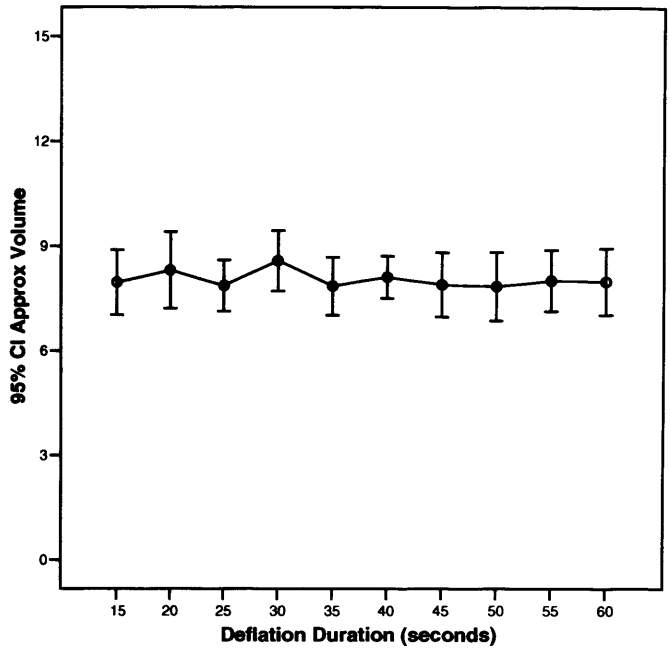


Figure 3.76 The approximate volume of venous blood flow post compression for deflation durations in the range 15 to 60 seconds, using the uniform thigh compression cuff. These results were obtained using the randomised method.

It appears that altering the deflation duration does not seem to impart an effect on the distal venous blood flow response following cuff deflation. This is supported by the one-way ANOVA, which demonstrated that there were no significant differences between deflation durations for peak velocity, p=0.928, duration of venous blood flow, p=0.837, and approximate volume, p=0.977.

Therefore, for uniform thigh compression, the optimal pressure and deflation duration would be consequent upon the results of the arterial study.

The effect of altering the deflation duration of an IPC regime appears to impart a different effect on the distal venous circulation dependant on whether uniform whole leg or uniform thigh compression is being used. Investigations of uniform thigh compression did not reveal any differences in the distal venous response achieved for the range of deflation periods implemented, whilst uniform whole leg compression demonstrated an increase in peak venous velocity following cuff deflation for increasing deflation durations. This could be related to the location of the compression cuff; the Huntleigh DVT 30 cuff being in closer proximity to the distal circulation than the thigh cuff.

Laser Doppler flowmetry was similarly implemented with the uniform thigh cuff to determine the effect of compression on distal tissue blood perfusion. Figure 3.77 displays the signal obtained.

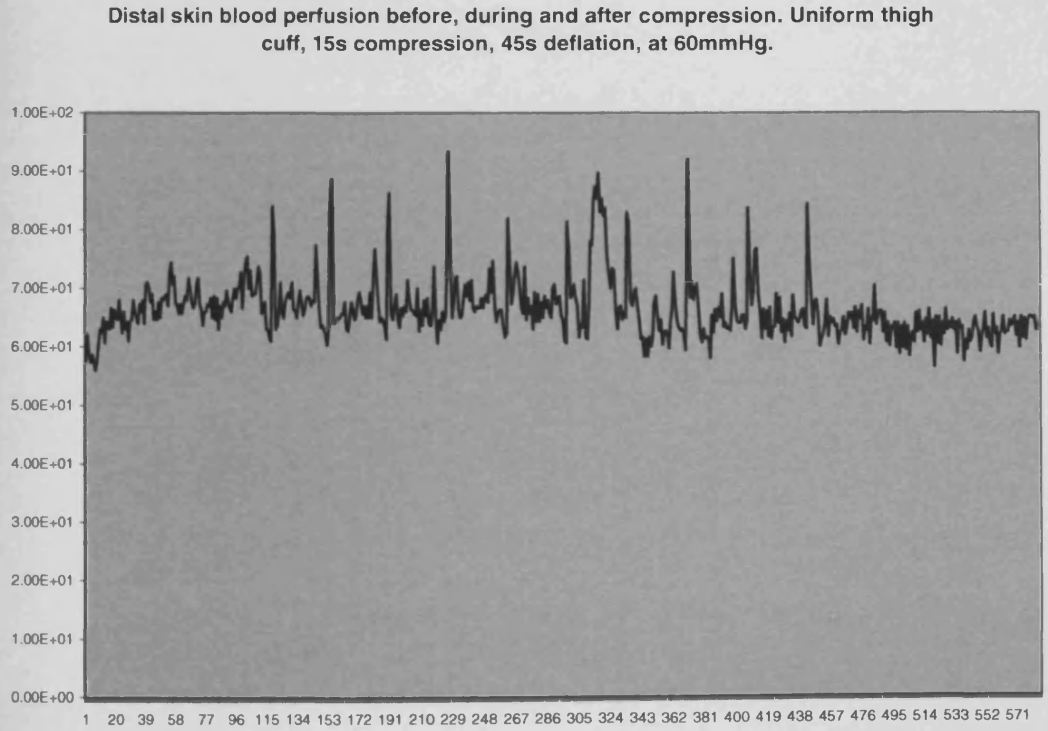


Figure 3.77 Distal skin blood perfusion in the foot of a healthy volunteer during compression with the uniform thigh compression cuff.

The graph above demonstrates that uniform thigh compression does increase blood perfusion in distal tissues; however, the magnitude of the increase is greater for uniform whole leg compression than for uniform thigh compression.

3.3.2.1 Summary of uniform thigh cuff findings

The investigations carried out have revealed that there is a distal haemodynamical response associated with the uniform thigh compression garment. In summary, the optimal uniform thigh compression cycle for enhancing both the distal arterial and venous blood flows would involve a pressure of 60mmHg, a compression period of 25 seconds and a deflation period of 45 seconds.

3.4 *Conclusions for Investigations with Uniform Compression Cuffs*

Investigations of the distal haemodynamical effects of uniform whole leg and uniform thigh compression have revealed that, in the first instance, there is a distal blood flow response to compression of the entire leg, and to compression of part of the leg; and in the second instance, that this distal haemodynamical response may be optimised by varying different aspects of the compression sequence.

The following six figures (figures 3.78 – 3.82) summarise and compare the results obtained for varying the compression duration for the two uniform compression garments.

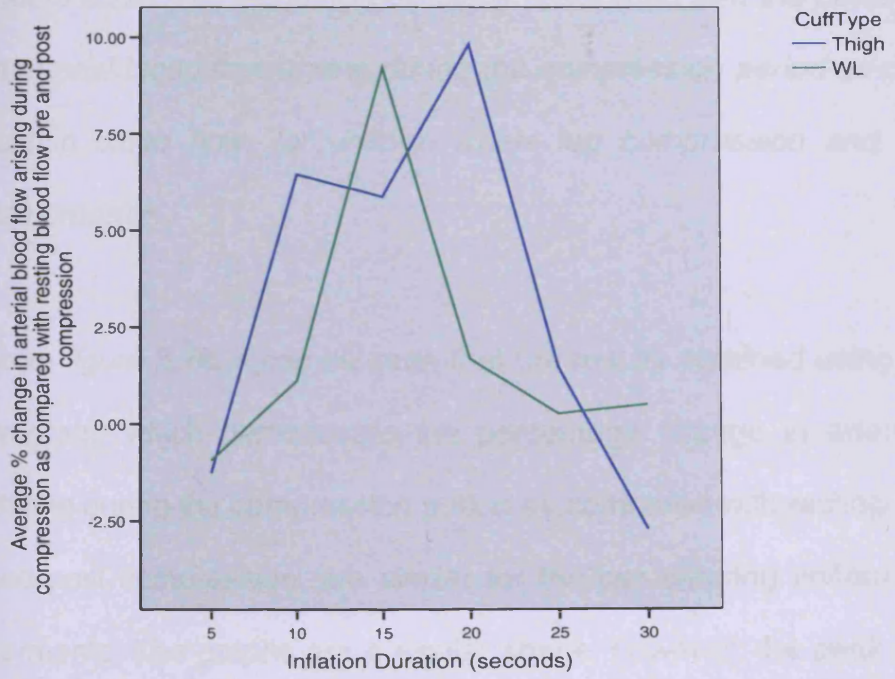


Figure 3.78 A comparison of the percentage change in arterial blood flow arising during compression as compared with resting blood flow pre and post the compression period for uniform whole leg compression and uniform thigh compression.

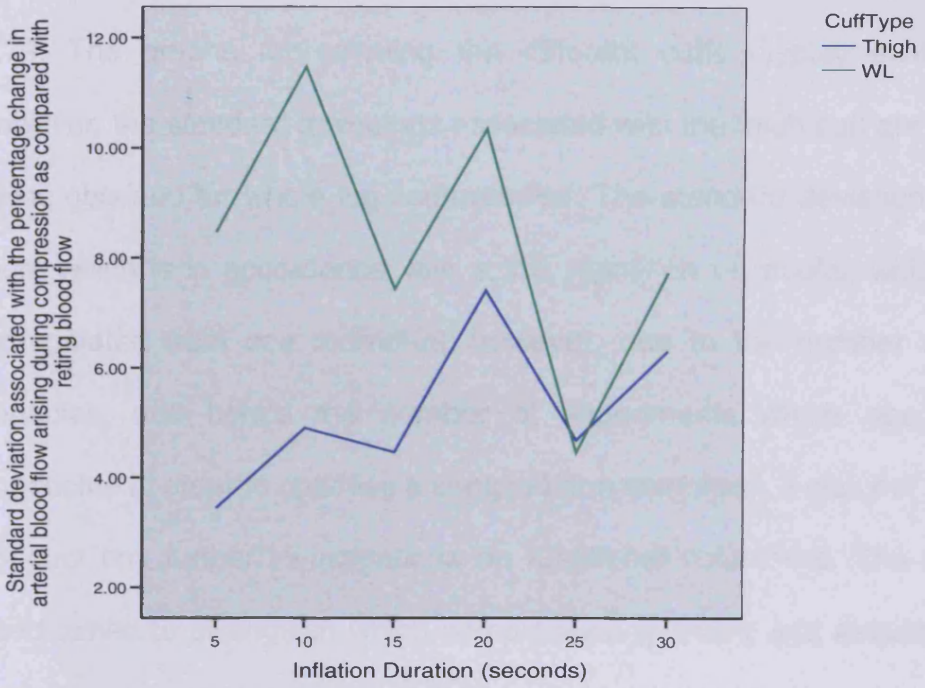


Figure 3.79 The standard deviations associated with the percentage change in arterial blood flow arising during the compression period as compared with resting blood flow, for uniform whole leg compression and uniform thigh compression.

From figure 3.78, it can be seen that the results obtained using the computer program, which demonstrate the percentage change in arterial blood flow arising during the compression period as compared with resting blood flow pre and post compression, are similar for the two differing uniform compression garments. The graphs are a similar shape; however, the peak in each graph corresponds to a different inflation duration; 15 seconds for whole leg compression, and 20 seconds for thigh compression. The physiology behind the arterial hyperaemia is unclear; however it appears to have been induced by changes arising in the venous circulation during compression.

The standard deviations of the computer program results are shown in figure 3.79. The graphs representing the different cuffs display similar trends; however, the standard deviations associated with the thigh cuff are lower than those obtained for whole leg compression. The standard deviations are quite high, which is in accordance with a low repetition of results, which were all extrapolated from one individual; however, due to the number of differing variables, and hence the number of experiments which needed to be conducted in order to optimise a compression technique, it was not possible to conduct any further investigations on additional volunteers. The techniques used aimed to distinguish which compression garment and sequence should be further investigated on a number of healthy individuals and patients with leg ulcers, in the most scientific / objective method possible. It is assumed that if the results had been repeated a greater number of times, these standard deviations would reduce.

Therefore, from figures 3.78 and 3.79, there does not appear to be a significant difference between the effect imparted on distal arterial blood flow by uniform whole leg compression and uniform thigh compression, except that a longer compression duration is required with the thigh cuff in order to produce a similar increase in arterial blood flow to that produced with a shorter duration of whole leg compression.

Figures 3.80 – 3.82 compare the results obtained from the venous studies for each of the uniform compression garments.

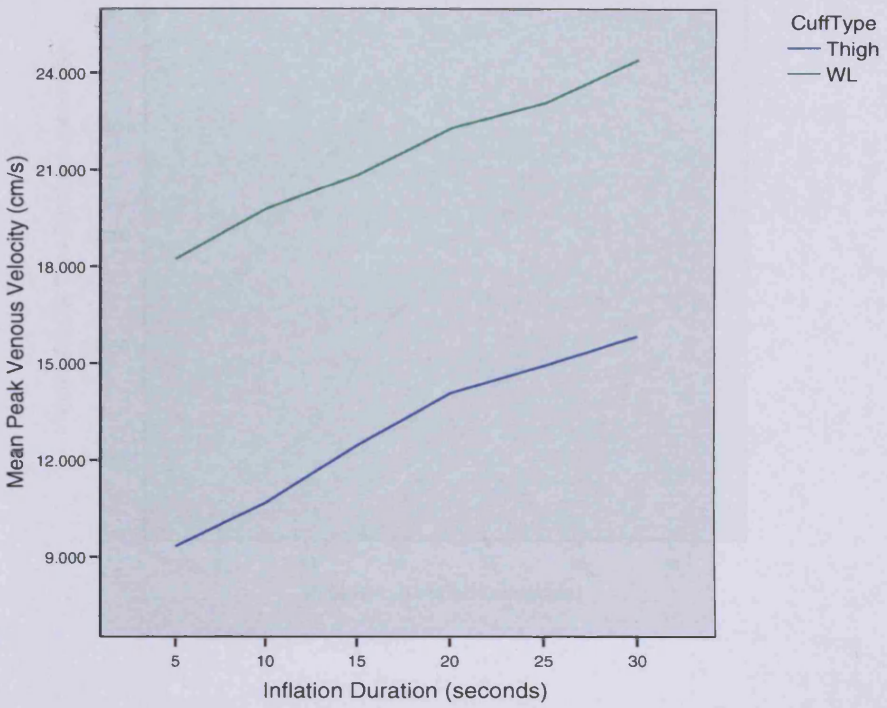


Figure 3.80 A comparison of the mean peak venous velocities obtained post compression associated with varying compression durations, for uniform whole leg and uniform thigh compression.

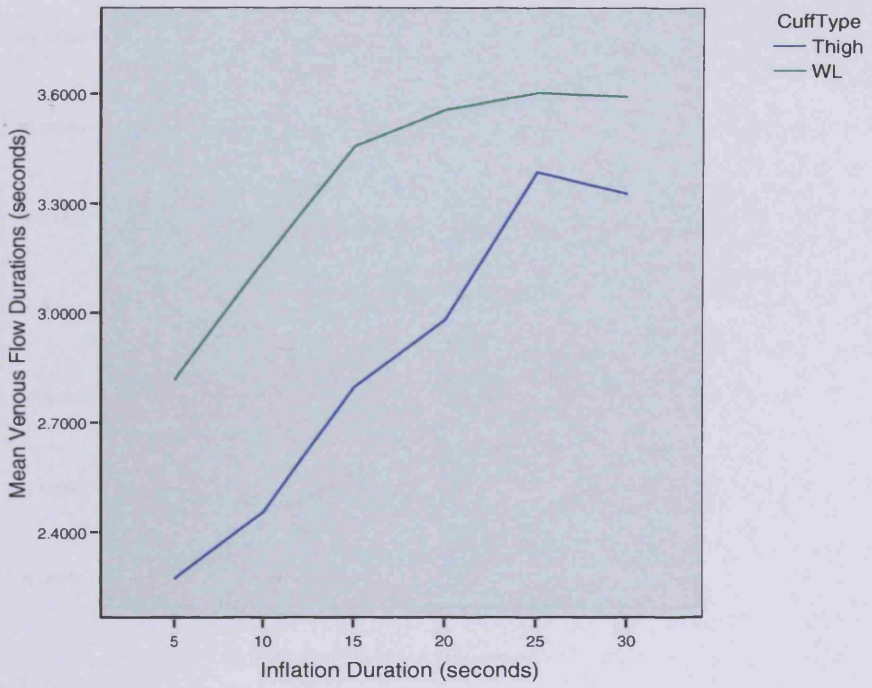


Figure 3.81 A comparison of the mean venous blood flow durations obtained post compression, associated with varying inflation durations, for uniform whole leg and uniform thigh compression.

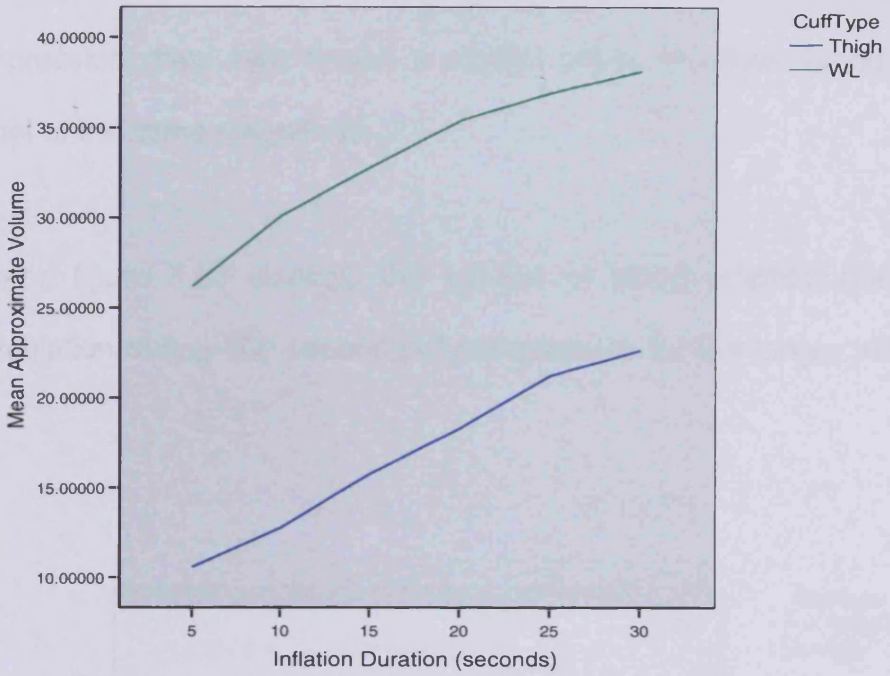


Figure 3.82 A comparison of the approximate venous volume post compression, associated with varying inflation durations, for uniform whole leg and uniform thigh compression.

It can be seen from figures 3.80 – 3.82 above that there is a very clear trend in the distal venous response to compression. As previously mentioned, the longer the compression duration the greater the peak velocity, duration and approximate volume of distal venous blood flow. The graphs above display the conformity of the results obtained for the different compression garments; thigh compression however produces much lower results to those obtained using whole leg compression. As demonstrated earlier in the chapter, blood is trapped distally in the foot during whole leg compression and in the foot and calf during thigh compression. Blood trapped in the foot will be at a much greater pressure than blood trapped in the foot and calf, producing higher

venous velocities and volumes when the trapped blood is released. However, thigh compression does also impart a similar effect on distal blood flow, although not of the same magnitude.

The following figure 3.83 displays the volume of blood emptied from the venous circulation during 600 seconds of compression for the longer inflation durations.

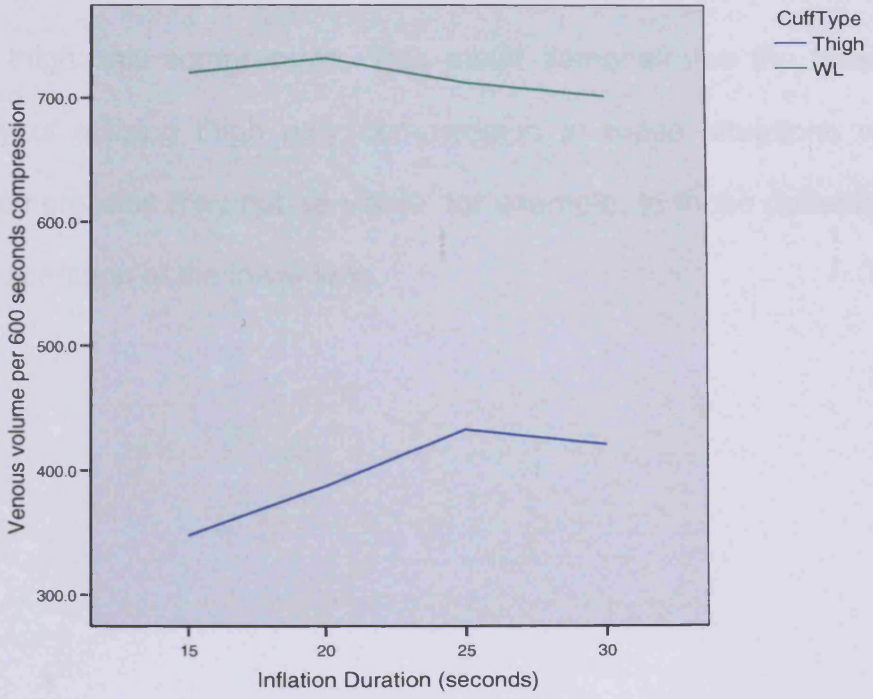


Figure 3.83 A comparison of the volume of venous blood emptied during 600 seconds of compression associated with varying inflation durations for uniform whole leg and uniform thigh compression.

Similarly, the volumes of venous blood emptied over a period of 600 seconds, are greater for whole leg compression than for thigh compression, and the

peak values correspond to differing compression durations; 20 seconds for whole leg compression, and 25 seconds for thigh compression. It can therefore be inferred from these results that the compression duration which produces the optimal venous emptying would also produce the optimal arterial supply.

By comparison of the results obtained using the different uniform compression garments, it can be seen that the underlying mechanisms which initiate changes in the distal circulation are the same, although activated to a lesser extent with thigh only compression. This result demonstrates the feasibility and efficacy of utilising thigh only compression in those situations where whole leg compression may not be viable, for example, in those patients with chronic leg ulceration of the lower limb.

Chapter 4: Preliminary Investigations: Multiple Chamber Compression

4.1 Introduction

In chapter 3, it was discovered that uniform compression of the whole leg and of the thigh imparted an effect on the distal circulation of a healthy volunteer; and optimal compression sequences were obtained for each of the garments. In this chapter, using results obtained from the previous chapter, investigations aim to discover whether multiple chamber compression similarly affects the distal blood flow of a healthy volunteer, and also to obtain the optimal operating sequence for each of the garments.

4.2 Methods

4.2.1 Variables

The investigations in this chapter implemented the 3 chamber whole leg compression cuff and the 3 chamber thigh compression cuff. In each of the garments, the widths of the individual chambers were approximately equal.

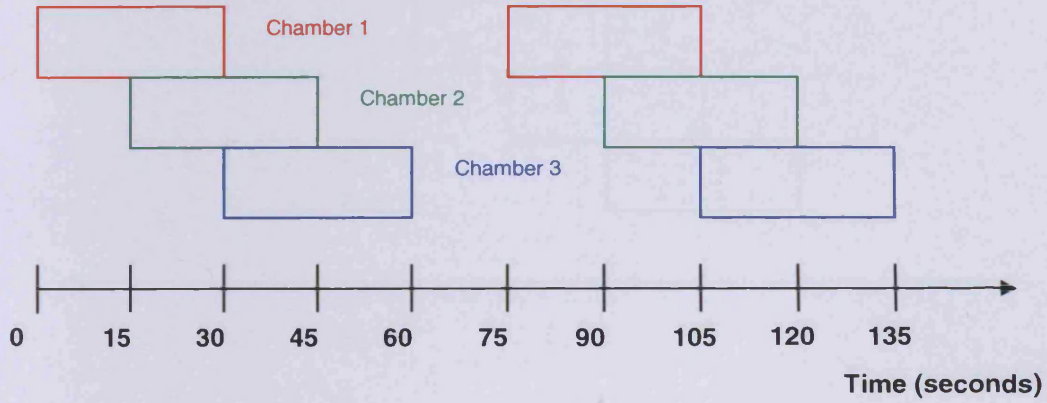
For the purpose of investigating the distal haemodynamical response of the multiple chamber garments, seven different cycles were constructed which covered all possible variations in the compression sequence. In each of the block diagrams, the red box represents the first chamber, which is the most distal of the three chambers; the green box represents the middle chamber, and the blue box represents the most proximal chamber. The seven cycles are as follows.

Cycle 1

Pressure: 60mmHg,

Sequence: 30s compression, 45s deflation in each chamber, staggered by 15s,

Single cycle time: 75s.

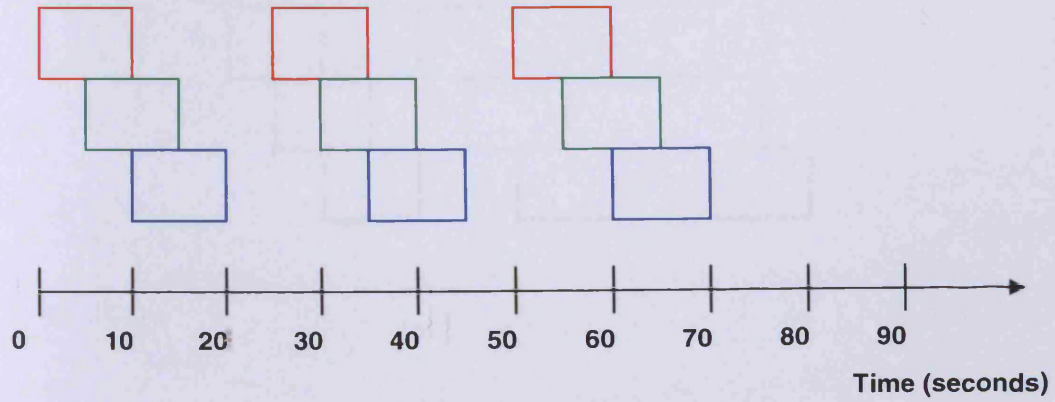


Cycle 2

Pressure: 60mmHg,

Sequence: 10s compression, 15s deflation in each chamber, staggered by 5s.

Single cycle time: 25s.

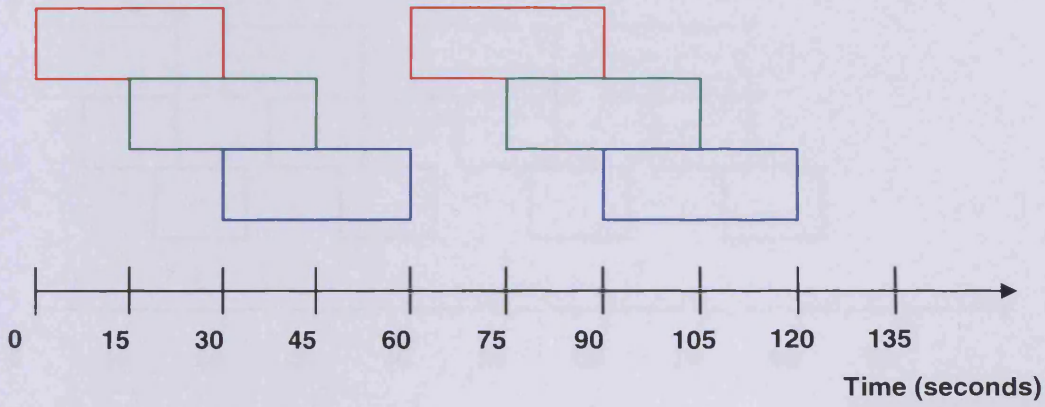


Cycle 3

Pressure: 60mmHg,

Sequence: 30s compression, 30s deflation in each chamber, staggered by 15s.

Single cycle time: 60s.

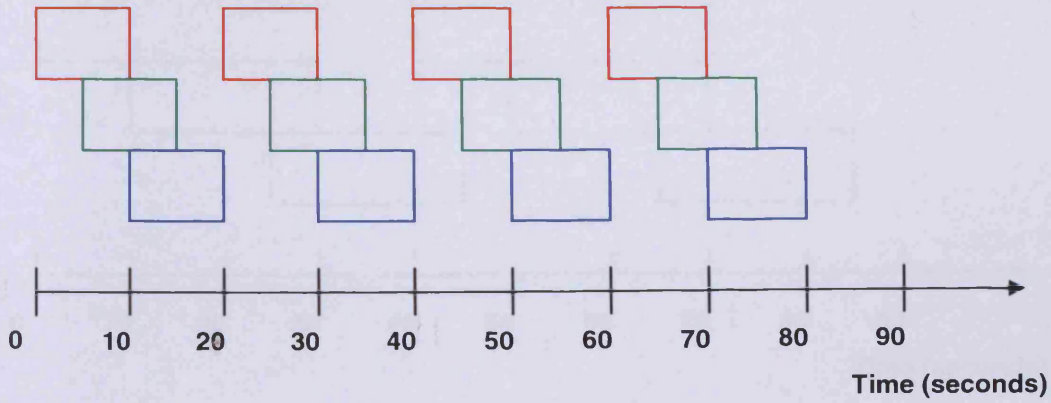


Cycle 4

Pressure: 60mmHg,

Sequence: 10s compression, 10s deflation in each chamber, staggered by 5s.

Single cycle time: 20s.



Cycle 5

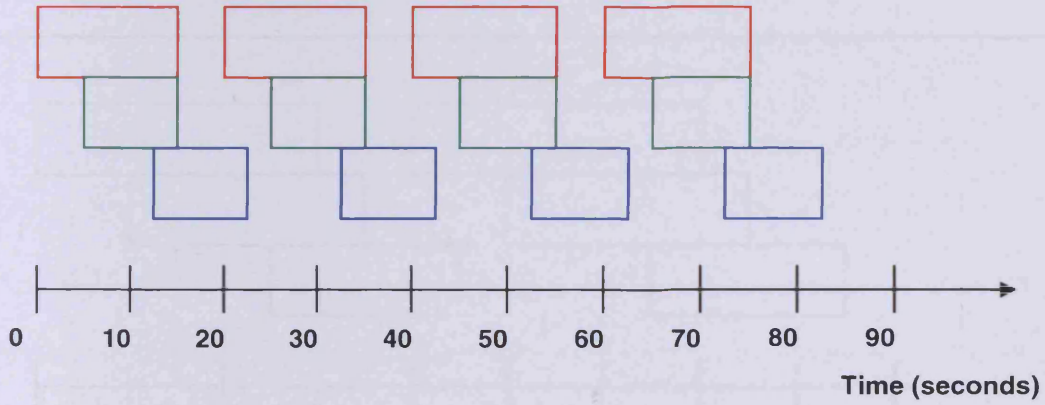
Pressure: 60mmHg,

Sequence: Chamber 1: 15s compression, 5s deflation,

Chamber 2 & 3: 10s compression, 10s deflation,

Chamber 2 starts at 5s, chamber 3 starts at 12s.

Single cycle time: 20s.



Cycle 6

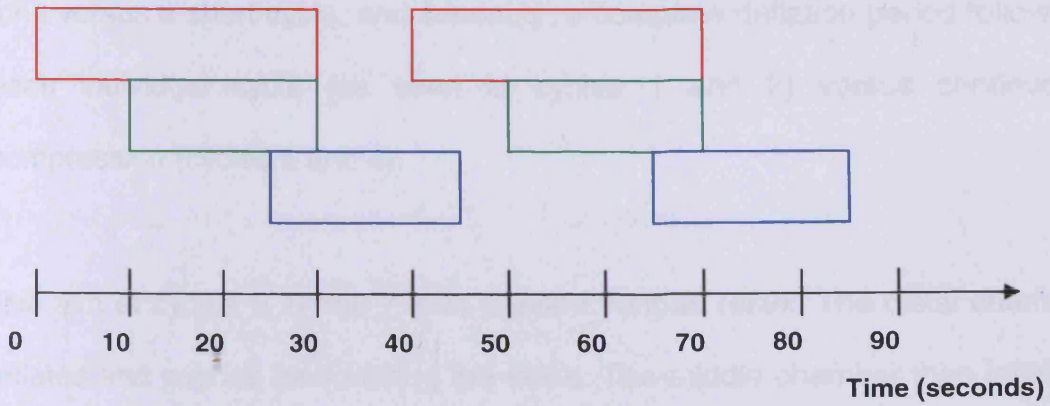
Pressure: 60mmHg,

Sequence: Chamber 1: 30s compression, 10s deflation,

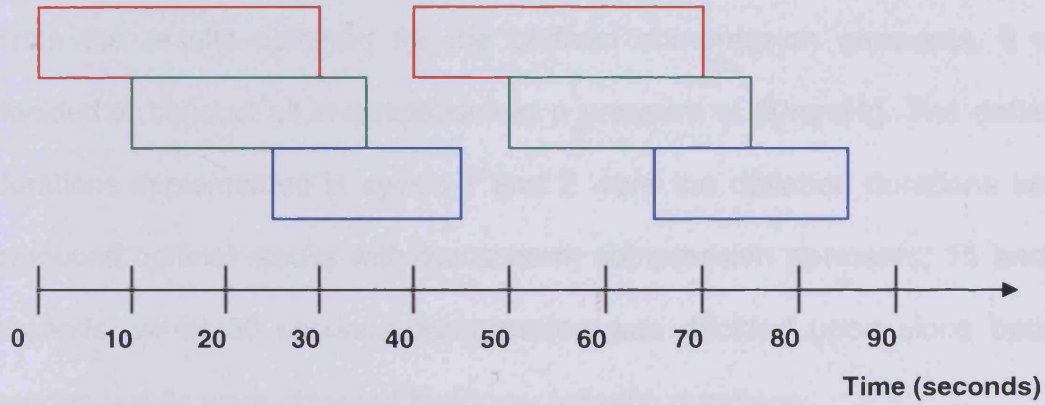
Chamber 2 & 3: 20s compression, 20s deflation,

Chamber 2 starts at 10s, chamber 3 starts at 25s.

Single cycle time: 40s.



Cycle 7	
Pressure:	60mmHg,
Sequence:	Chamber 1: 30s compression, 10s deflation,
	Chamber 2: 25s compression, 15s deflation,
	Chamber 3: 20s compression, 20s deflation,
	Chamber 2 starts at 10s, chamber 3 starts at 25s.
Single cycle time:	40s.



Cycles 1 and 2 involve a similar configuration; however, cycle 2 is a shorter duration version of cycle 1. The same is true of cycles 3 and 4. Cycles 1, 2, 3 and 4 were decided upon in order to compare a variety of factors; firstly, a long versus a short cycle; and secondly, a complete deflation period following each individual cycle (as seen in cycles 1 and 2) versus continuous compression (cycles 3 and 4).

The aim of cycles 5, 6 and 7 is to prevent venous reflux. The distal chamber inflates and pushes blood along the veins. The middle chamber then inflates, pushing blood further along the venous circulation. The proximal chamber

inflates before the first and second chambers deflate, therefore when the distal chambers simultaneously deflate, the inflated proximal chamber prevents reverse venous flow. The distal chamber then re-inflates before the proximal chamber deflates. This cycle is proposed to be beneficial in those patients with incompetent venous valves. Cycle 5 is a shorter duration version of cycle 6, whilst cycle 7 is similar to 6; although the first and second chambers deflate independently.

From the results obtained for the uniform compression garments, it was decided to conduct all investigations at a pressure of 60mmHg. The deflation durations implemented in cycles 1 and 2 were the deflation durations which produced optimal results with the uniform compression garments; 15 and 45 seconds, whilst 30 seconds compression was decided upon since optimal venous results were obtained for longer inflation durations.

4.2.2 Data Acquisition

The methods of data collection were similar to those implemented for the uniform compression cuffs, as described in chapter 3.2.2.

However, it was not possible to obtain a single pump which was capable of sequentially inflating the three chambers in each cuff; therefore three Flowpac pumps were used, where each chamber was connected to an individual Flowpac pump. This required each pump to be started at a different time, dependant upon the timings of the cycle.

4.2.3 Data Analysis

The arterial studies were repeated three times. The results were then analysed as described in chapter 3.2.3.

The venous results were repeated three times, providing 20 data values for each cycle investigated. The results were similarly analysed as detailed in chapter 3.2.3.

PPG signals were collected for each cycle. At least three signals of varying lengths (between 600 and 1800 seconds) were collected per cycle, however it was not possible to average the signals together, due to differences in the start time, and duration of each signal. The PPG results were used to determine whether the compression sequence of the multiple chamber garments had an effect on distal microcirculatory blood volume.

4.3 Results and Discussion

4.3.1 Three Chamber Whole Leg Cuff

Sequential compression is routinely implemented for enhancing venous return. The compression 'wave' which progresses up the limb accelerates venous blood back towards the heart. The first objective of the studies with the three chamber whole leg cuff was to determine whether or not sequential compression impinged on a distal arterial hyperaemia. However, results indicated that sequential compression produced both a distal venous and a distal arterial blood flow response.

The following figures demonstrate the distal arterial response to three chamber whole leg compression for each of the seven differing cycles. The time averaged maximum (TAM) blood flow velocity was recorded every 5 seconds, as with previous studies, for a test which comprised 180 seconds without compression, ten cycles of compression, and a further 180 seconds without compression. In figures 4.1 – 4.7, the coloured vertical lines represent the start of compression for each of the three chambers; red for chamber 1, green for chamber 2 and blue for chamber 3. The grey line indicates the end of ten cycles of compression.

Three sets of data were collected for each cycle, which were normalised and averaged together and plotted in the following graphs.

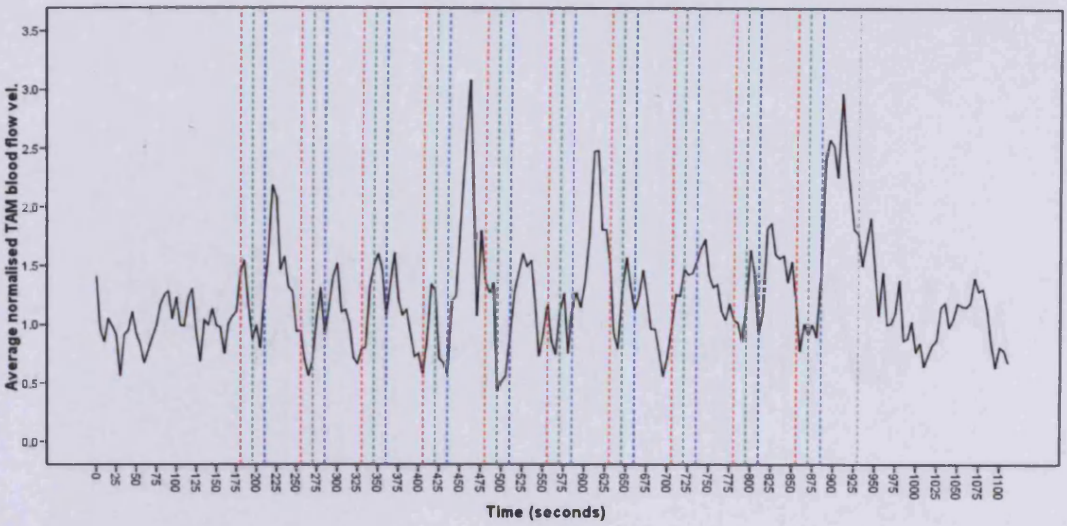


Figure 4.1 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 1 (30 s compression, 45 s deflation in each chamber, staggered by 15 s).

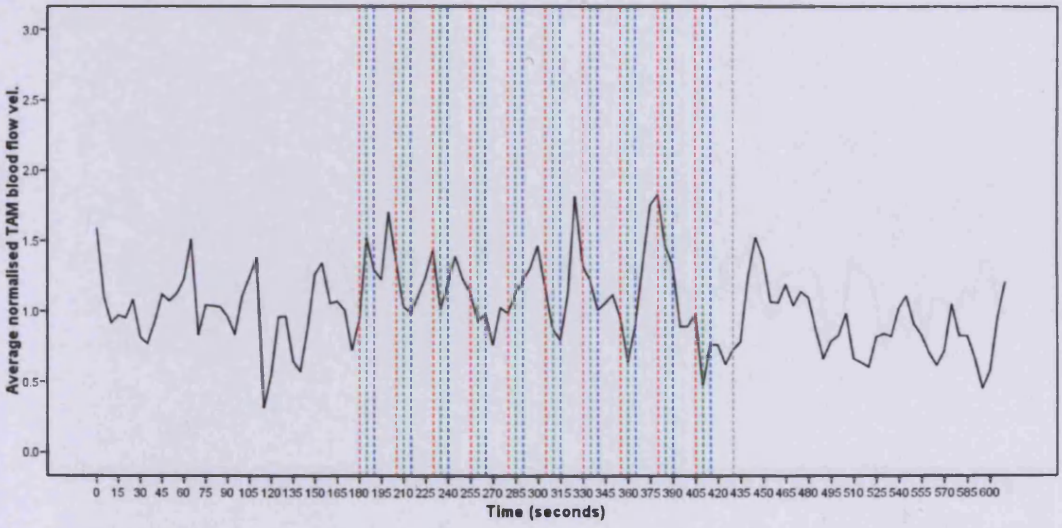


Figure 4.2 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 2 (10 s compression, 15 s deflation in each chamber, staggered by 5 s).

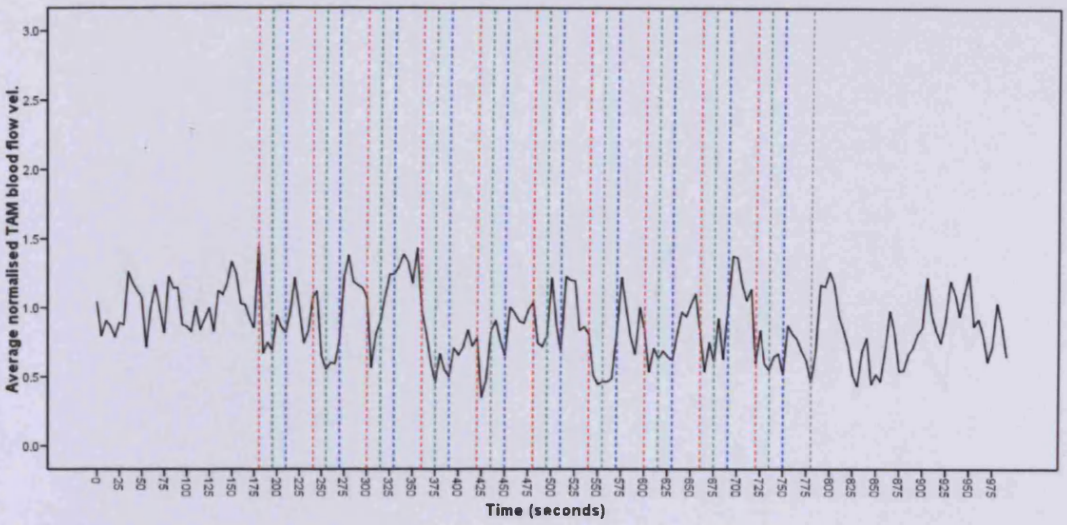


Figure 4.3 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 3 (30 s compression, 30 s deflation in each chamber, staggered by 15 s).

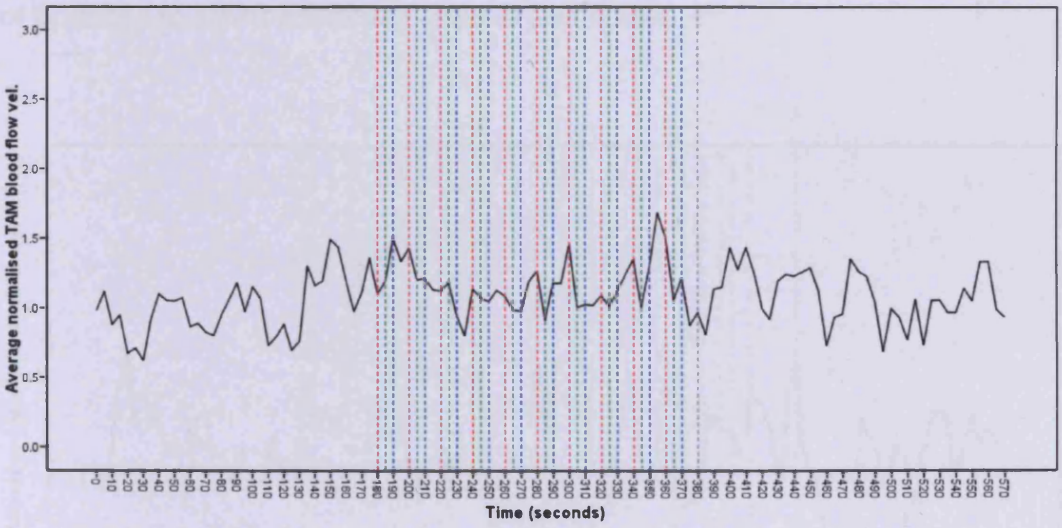


Figure 4.4 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 4, (10 s compression, 10 s deflation in each chamber, staggered by 5 s).

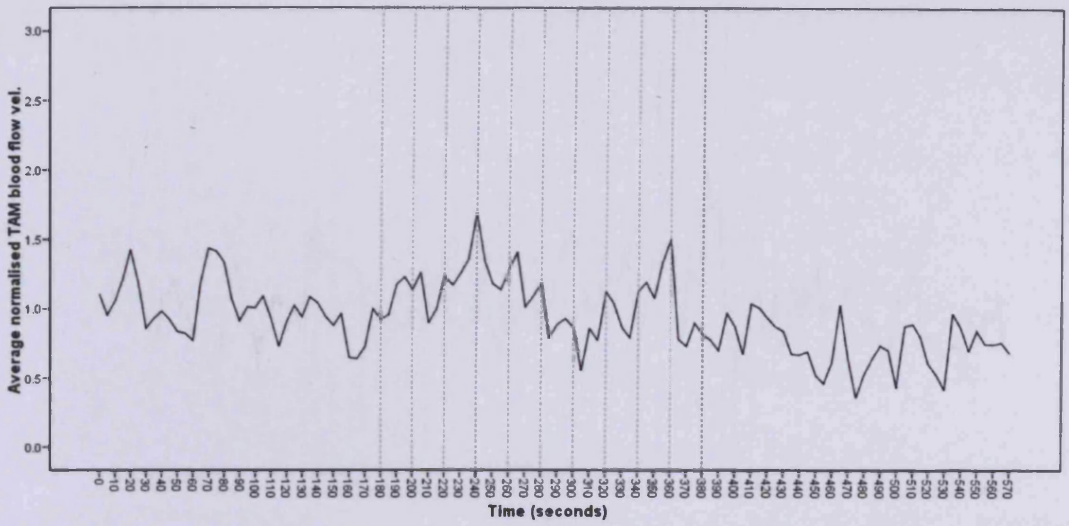


Figure 4.5 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 5, (15 s compression, 5 s deflation in chamber 1; and 10 s compression, 10 s deflation in chamber 2 and 3). The grey lines represent the start of each compression cycle. It was not possible to insert additional lines in this figure.

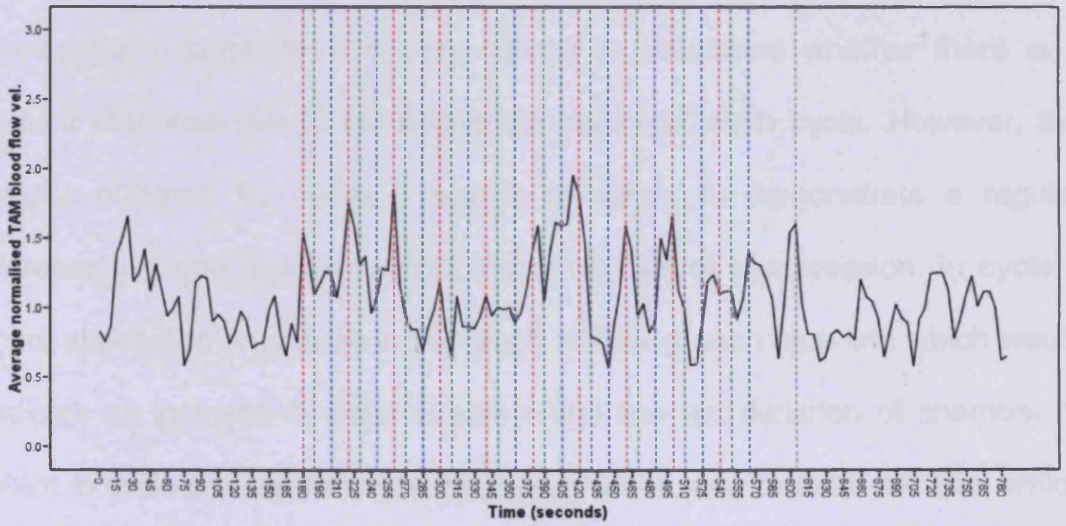


Figure 4.6 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 6, (30 s compression, 10 s deflation in chamber 1; and 20 s compression, 20 s deflation in chambers 2 and 3).

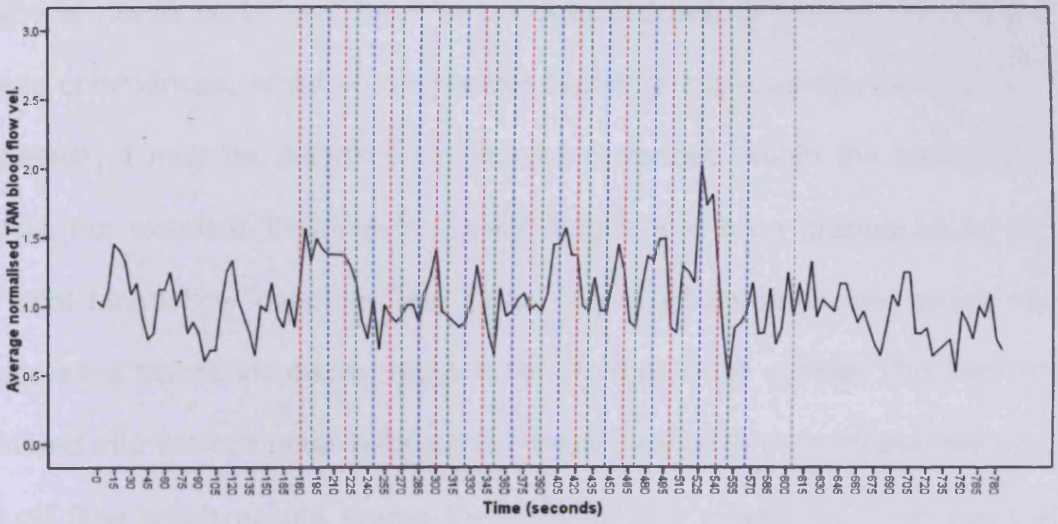


Figure 4.7 The distal arterial blood flow response obtained whilst using the three chamber whole leg compression cuff for cycle 7, (30 s compression, 10 s deflation in chamber 1; 25 s compression, 15 s deflation in chamber 2; and 20 s compression, 20 s deflation in chamber 3).

These graphs are more complicated than those obtained for the uniform compression garments. It is very difficult to determine whether there is a regular response due to the sequential nature of each cycle. However, the graphs obtained for cycles 1 and 6 do seem to demonstrate a regular increase in blood flow throughout the ten cycles of compression. In cycle 1 there appears to be a peak in the graph following each blue line which would indicate an increase in distal arterial blood flow on deflation of chamber 1; whilst in cycle 6 there seems to be a peak on or near to each red line, which would correspond to an increase in blood flow following the simultaneous deflation of chambers 1 and 2. Cycles 1 and 6 are long cycles in comparison with cycles 2, 4 and 5. The length of the cycle could determine whether or not a response is demonstrated in the graphs. A long cycle would enable a

hyperaemia to occur and for it to be detected before another compression cycle commences; whilst in the shorter cycles, a hyperaemia may still occur, however, it may be detected at different instances within the compression cycle. For example, in figure 4.5, there appears to be a gradual increase in arterial blood flow over the first three cycles of compression, which then decreases before increasing again over the last three cycles. The data was entered into the computer program for determining the percentage change in blood flow which occurs during the compression period as compared with resting flow pre and post compression; and hence an objective comparison of the differing sequential cycles was obtained. The results, along with their associated standard deviations are displayed in table 4.1.

Cycle	**1**	**2**	**3**	**4**	**5**	**6**	**7**
% change in blood flow	*23.10*	*19.66*	*-5.09*	*9.33*	*22.53*	*17.72*	*15.77*
% standard deviation (2 d.p)	*21.61*	*14.81*	*2.20*	*6.44*	*26.59*	*7.49*	*14.23*

Table 4.1 The percentage change in blood flow arising during compression with the three chamber whole leg cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for the seven different cycles; and the associated standard deviations.

The lowest percentage change in arterial blood flow occurs for cycles 3 and 4, which do not have a total deflation period. This could imply that for a hyperaemia to occur, a period of no compression is required; this would accord with previous studies of proximal effects (Morris and Woodcock 2002).

The results obtained for the percentage change in blood flow do appear to agree with the graphs (figures 4.1 – 4.7). The graphs obtained for cycles 3 and 4 do not seem to demonstrate any variation in distal arterial blood flow during the compression period from the resting periods, which would concur with the results obtained from the computer program. The greatest arterial response was obtained for cycle 1, which again corresponds with the noticeable increases in blood flow displayed in the graph. Cycle 5 however, produces an unexpectedly high increase in arterial blood flow during compression, which is comparable to that which was obtained with cycle 1. Cycle 5 is a very rapid cycle; each rotation is only of 20 seconds duration, however, as previously described, a gradual increase in arterial blood flow is apparent over the first three and last three cycles of compression, which would explain the high percentage increase in arterial blood flow during the compression period.

The standard deviations associated with these percentage changes vary considerably between the different cycles. The low standard deviations for cycles 3, 4 and 6 would imply that their results are fairly reliable; however, the standard deviations associated with cycles 1 and 5 are very high, which would indicate that there is a considerable range in the data values. Further repetitions of the tests would aim to reduce the degree of error and therefore the standard deviation associated with the results; however, due to the number of variables being investigated and consequently the number of studies, along with a limited timescale, this was not possible, and therefore the most scientific conclusions were to be drawn from the results obtained.

It would seem therefore that the optimal sequential cycles for improving distal arterial blood flow with the 3-chamber whole leg garment are cycles 1, 2 and 5. The results of the venous studies in conjunction with the results of the arterial studies should clarify whether one of these cycles is more favourable than the others.

The seven different cycles were investigated for their effects on the distal venous circulation. The peak velocity, duration and approximate volume were recorded following each chamber deflation. For cycles 1, 2 3, 4 and 7 this implied recording measurements three times per cycle; whilst cycles 5 and 6 only incurred 2 deflations, since the distal and middle chambers deflated simultaneously. However, it was found that not all deflations incurred a result. Cycles 1, 2, 3 and 4 only produced a result for the deflation of the most distal and middle chambers. The proximal chamber could be too far away to impart any considerable effect on the distal vasculature which is capable of being detected by Doppler ultrasound. Similarly, for cycles, 5, 6 and 7 there was no distal venous response detected when the proximal chamber deflated. In this case however; the first chamber has re-inflated before the proximal chamber has deflated, therefore hindering a distal venous response when the proximal chamber does deflate.

The number of results produced per individual cycle varied between the different sequences, therefore, in order to compare the results obtained from differing cycles, the results were added together for the different chamber

deflations, before mean values were calculated in SPSS. This enabled direct comparison of the results obtained for a single repetition of each cycle.

The following graphs (figures 4.8 – 4.10) demonstrate the results obtained for the mean peak velocity, mean duration and mean approximate volume of distal venous blood flow for each of the seven different cycles.

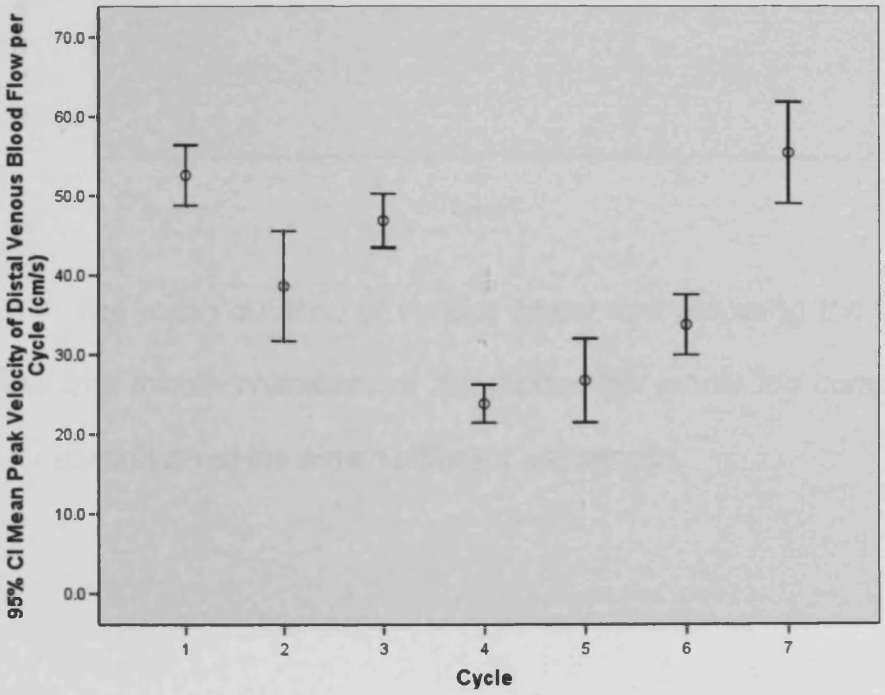


Figure 4.8 The mean peak venous blood flow velocity following the deflation of the distal and middle chambers of the 3-chamber whole leg compression garment for each cycle of the seven different sequences.

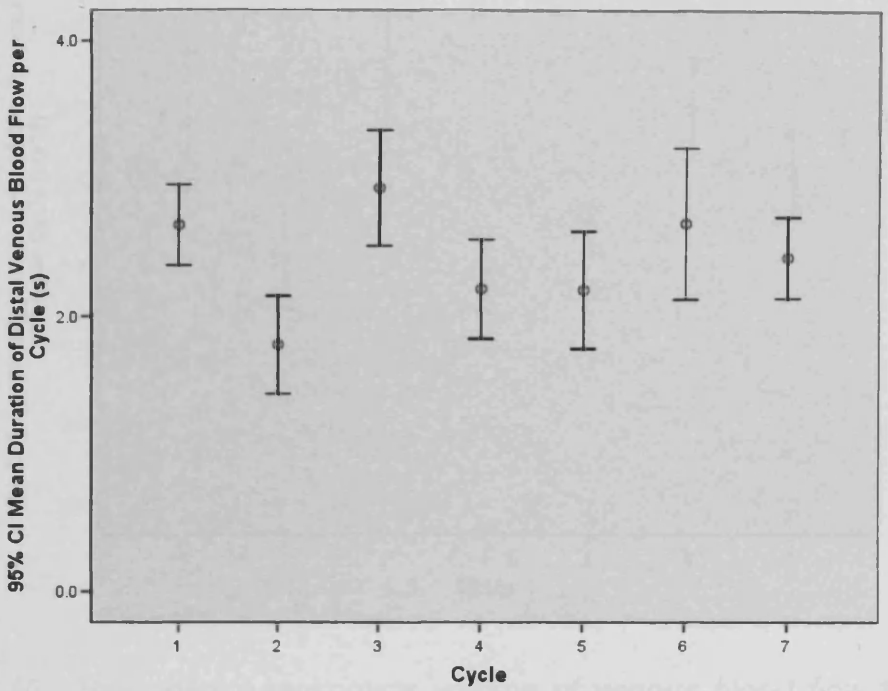


Figure 4.9 The mean duration of venous blood flow following the deflation of the distal and middle chambers of the 3-chamber whole leg compression garment for each cycle of the seven different sequences.

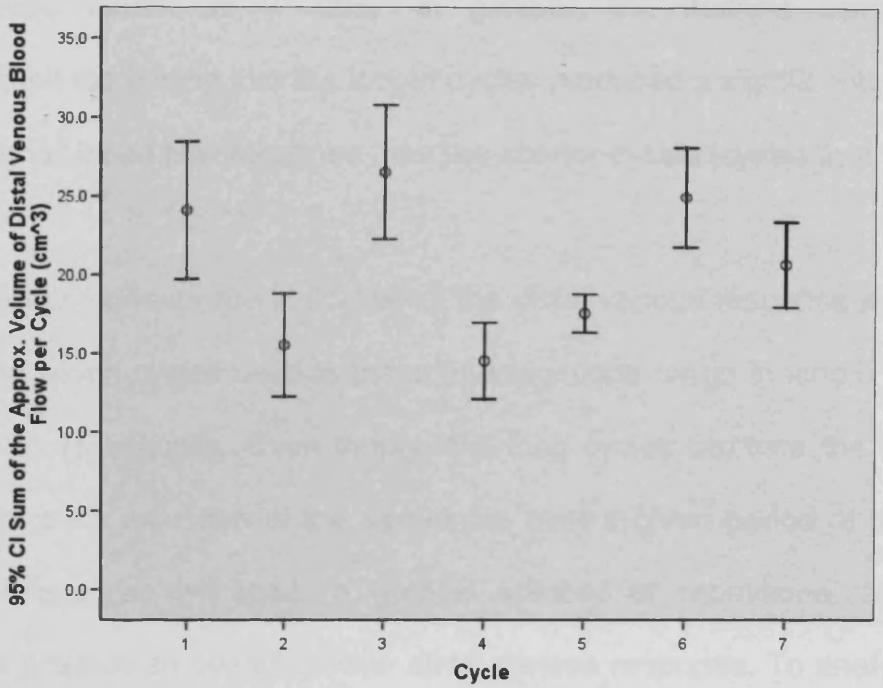


Figure 4.10 The mean, approximate volume of venous blood flow following the deflation of the distal and middle chambers of the 3-chamber whole leg compression garment for each cycle of the seven different sequences.

Figures 4.8 – 4.10 demonstrate the results obtained per individual cycle. As can be seen from these graphs, the longer cycles (cycles 1, 3, 6 and 7) produce the greatest distal venous response per cycle. This is a reasonable result to acquire. The longer the compression period, the greater the volume of blood which is trapped distally in the foot and therefore the greater the peak velocity, duration and volume of venous blood which is accelerated along the venous circulation back towards the heart on deflation of each chamber of the compression cuff.

The one way ANOVA confirmed the presence of significant differences between the cycles for peak velocity ($p < .005$), duration ($p=.001$), and

approximate volume ($p < .005$). In general, the multiple comparisons corroborated the finding that the longer cycles produced a significantly greater distal venous blood flow response than the shorter cycles (cycles 2, 4 and 5).

These results however are indicative of the distal venous response *per cycle,* where the seven cycles used in these investigations range in length from 20 seconds to 75 seconds. Even though the long cycles produce the greatest results for each repetition of the sequence, over a given period of time, the shorter sequences will incur a greater number of repetitions, and may therefore produce an overall greater distal venous response. To analyse this, the volume of venous blood emptied from the distal vasculature over 600 seconds compression was determined for each cycle. The results are demonstrated in table 4.2, and figure 4.11.

Cycle	**Approx. volume per 600 seconds compression (cm^3, 3s.f.)**
1	*582*
2	*915*
3	*639*
4	*820*
5	*1756*
6	*1353*
7	*1139*

Table 4.2 The approximate volume of venous blood emptied with the 3-chamber whole leg compression cuff during 600 seconds of compression for each of the seven different cycles.

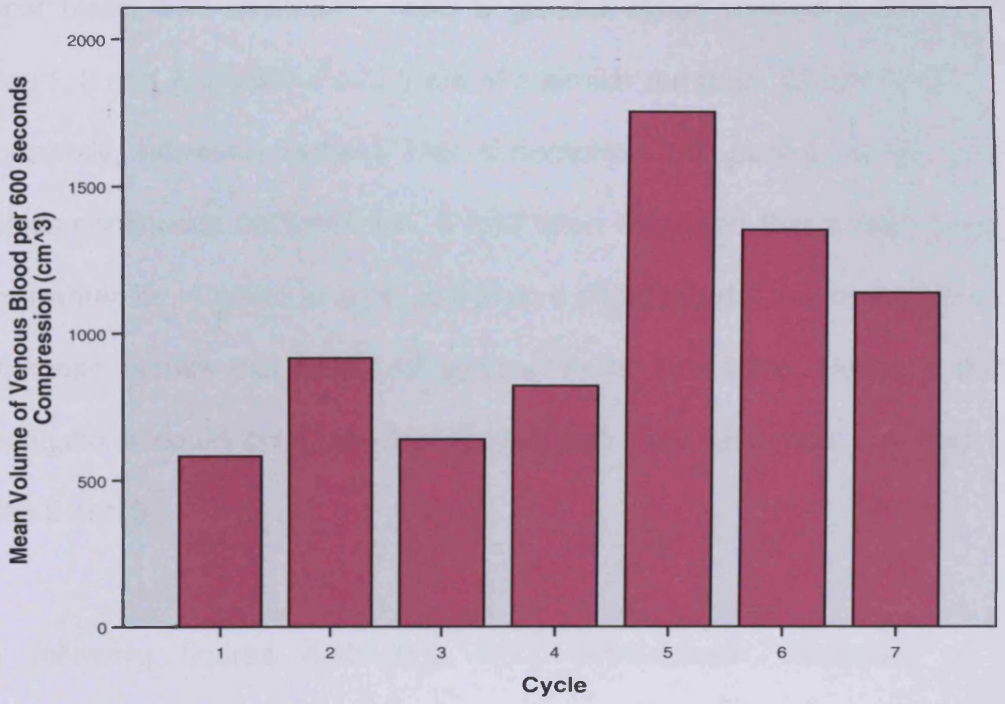


Figure 4.11 The mean volume of distal venous blood emptied with the 3-chamber whole leg compression cuff during 600 seconds of compression for each of the seven different cycles.

This graph displays a completely different result to that which was obtained per cycle. Over a period of 600 seconds, the shorter cycle 5 produces the greatest distal venous emptying. This result is in agreement with the results obtained from the distal arterial studies, where cycle 5 produced an increase in arterial blood flow during compression of 22.53% as compared with the resting period's pre and post compression. It is also to be expected that the cycle which produces the greatest arterial supply should also as a consequence produce the greatest venous drainage. Cycle 2 produces an interesting result between the two studies, generating an increase in distal

arterial blood flow of 19.66%, and a greater distal venous response than cycles 1, 3 and 4. Cycles 2 and 5 are of a similar duration, 25 and 20 seconds respectively, however, cycle 2 has a complete 'off' period, whilst cycle 5 involves continuous compression. It had been expected that a total deflation period would be required in order to obtain a distal arterial response; however, from these results this does not appear to be the case. Perhaps further investigations could compare the distal blood flow response obtained with cycles 2 and 5.

The following figures 4.12 and 4.13 demonstrate examples of the photoplethysmography (PPG) signals obtained for cycles 2 and 5. The cycle 2 signal is of 1200 seconds duration, whilst the cycle 5 signal is of 900 seconds duration. The difference in the length of the signal is attributed to the timing of the Flowpac pumps losing their synchronicity. This proved to be a problem when a long test was being undertaken. The Flowpacs would be started at their correct timings, and within a few minutes, the pumps would have lost their co-ordination. This was also more of a problem with the shorter cycles, and especially with cycle 5, which required the simultaneous deflation of two of the chambers.

PPG sensors were placed on the sole of the foot, and also above the medial malleolus. In the following graphs, the pink line represents the signal obtained from the sole of the foot, and the blue line from the ankle.

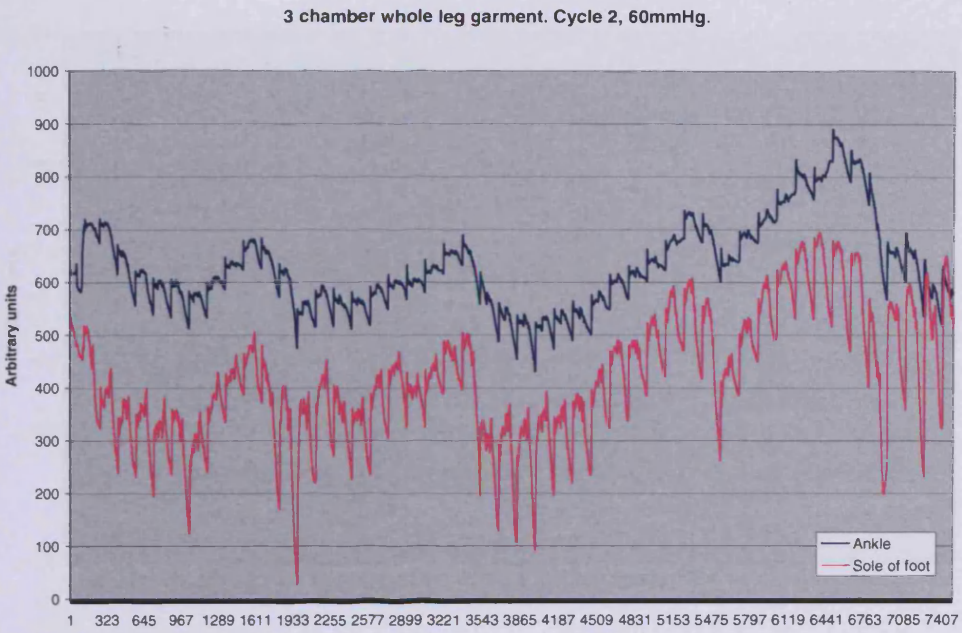


Figure 4.12 The photoplethysmography signal obtained from the sole of the foot and the ankle, whilst using the 3-chamber whole leg compression cuff with cycle 2.

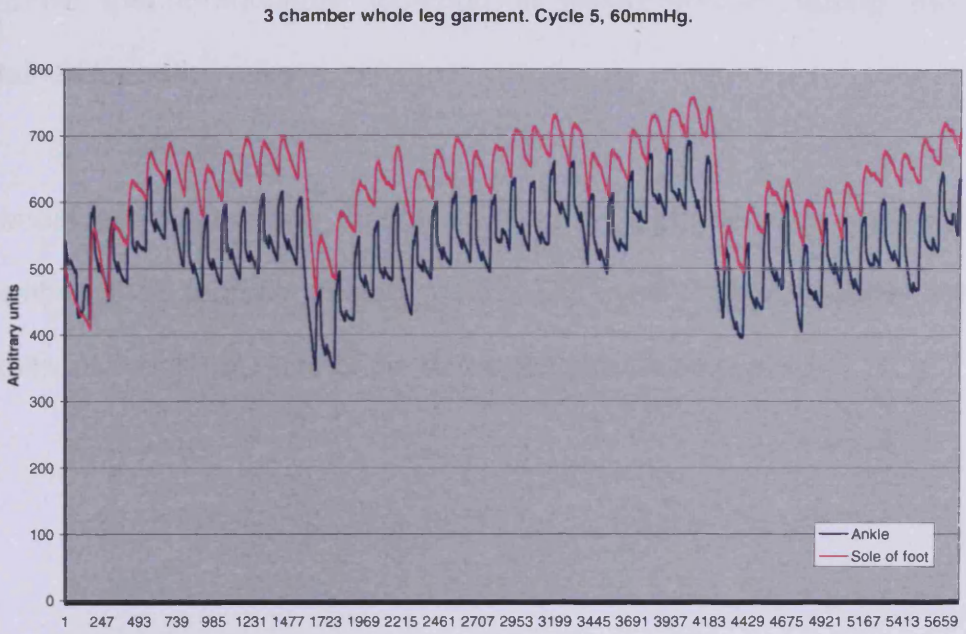


Figure 4.13 The photoplethysmography signal obtained from the sole of the foot and the ankle, whilst using the 3-chamber whole leg compression cuff with cycle 5.

In both figures 4.12 and 4.13, there appears to be a generally increasing trend to the signals, which implies that the microcirculatory blood volume is decreasing. In the graphs obtained from the PPG studies, an increase in the signal represents a decrease in blood volume, whilst a decrease in the signal is indicative of an increase in blood volume. Therefore, a decrease in the venous microcirculatory blood volume indicates that compression is promoting the return of venous blood to the heart.

In conjunction with the variation in blood volume per cycle, and the general trend for the blood volume to be gradually decreasing, there could also be a

rhythmic thermoregulatory variation in blood volume during the signals obtained for both cycles.

It would seem therefore, that cycle 5 is the optimal sequence with the 3-chamber whole leg compression cuff, whilst cycle 2 also produces favourable results, although not quite of the same magnitude as cycle 5.

4.3.2 Three Chamber Thigh Cuff

The same seven cycles were investigated using the 3-chamber thigh garment; however, prior to the commencement of the tests, the effects of the sizes of the chambers in the thigh garment were investigated using photoplethysmography and Doppler ultrasound. It was queried whether the distal and proximal chambers could be narrower than the central chamber, which would consequently allow the central chamber to be considerably wider. The theory behind this configuration was that the distal and proximal chambers were acting as valves, preventing venous reflux, and that the larger central chamber was accelerating the venous blood back towards the heart. However, when the effectiveness of the narrow chambers was examined, they were demonstrated to be too narrow to produce any variation in the distal microcirculatory blood flow, although on examination of proximal venous blood flow, a response was detected for both the narrow and the larger chambers. The proximal venous response however, was greater for the wider chamber than for the narrower chambers. It was decided that three equal sized chambers should be used, whereby the proximal and distal chambers would still prevent venous reflux, whilst all three chambers would contribute to enhancing venous return.

The seven graphs below (figures 4.14 – 4.20) demonstrate the distal arterial blood flow response to compression using the 3-chamber thigh garment for each of the seven different compression sequences.

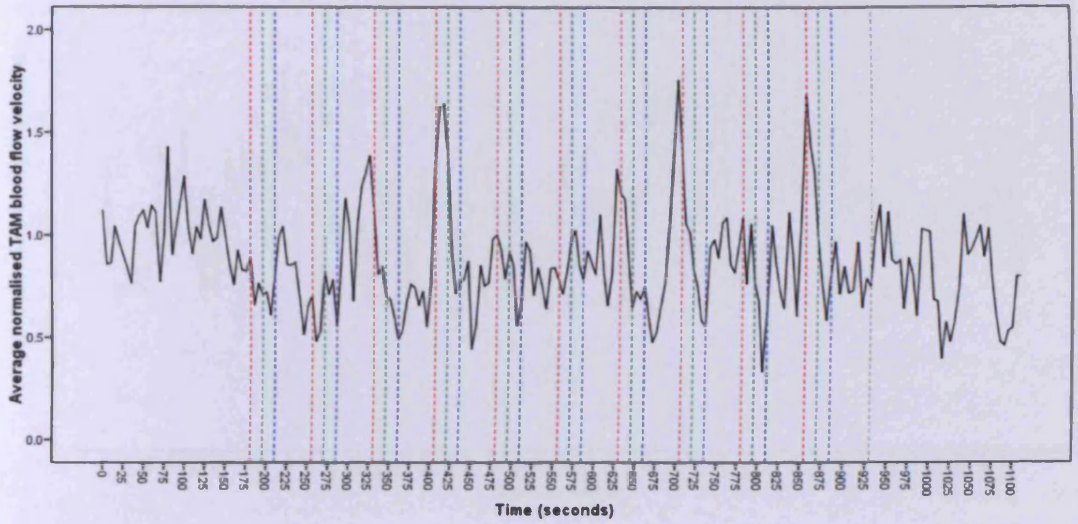


Figure 4.14 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 1 (30 s compression, 45 s deflation in each chamber, staggered by 15 s).

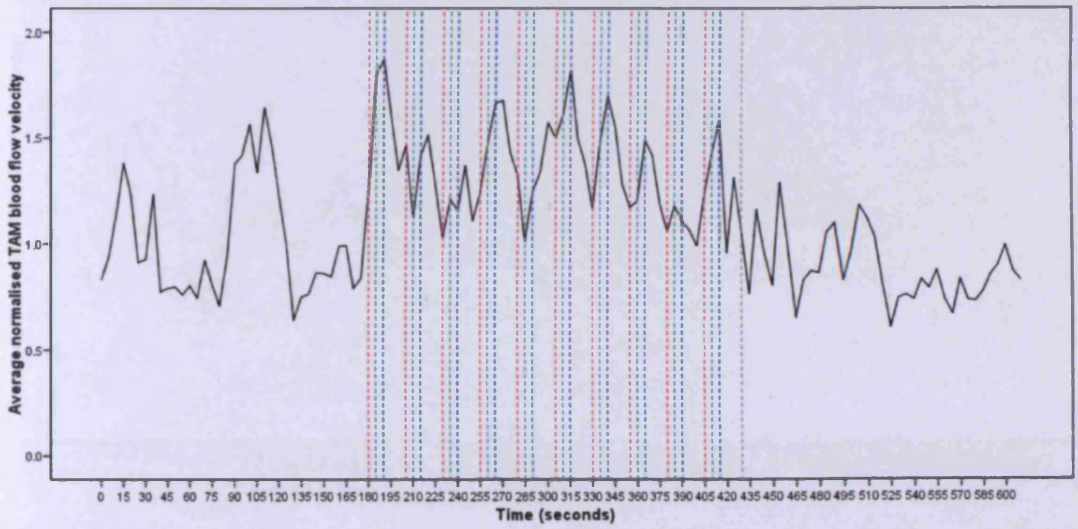


Figure 4.15 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 2 (10 s compression, 15 s deflation in each chamber, staggered by 5 s).

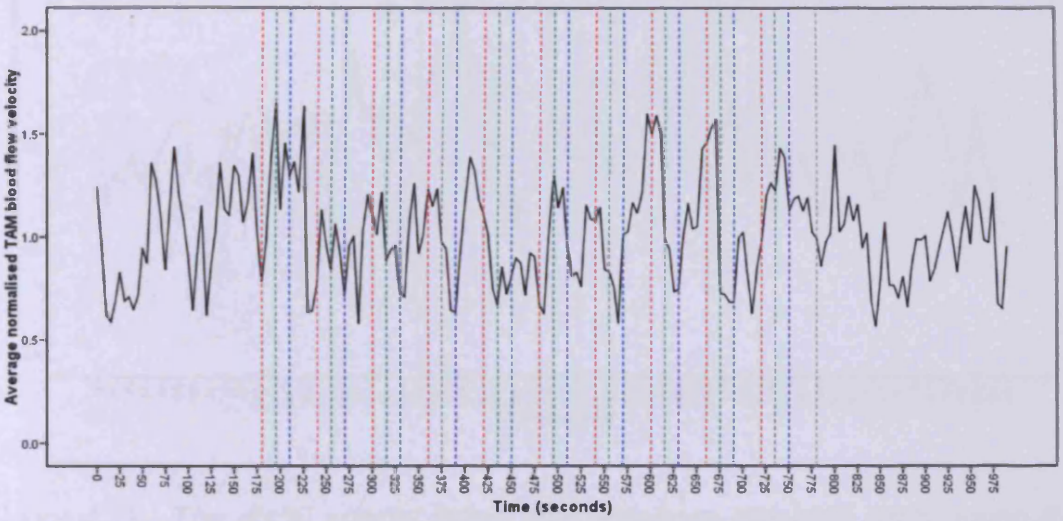


Figure 4.16 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 3 (30 s compression, 30 s deflation in each chamber, staggered by 15 s).

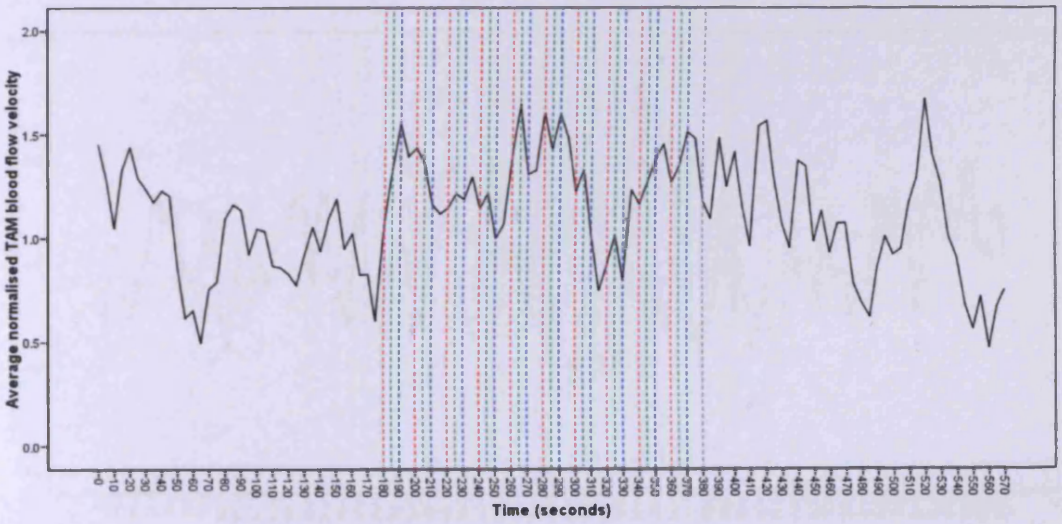


Figure 4.17 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 4 (10 s compression, 10 s deflation in each chamber, staggered by 5 s).

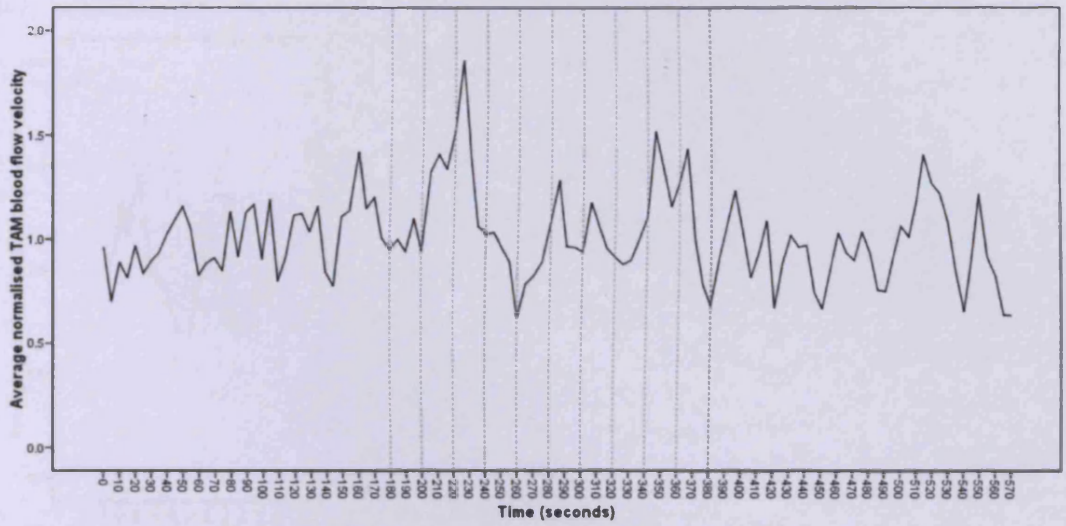


Figure 4.18 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 5 (15 s compression, 5 s deflation in chamber 1; and 10 s compression, 10 s deflation in chambers 2 and 3). In this graph, the grey lines represent the start of each compression cycle. It was not possible to insert additional lines in this figure.

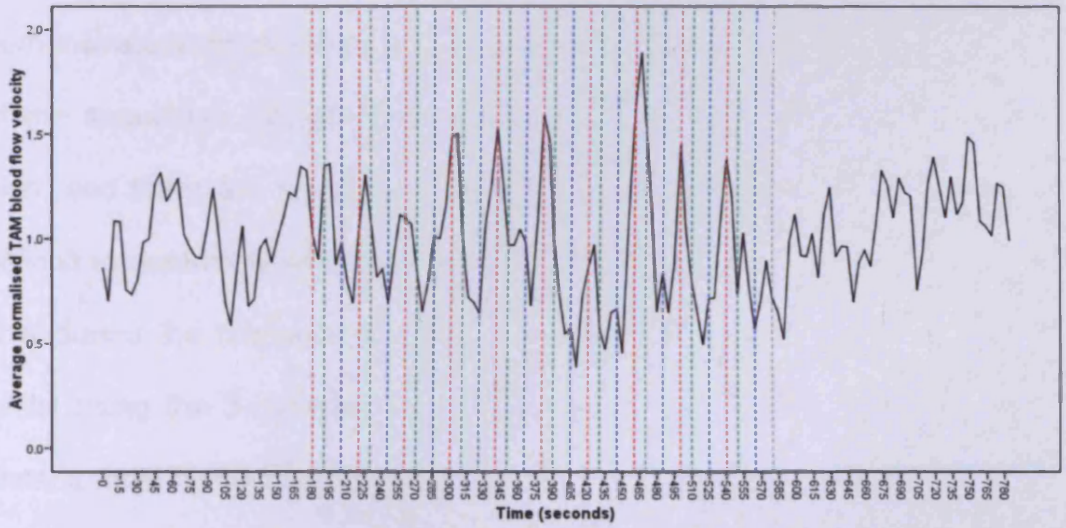


Figure 4.19 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 6, (30 s compression, 10 s deflation in chamber 1; and 20 s compression, 20 s deflation in chambers 2 and 3).

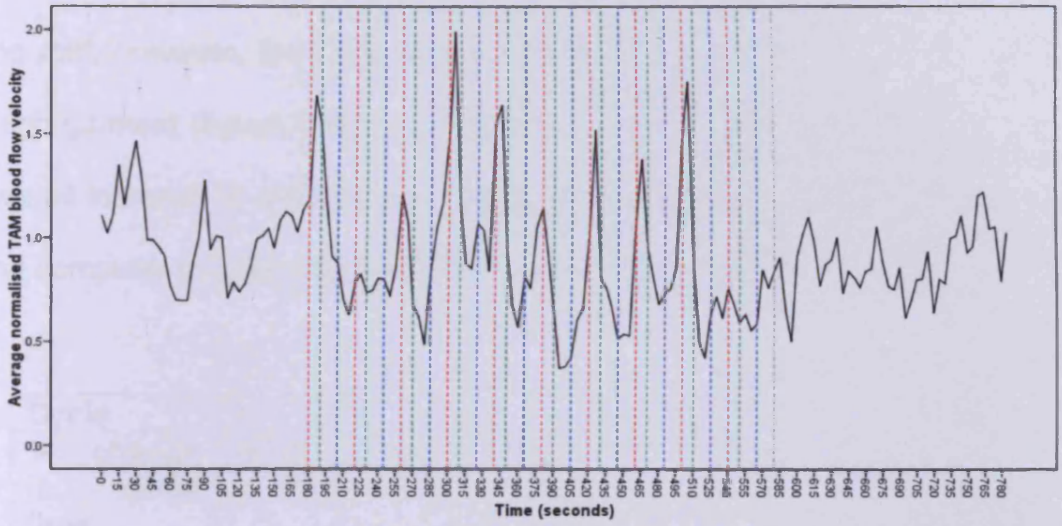


Figure 4.20 The distal arterial blood flow response obtained whilst using the three chamber thigh compression cuff for cycle 7, (30 s compression, 10 s deflation in chamber 1; 25 s compression, 15 s deflation in chamber 2; and 20 s compression, 20 s deflation in chamber 3).

Figure 4.19, which represents the results obtained for cycle 6, appears to demonstrate a regular increase in distal arterial blood flow for each repetition of the sequence. Nevertheless, since the baseline appears to be relatively high, and there are some large troughs during the compression period, it is difficult to determine whether or not cycle 6 produces a net increase in blood flow during the compression period. The remainder of the graphs obtained whilst using the 3-chamber thigh compression cuff demonstrate an irregular distal arterial blood flow response; there are hyperaemias observed during the compression periods, however, they do not occur regularly within the cycle. Figure 4.15 displays an interesting result whereby the distal arterial blood flow response is characterised by a gradual increase and decrease throughout the duration of the compression period, which indicates a large net increase in

arterial blood flow. Cycle 5 produced optimal results with the 3-chamber whole leg cuff, however, from the graph obtained for cycle 5 with the 3-chamber thigh garment (figure 4.18), it is difficult to say for certain whether there is an overall increase in distal arterial blood flow or not. The results obtained from the computer program aim to clarify the findings displayed in the graphs.

Cycle	**1**	**2**	**3**	**4**	**5**	**6**	**7**
% change in blood flow	*-5.71*	*37.02*	*7.87*	*23.90*	*10.64*	*-10.20*	*-8.63*
% standard deviation (2 d.p)	*13.72*	*77.19*	*6.30*	*12.38*	*8.64*	*4.22*	*7.96*

Table 4.3 The percentage change in blood flow arising during compression with the three chamber thigh cuff, as compared with a baseline extrapolated from the resting periods pre and post compression for the seven different cycles; and the associated standard deviations.

The first point worth noticing is that three out of the four longer cycles produce a negative percentage change in distal arterial blood flow. Cycles 1, 6 and 7 therefore all produced a decrease in distal arterial blood flow during the compression period as compared with resting blood flow. This is in complete contrast to the results obtained with the 3-chamber whole leg cuff, where these three cycles all produced relatively high increases in distal arterial blood flow of 23.10%, 17.72% and 15.77% respectively. This could be associated with the 'amount' of limb receiving compression. The difference in the results between the two cuffs could be as a direct consequence of whether or not the calf is being compressed.

Cycle 2 produces the greatest increase in distal arterial blood flow of 37.02%, confirming the results demonstrated in the graph, figure 4.15. However; the standard deviation associated with this result is very high at 77.19%. This raises the possibility of the result being an anomaly; however, since cycle 2 also produced a relatively high result with the 3 chamber whole leg cuff, it is possible that cycle 2 did produce an increase in distal arterial blood flow, but, an unusually high result could have been obtained for one data set as compared with the other two data sets, resulting in a large standard deviation. As previously mentioned, further repetitions of the tests would aim to clarify whether the result obtained is a true indication of the distal blood flow response; however, due to time constraints this was not possible. Cycle 5 has also produced a net increase in distal arterial blood flow during compression, however, the result is approximately half the result obtained for whole leg compression. This is a plausible result to have obtained since less of the leg is receiving compression with thigh only compression as compared with whole leg compression.

Therefore, it would seem that cycle 2 produces the optimal results with the 3-chamber thigh cuff, which also produced good results with the 3-chamber whole leg garment; whilst cycle 5, which was optimal with the 3-chamber whole leg cuff, produced a good result with the 3-chamber thigh cuff. Dependant upon the findings of the venous studies, this result could imply that further investigations should be carried out to compare the two different cycles for one of the multiple chamber garments, or the use of the two multiple chamber cuffs with one of the cycles.

The venous studies examined the effect of the seven different cycles on the peak velocity, duration and approximate volume of distal venous blood flow, with the 3-chamber thigh cuff. As with the 3-chamber whole leg garment, not all of the chamber deflations produced a result. In contrast to the 3-chamber whole leg cuff, the 3-chamber thigh cuff produced a result for all three chambers with cycles 1 and 3, for the middle and proximal chamber for cycle 2, and for the middle chamber only with cycle 4, whilst the other cycles remained the same. A result was recorded for each chamber with the longer cycles 1 and 3, possibly due to the closer proximity of the chambers in the thigh cuff, as compared with the whole leg garment; however, the discrepancies with cycles 2 and 4 could be associated with the rapidity of these two cycles, in addition to the size of the chambers. The results obtained from the different chamber deflations have been summed for each cycle, and plotted in the following graphs.

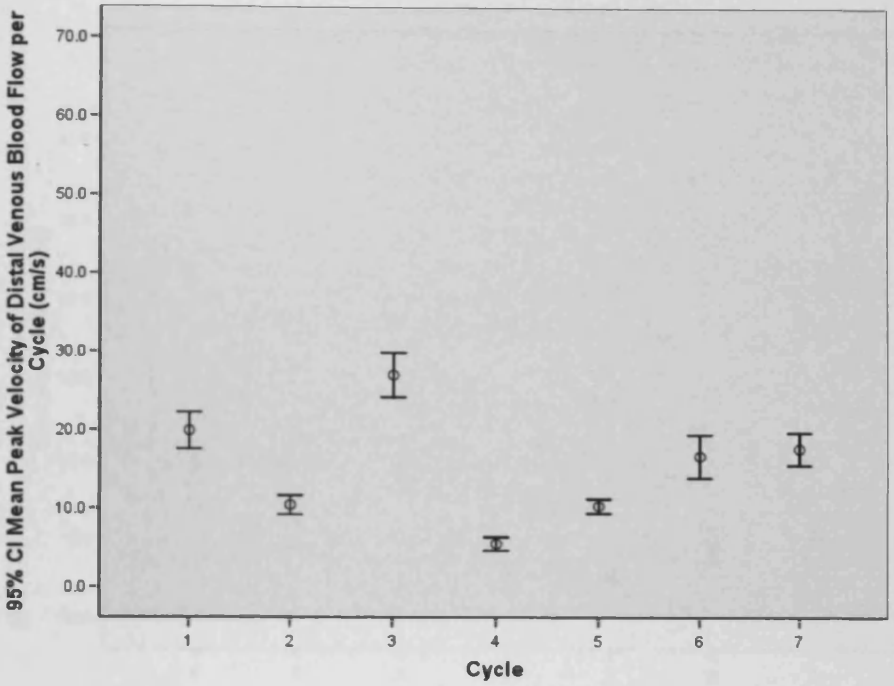


Figure 4.21 The mean peak venous blood flow velocity following the deflation of the chambers in the 3-chamber thigh compression garment for each cycle of the seven different sequences.

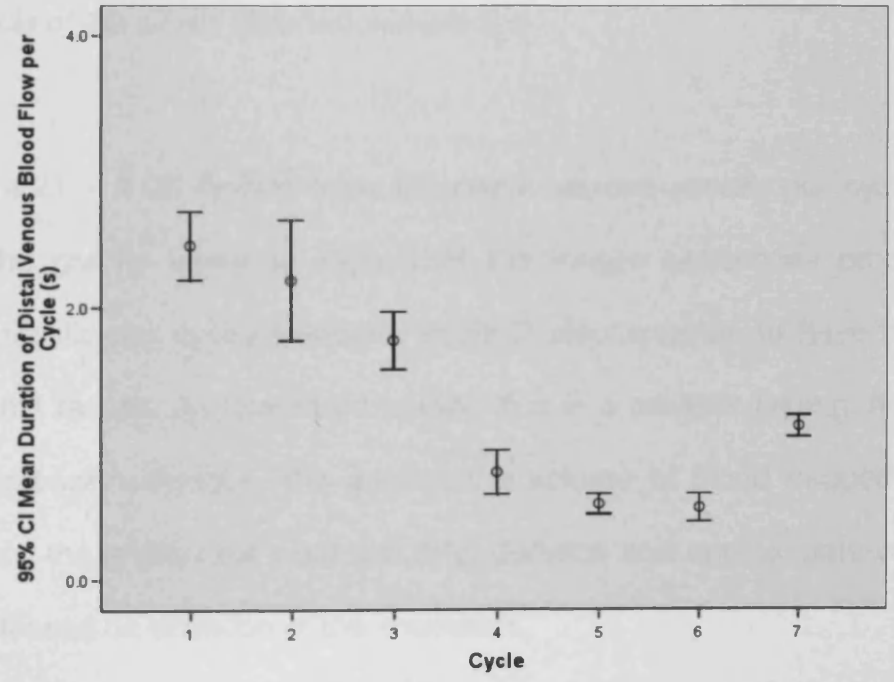


Figure 4.22 The mean duration of venous blood flow following the deflation of the chambers in the 3-chamber thigh compression garment for each cycle of the seven different sequences.

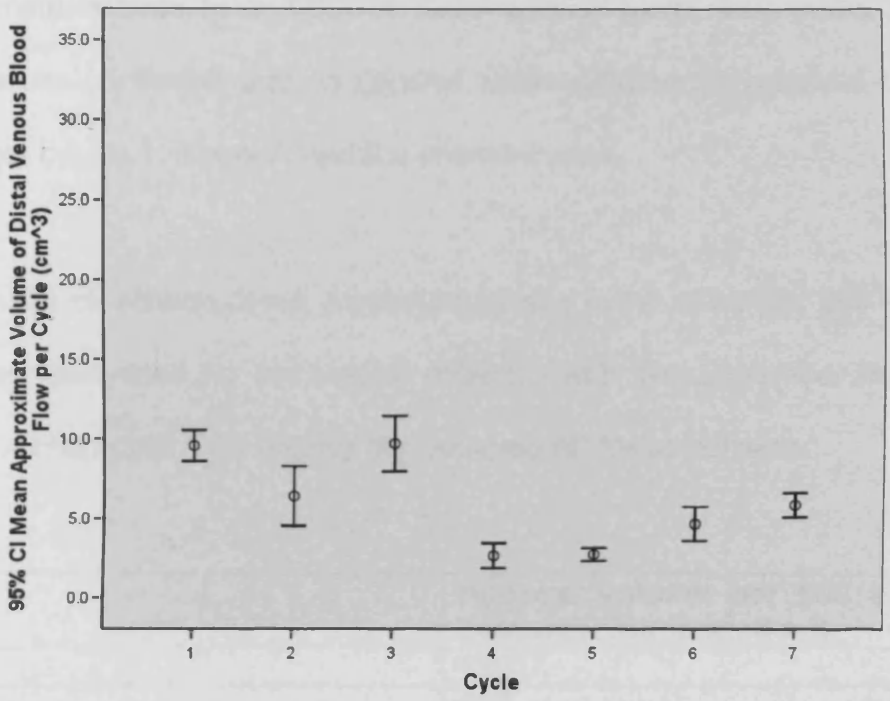


Figure 4.23 The mean, approximate volume of venous blood flow following the deflation of the chambers in the 3-chamber thigh compression garment for each cycle of the seven different sequences.

Figures 4.21 – 4.23 demonstrate the distal venous results per cycle. Once again, the graphs seem to imply that the longer sequences produce the optimal results per cycle; however, cycle 2 also appears to have produced reasonable results. As described earlier, this is a realistic finding; the longer the compression duration, the greater the volume of blood trapped distally, and hence the greater the peak velocity, duration and approximate volume of blood released on deflation of the chambers.

The one way ANOVA demonstrated that there were significant differences between the cycles for peak velocity ($p < .005$), duration ($p < .005$) and

approximate volume ($p < .005$) of distal venous blood flow, whilst multiple comparisons confirmed that, in general, these differences occurred between the longer cycles 1, 6 and 7, and the shorter cycles.

The volume of venous blood emptied from the distal veins per 600 seconds has been calculated for the results obtained with the 3-chamber thigh cuff. Table 4.4 and figure 4.24 display the outcome of this calculation.

Cycle	Approx. volume per 600 seconds compression (cm^3, 3 s.f)
1	136
2	357
3	161
4	130
5	171
6	132
7	156

Table 4.4 The approximate volume of venous blood emptied with the 3-chamber thigh compression cuff during 600 seconds of compression for each of the seven different cycles.

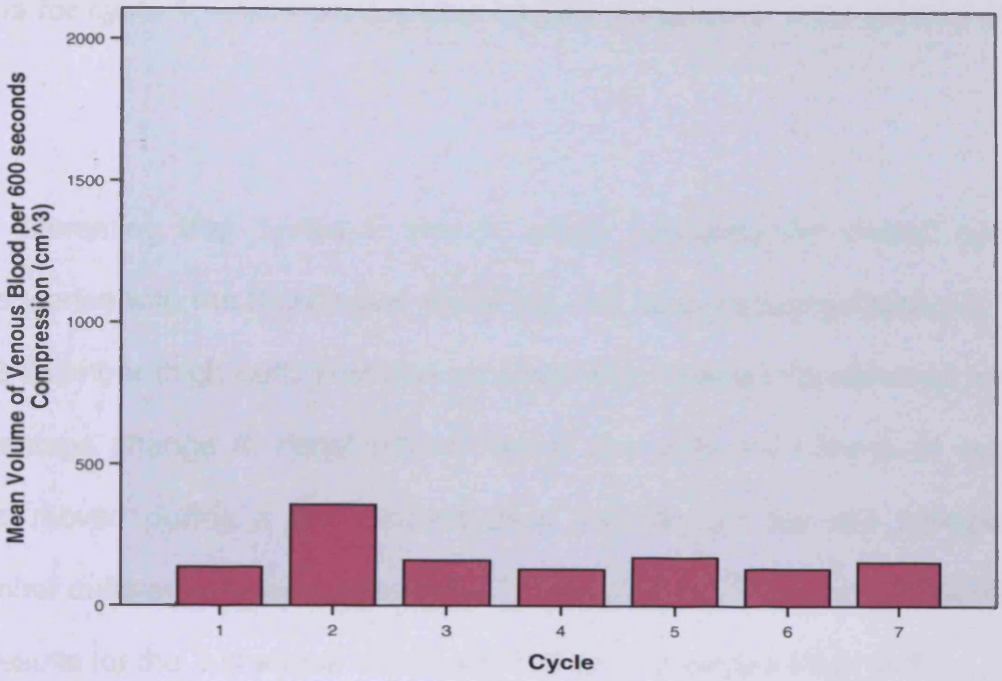


Figure 4.24 The mean volume of distal venous blood emptied with the 3-chamber thigh compression cuff during 600 seconds of compression for each of the seven different cycles.

The greatest volume of distal venous blood moved during the 600 second time period was produced for cycle 2, which emptied 357 cm^3 of blood per 600 seconds from the distal vasculature. This result is at least double the volume produced with any of the other remaining six cycles. Cycle 5 produced the second highest result of 171 cm^3 per 600 seconds. These results are demonstrated in figure 4.24.

The optimal venous result obtained for cycle 2 coincides with the optimal result obtained from the arterial study, where cycle 2 produced an increase in distal arterial blood flow of 37.02% during the compression period. The same

is true for cycle 5, which produced a 10.64% increase in distal arterial blood flow.

It is interesting that cycles 2 and 5, which produced the overall optimal performance with the 3-chamber whole leg cuff, also performed optimally with the 3-chamber thigh cuff. This can be seen when the results obtained for the percentage change in distal arterial blood flow and the volume of venous blood moved during a 600 second time duration for the two different 3-chamber cuffs are plotted on the same graph. Figures 4.25 and 4.26 compare the results for the 3-chamber whole leg and the 3-chamber thigh cuffs.

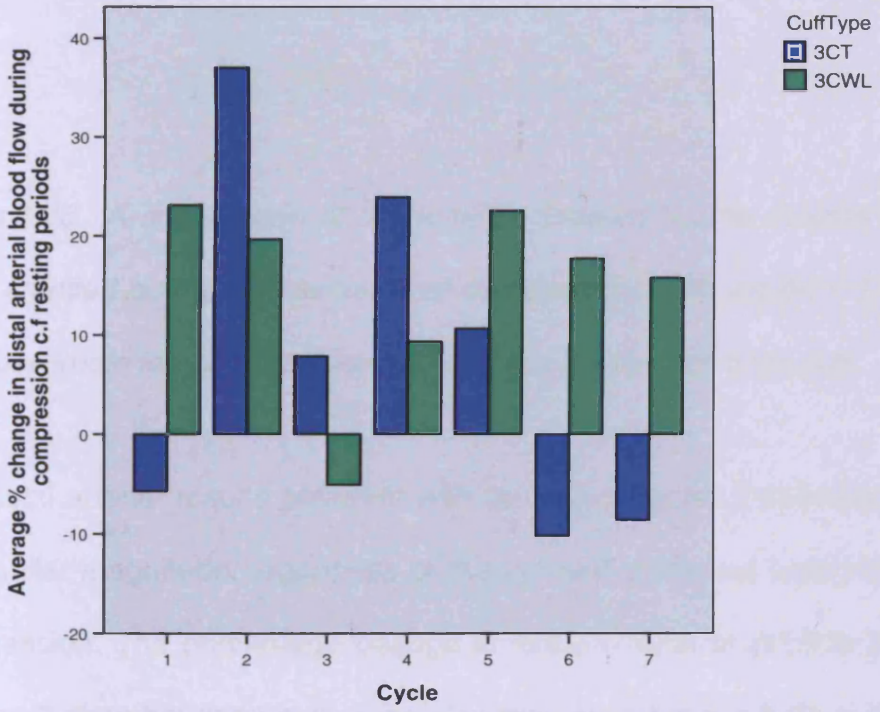


Figure 4.25 A comparison of the results obtained for the percentage change in distal arterial blood flow during compression with cycles 1-7, for the 3-chamber whole leg compression cuff and the 3-chamber thigh cuff.

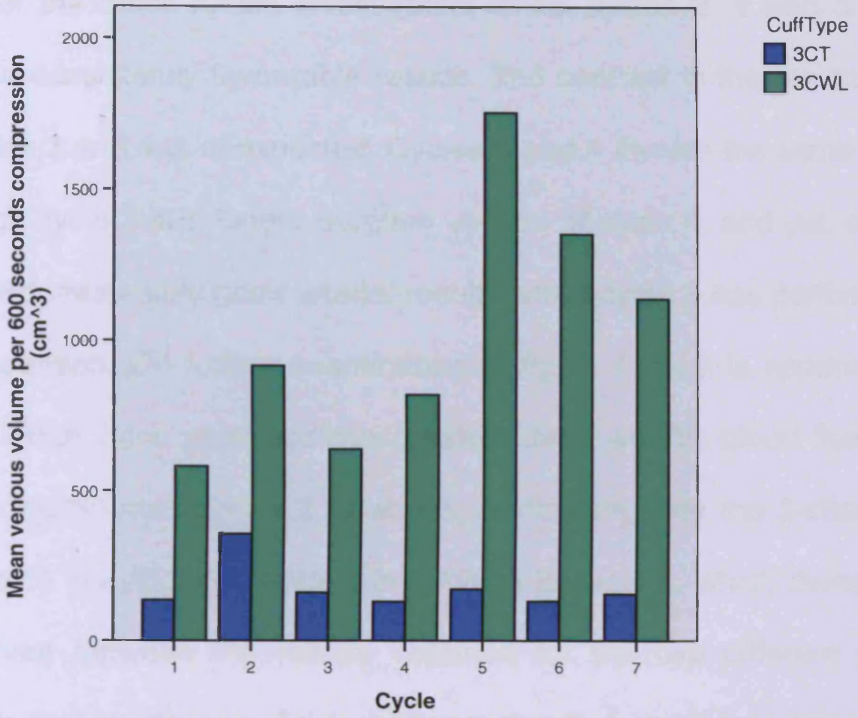


Figure 4.26 A comparison of the results obtained for the volume of venous blood emptied during 600 seconds of compression with cycles 1-7, for the 3-chamber whole leg compression cuff and the 3-chamber thigh cuff.

The distal arterial results obtained with the two different 3-chamber cuffs are of a similar magnitude, regardless of the amount of the leg which is receiving compression. The percentage change in distal arterial blood flow for cycle 2 with the 3-chamber thigh cuff, is greater than any of the results obtained with the 3-chamber whole leg garment, although, it is also worth mentioning that the standard deviation associated with this result is a very high 77.19%. One of the interesting aspects of figure 4.25 is the consistency of the results obtained for the different cuffs. For example, it seems clear that cycle 3 is of no particular benefit to distal arterial blood flow, especially in comparison with

some of the other cycles investigated; whilst cycles 2, 4 and 5 appear to produce consistently favourable results. The contrast in the results produced by cycles 3 and 4 is unexpected. Cycles 3 and 4 involve the same sequence; although cycle 3 is a longer duration version of cycle 4, and yet, cycle 4 has produced reasonably good arterial results whilst cycle 3 has performed poorly in comparison. On further examination of figure 4.25, it is apparent that the cycles which have produced the greatest distal arterial blood flow response are the more rapid cycles 2, 4 and 5; particularly with the 3-chamber thigh cuff, and it is also these cycles, in addition to cycle 3, which demonstrate an agreement between the results obtained for the two different cuffs. It is possible that the timings of the shorter cycles 2, 4 and 5, which involve single cycle durations of 25, 20 and 20 seconds respectively, are such that the distal arterial response is optimised.

Figure 4.26 compares the results obtained for the volume of venous blood emptied per 600 seconds of compression for each of the 3-chamber cuffs. The magnitude of the results obtained for the 3-chamber whole leg cuff significantly exceeds the magnitude of the results obtained for the 3-chamber thigh cuff; however, as previously mentioned, this was to be expected when the 'amount' of limb being compressed was compared. If the difference in the magnitude of the results is put aside, on examination of the graphs it can be seen that there is a resemblance between the results. Cycles 2 and 5 produce optimal results for each of the 3-chamber cuffs. This result in combination with the results demonstrated in figure 4.25 is very encouraging; both figures

support the advantages of cycles 2 and 5 for optimally enhancing the distal arterial and the distal venous circulations.

Initially, it was presumed that a longer compression cycle would induce maximal arterial inflow and venous outflow. This supposition was based upon the concept that the longer the compression duration, the greater the volume of blood trapped distally, the greater the volume of blood released back to the heart on deflation of the cuff, and consequently the greater the resulting arterial hyperaemia. However, this presumption, whilst true for a single cycle of compression, did not prove to be accurate when the compression cycle was prolonged over a given length of time. The results have demonstrated that the shorter cycles are more efficient in enhancing venous return and consequently improving the arterial supply over the given time duration. Cycles 2, 4 and 5 are executed very rapidly as a consequence of their short cycle times, and this fast turnaround of the sequence maintains a continuous 'wave' of compression up the leg, accelerating blood back towards the heart. Although the longer sequences, cycles 1, 3, 6 and 7, similarly implement a 'wave-like' action up the leg, they are much slower systems, which in the first instance would not be moving the same volume of blood in a given time period, and secondly, may be impeding the arterial blood flow. The veins have a limited distensibility; therefore, during compression with the longer cycles, after a specific time duration the veins distal to the compression cuff may have been distended to their maximum capabilities, and are no longer able to accommodate any more blood; prolonging compression any further would be futile. In addition, the arteries could be affected by the extended compression

period, whereby they are partially compressed, and hence the arterial flow could be reduced as a consequence.

The difference in the arterial results obtained for the two cuffs for cycles 1, 6 and 7 could be associated with the 'amount' of the leg receiving compression. The 3-chamber thigh cuff produced negative results for these three cycles, whilst the 3-chamber whole leg cuff produced very high positive results. Since high percentage changes have been obtained for the 3-chamber thigh cuff with other cycles, for example cycles 2 and 4, the answer is not that the cuff is not capable of achieving a comparable arterial response to the whole leg garment. The solution could be related to whether or not the calf is being compressed. The high results demonstrated with the 3-chamber whole leg cuff could be as a consequence of a hyperaemia occurring due to the compression of the veins in the calf; whilst the negative results obtained with the 3-chamber thigh cuff represent an absence of an effect in the calf.

As yet, the complication of external factors has not been mentioned. Blood flow is highly sensitive to variations in temperature; if the surrounding temperature was too hot or too cold, the blood flow was affected, resulting in continuous forward flow (hyperaemia), as the arteries dilated or constricted (dependant on whether the individual was too hot or too cold) to try and resume a normal temperature.

Other factors which could have affected the results include the amount of time that the individual allowed for the blood flow to relax before commencing the

study; how long the individual had been lying down collecting results for; whether there were any unexpected distractions or disturbances in the department which could have increased the heart rate and consequently the blood flow; whether the individual had recently consumed food or a caffeinated drink; any medications that the individual may have been taking, and also whether the individual smoked cigarettes. In this particular case, since all of the investigations were conducted on a single healthy individual, many of these factors were controlled, for example, the individual does not smoke, does not drink any caffeinated drinks during the day, and a period of at least 600 seconds was allowed prior to the commencement of any tests to let the blood flow relax.

Many PPG signals were collected for the 3-chamber thigh cuff, and as with the 3-chamber whole leg cuff, they varied in duration and start time, and therefore could not be averaged together. In order to compare with the signals included for the 3 chamber whole leg cuff, the following signals (figures 4.27 and 4.28) were obtained for cycles 2 and 5 with the 3-chamber thigh cuff.

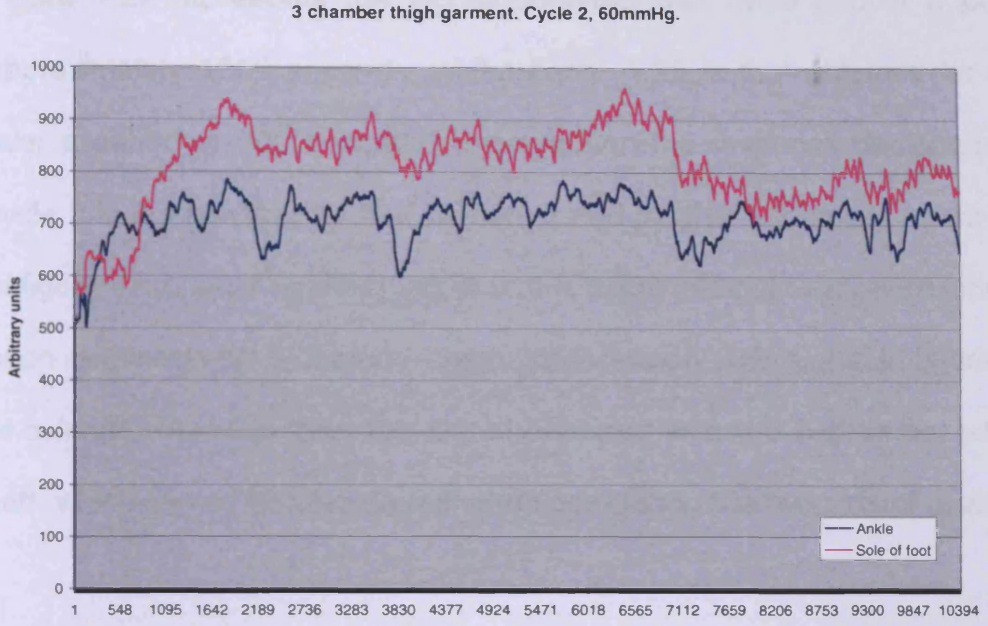


Figure 4.27 The photoplethysmography signal obtained from the sole of the foot and the ankle, whilst using the 3-chamber thigh compression cuff with cycle 2.

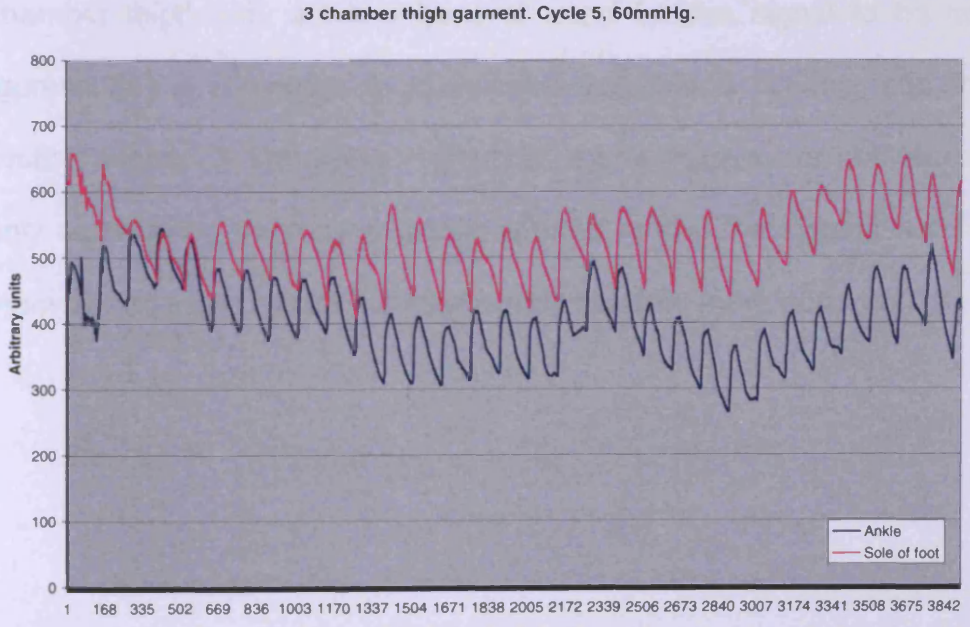


Figure 4.28 The photoplethysmography signal obtained from the sole of the foot and the ankle, whilst using the 3-chamber thigh compression cuff with cycle 5.

Figure 4.27 represents the signal obtained with cycle 2 over a period of approximately 1600 seconds, whilst figure 4.28 is that obtained for cycle 5 over a period of 600 seconds. Even though the response demonstrated for cycle 2 is not as clear as that demonstrated for the 3 chamber whole leg cuff in figure 4.12, what is important is that a distal microcirculatory response has been obtained with 3-chamber thigh compression. The signal in figure 4.27 is of a longer duration than the signal obtained with the 3-chamber whole leg cuff, which should be considered when comparing the two sets of results.

The signal obtained for cycle 5 (figure 4.28) displays a very clear response. The amplitude of the signal is comparable if not greater than the amplitude of the response obtained with the 3-chamber whole leg cuff (figure 4.13). The effects which do not seem to be appearing in the signals obtained with the 3-chamber thigh cuff, are the general trend for the signal to be increasing, representing a decrease in microcirculatory blood volume, and the longer cyclic variation in the signal. However, these signals are not averages, and only represent a very short period of time, and if the signals were repeated many times, these effects could possibly become more apparent.

4.4 Conclusion for the Preliminary Investigations

In summary, it would appear that multiple chamber compression does not hinder a distal arterial response, and that in some instances a net increase in distal arterial blood flow was observed. From the investigations carried out, it appeared that there were two cycles which generally exceeded the performance of the other five sequences with both the 3-chamber whole leg cuff and the 3-chamber thigh cuff; these were cycles 2 and 5, which have a cycle time of 25 and 20 seconds respectively.

The preliminary investigations, which have been discussed in chapters 3 and 4, were conducted as a means of determining the optimal compression garment and compression sequence for enhancing the distal circulation. The methods used were considered to be the most practical and scientific given the number of different compression cuffs and sequence variations which required investigation within a restricted period of time. The results obtained are deemed to be a reasonable indication of the effects of compression on the distal haemodynamics. It remains to be decided which of the cuffs, with which sequence should be investigated further on healthy volunteers and subsequently on patients with chronic leg ulcers.

The optimal compression sequence obtained for each of the four compression garments has been compared in the following figures (figures 4.29 – 4.34). The figures compare the results obtained for the percentage change in distal arterial blood flow during compression and the associated standard deviation, the peak velocity, duration and approximate volume of distal venous blood

flow per cycle, and the volume of distal venous blood flow during 600 seconds of compression. The optimal compression sequences for the different compression cuffs are given in table 4.5.

Cuff	Optimal compression sequence
Huntleigh DVT 30	*60mmHg,* *20 seconds inflation,* *45 seconds deflation.*
Uniform thigh	*60mmHg,* *25 seconds inflation,* *45 seconds deflation.*
3-chamber whole leg	*60mmHg,* *Cycle 5.*
3-chamber thigh	*60mmHg,* *Cycle 2.*

Table 4.5 The optimal compression sequence for each of the different cuffs investigated.

Figures 4.29 and 4.30 compare the percentage change in distal arterial blood flow and the standard deviation which was obtained for each of the different cuffs and their associated compression sequence.

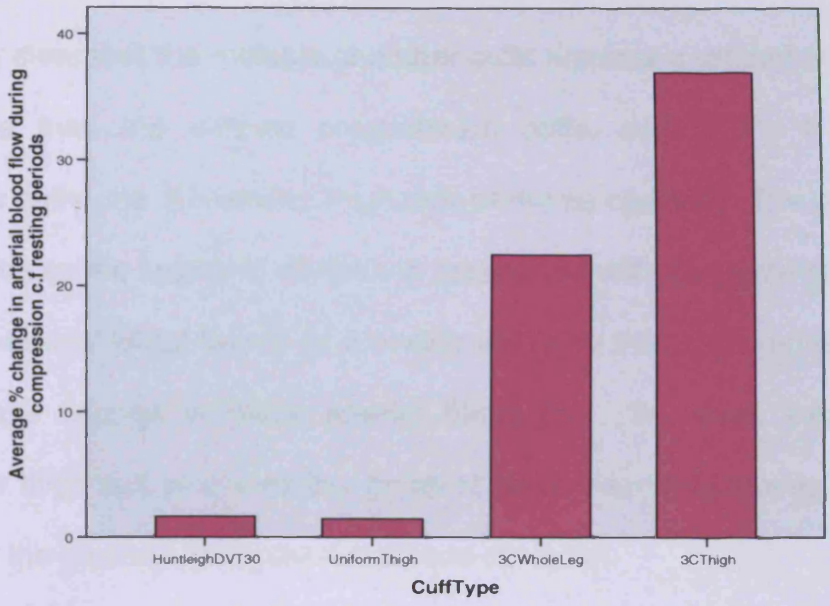


Figure 4.29 A comparison of the results obtained for the percentage change in distal arterial blood flow during compression for the four different compression cuffs and their optimal compression sequences.

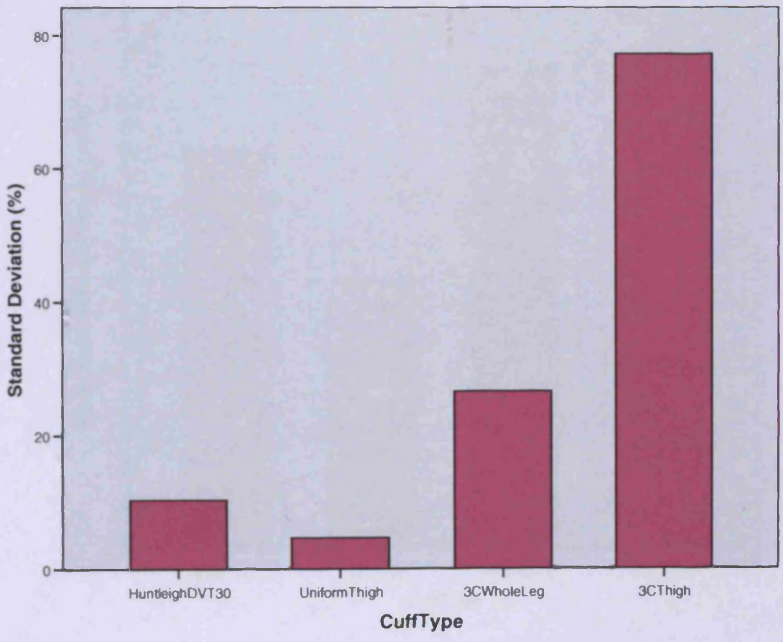


Figure 4.30 A comparison of the results obtained for the standard deviation associated with the percentage change in distal arterial blood flow during compression for the four different compression cuffs and their optimal compression sequences.

It is very clear that the multiple chamber cuffs produce a greater distal arterial response than the uniform compression cuffs, and of the two multiple chamber cuffs, the 3-chamber thigh cuff performs optimally. The graph which demonstrates the standard deviations associated with the percentage change in distal arterial blood flow is of a similar shape to the graph representing the percentage change in distal arterial blood flow. So, even though the 3-chamber thigh cuff produces the greatest distal arterial response, it has also incurred the greatest associated standard deviation.

The following figures are indicative of the distal venous response obtained *per cycle.*

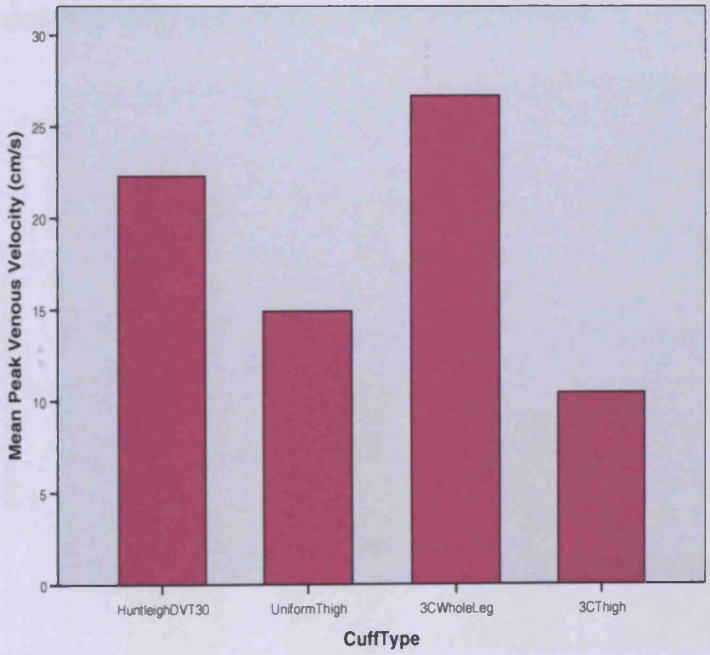


Figure 4.31 A comparison of the results obtained for the peak velocity of distal venous blood flow following deflation, for the four different compression cuffs and their associated optimal compression sequences.

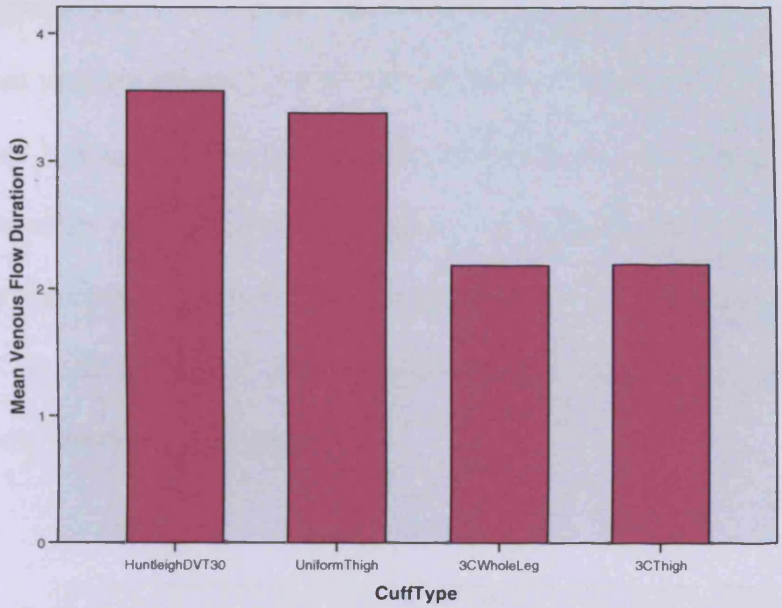


Figure 4.32 A comparison of the results obtained for the duration of distal venous blood flow following deflation, for the four different compression cuffs and their associated optimal compression sequences.

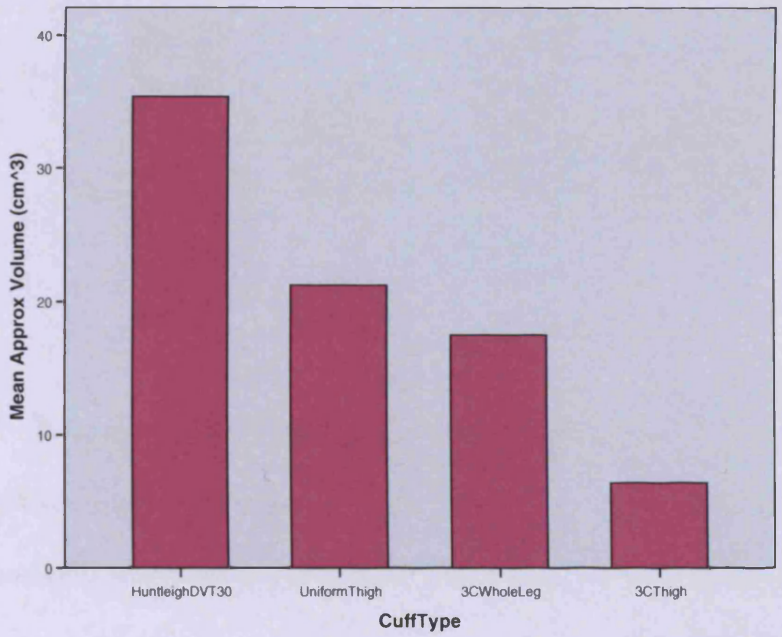


Figure 4.33 A comparison of the results obtained for the approximate volume of venous blood flow following deflation, for the four different compression cuffs and their associated optimal compression sequences.

It would appear that in general, the uniform compression cuffs produced a greater distal venous response than the multiple chamber compression cuffs, although the 3-chamber whole leg cuff produced the greatest peak venous velocity following cuff deflation. However, as previously, the best way of determining the optimal cycle for enhancing distal venous return is to compare the volume of venous blood flow emptied over a 600 second duration. The results are demonstrated in figure 4.34.

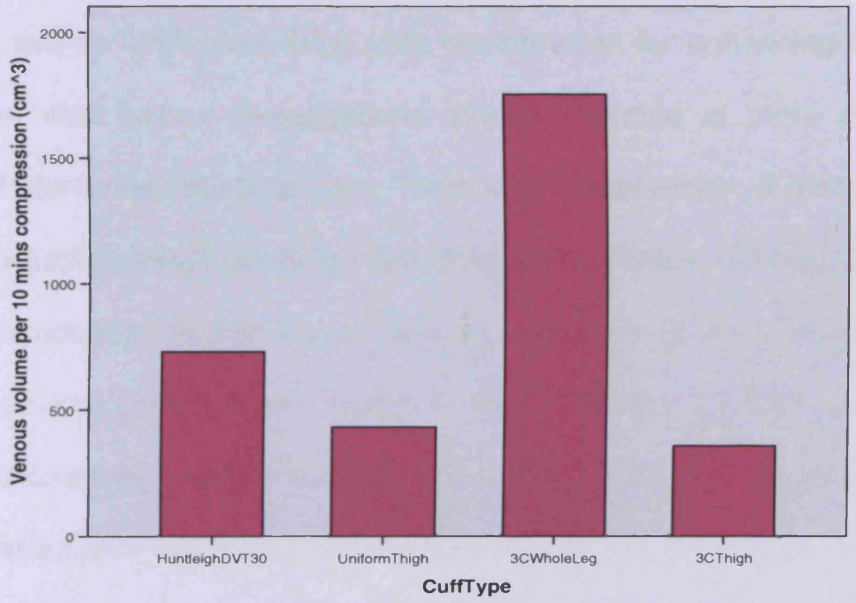


Figure 4.34 A comparison of the results obtained for the volume of venous blood emptied during a 600 second duration, for the four different compression cuffs and their associated optimal compression sequences.

Figure 4.34 demonstrates that the optimal compression regime for improving distal venous return is the 3-chamber whole leg cuff. The results obtained for

the thigh cuffs appear to be very similar, whilst the Huntleigh DVT 30 has performed slightly better.

When the findings of the venous studies are combined with those obtained from the arterial studies, it would seem that the 3-chamber thigh cuff produces the optimal arterial results whilst the 3-chamber whole leg cuff produces the optimal venous results. Further investigations carried out on healthy volunteers could compare the two different 3-chamber cuffs, or could compare two different cycles with one of the cuffs. It was decided that since the original objective was to implement thigh only compression for enhancing the distal circulation, that further investigations should examine in more detail the effects of the 3-chamber thigh cuff. Thigh only compression, if demonstrated to be successful, would be more agreeable to the patient with leg ulceration, as it would not interfere the wound itself, and would be easier for the patient to use in the home environment. Therefore, it was decided that investigations on healthy volunteers would compare the distal haemodynamical effects of cycles 2 and 5 with the 3-chamber thigh cuff; and the optimal cycle would then be examined on patients with leg ulcers of arterial, venous, diabetic and / or mixed aetiologies.

Chapter 5: Healthy Volunteers

5.1 Introduction

Chapters 3 and 4 described the preliminary investigations of this research; the purpose of which were to determine the optimal intermittent pneumatic compression system for enhancing the distal circulation in a healthy volunteer. The effects of different compression cuffs, compression sequences and pressures on distal blood flow were examined, and it was concluded that the 3-chamber compression garments were the most effective in increasing distal blood flow. Since the ultimate objective of the research is to treat patients with chronic leg ulceration, it was decided that the 3-chamber thigh compression garment would be more agreeable to patients, as it would not interfere with the wound itself, and would be easier for the patient to use in the home environment. Following on from the work carried out in the previous chapters, further investigations on a number of healthy volunteers compared the effects of cycles 2 and 5 with the 3-chamber thigh compression garment, on distal blood flow.

5.2 Methods

5.2.1 Variables

The 3-chamber thigh compression cuff was investigated with cycles 2 and 5 (see chapter 4.2.1), at a pressure of 60mmHg on a number of healthy volunteers for distal arterial and venous effects.

5.2.2 Data Acquisition

The methods of data acquisition did not vary significantly from those mentioned in chapters 3.2.2 and 4.2.2. Volunteers were recruited from the Department of Medical Physics, UHW, and asked to sign a consent form after reading a participant information sheet. A favourable ethical opinion had been obtained for the research from the South East Wales Local Research Ethics Committee Panel C.

The volunteer was asked to lie supine on a scanning couch in a temperature controlled room, with their head on a pillow. The 3-chamber thigh cuff was placed about the left leg of the volunteer, over their trousers, and connected to three Flowpac pumps. The QVL Doppler ultrasound system (see chapter 2) and an 8MHz flat transducer were used to locate the dorsalis pedis artery for the arterial studies, and the posterior tibial vein for the venous studies. Once the required blood vessel had been located, the ultrasound transducer was secured in place using micropore tape. A blanket was then placed over both legs and feet of the volunteer to prevent cooling. Before starting the study, a period of approximately 10 minutes was considered necessary to allow blood flow to stabilise.

Measurements were repeated for cycles 2 and 5. The arterial study involved recording the TAM blood flow velocity (see chapter 3.2.2) every 5 seconds throughout a test comprising 180 seconds of resting followed by ten cycles of compression and then a further 180 seconds of resting; whilst in the venous study the peak velocity and duration of venous blood flow were recorded

following the deflation of each chamber within each cycle. This was repeated ten times. Photoplethysmography signals were also recorded for 600 seconds, at the same time as the venous study.

5.2.3 Data Analysis

Data was collected from 20 volunteers. The arterial results were normalised and averaged together and plotted as a line graph in SPSS. Additional graphs were plotted which compared the results obtained from the male and female volunteers, and also compared the results obtained from the volunteers of 25 years and under and the volunteers over 25 years.

The percentage change in distal arterial blood flow which occurred during the compression period as compared with resting blood flow pre and post compression was calculated using the computer program written in Turbo Pascal, as previously. Mann-Whitney U tests were performed to compare the differences between the results which were obtained for male and female volunteers, and volunteers 25 years and under with volunteers over 25 years.

Ten results were obtained for each volunteer for the peak velocity and the duration of distal venous blood flow following the deflation of each chamber within each cycle of the sequence. Where multiple results were obtained for a single repetition of the sequence, the results were added together in order to allow comparisons between cycles 2 and 5. An approximate volume of distal venous blood moved per cycle was calculated by multiplying the duration of venous blood flow by the average maximum velocity of blood flow (TAM

velocity). However, since cycles 2 and 5 vary in duration, the volume of venous blood moved during 600 seconds was determined by multiplying the approximate volume per cycle by the number of cycles which occur during 600 seconds. The data was entered into SPSS where error bar charts were plotted of the means and a two sample T-test was performed to compare the mean data values for each of the cycles.

PPG signals were recorded for each volunteer; however, it was not possible to average them together since the start times varied.

5.3 Results and Discussion

Initially, investigations were carried out on seven healthy volunteers and the results were examined. A problem was encountered with the results obtained from the arterial studies. It was found that, in all instances, the arterial blood flow was decreasing during the ten cycles of compression, and that a hyperaemia was occurring following the end of the compression period. This was in conflict with the results previously obtained in the preliminary investigations (see figures 4.15 and 4.18), whereby net increases in distal arterial blood flow during the compression period of 37.02% and 10.64% were calculated by the computer program for cycles 2 and 5 respectively. A decrease in the arterial blood flow during compression would not be very beneficial to the patient with leg ulceration and could cause further damage if, as was originally proposed, the patient received continuous compression for a minimum of two hours daily. The results obtained for cycles 2 and 5 are demonstrated in figures 5.1 and 5.2.

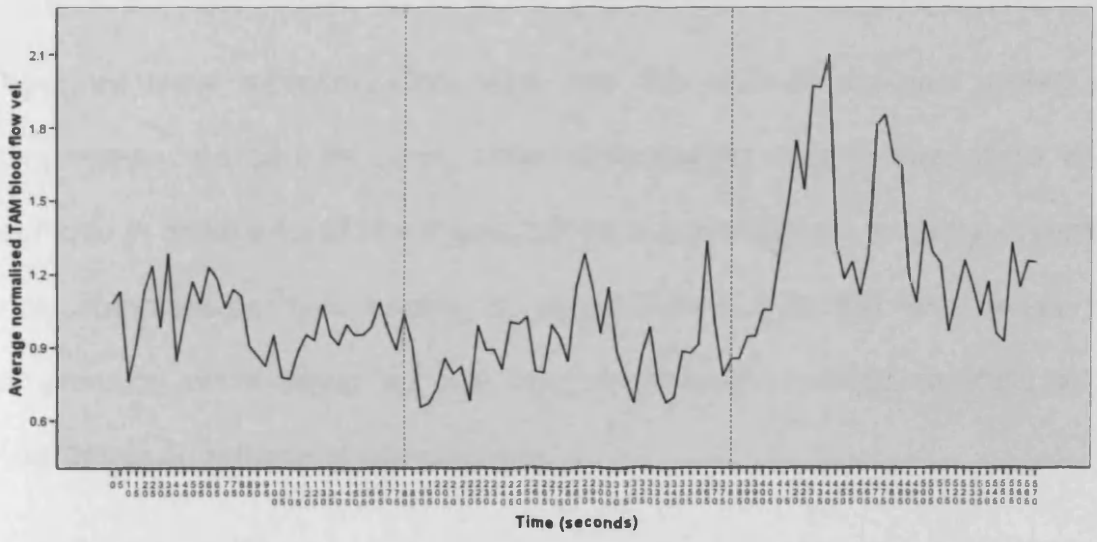


Figure 5.1 The average of the normalised distal arterial blood flow response obtained from seven healthy volunteers. The grey lines represent

the start and end of ten cycles of compression using cycle 5 with the 3-chamber thigh cuff.

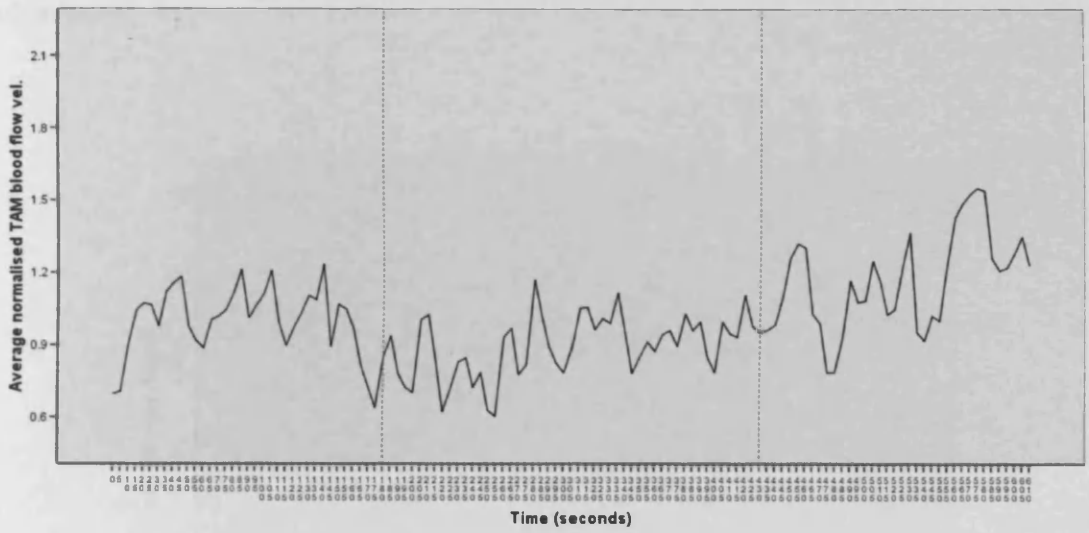


Figure 5.2 The average of the normalised distal arterial blood flow response obtained from seven healthy volunteers. The grey lines represent the start and end of ten cycles of compression using cycle 2 with the 3-chamber thigh cuff.

The grey lines represent the start and the end of the ten cycles of compression. As can be seen, once compression commences, there is a decrease in distal arterial blood flow, which is followed by a large hyperaemia once compression has ended. It would seem that the ten cycles of compression were acting as one long compression period, resulting in a hyperaemia on release of compression.

It was very clear from the results obtained from the seven volunteers that cycle 5 was having a greater effect on distal blood flow than cycle 2. This was

apparent from the graphs above (figures 5.1 and 5.2), whereby the hyperaemia observed for cycle 5 is far greater than that observed for cycle 2; and, in the venous studies, cycle 2 did not produce results in all of the volunteers.

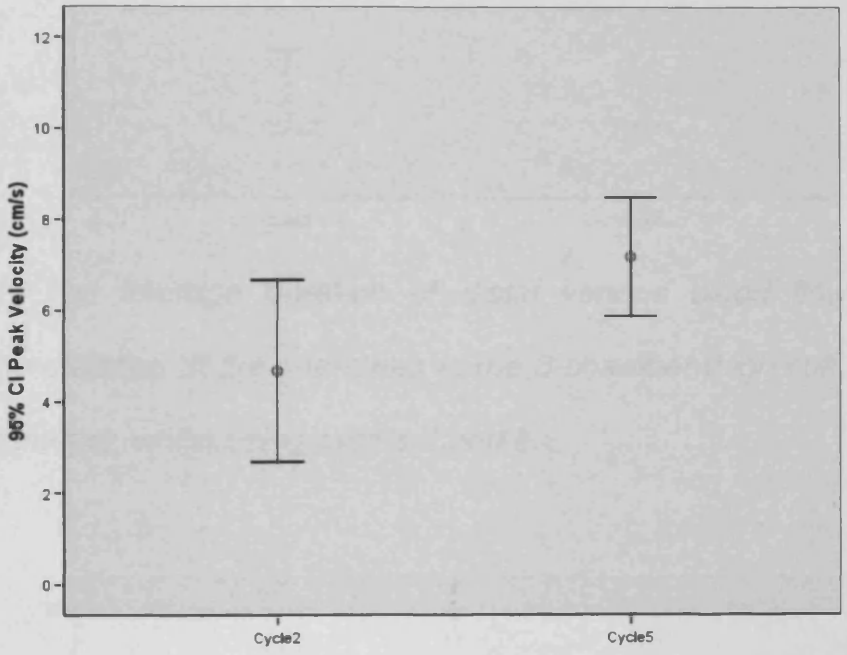


Figure 5.3 The average peak velocity of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for seven healthy volunteers, whilst using cycles 2 and 5.

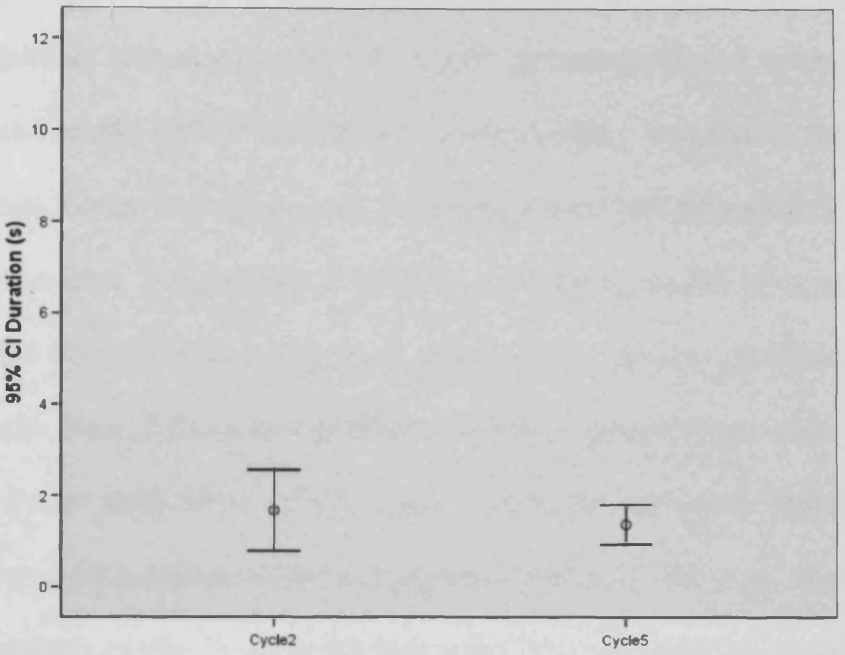


Figure 5.4 The average duration of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for seven healthy volunteers, whilst using cycles 2 and 5.

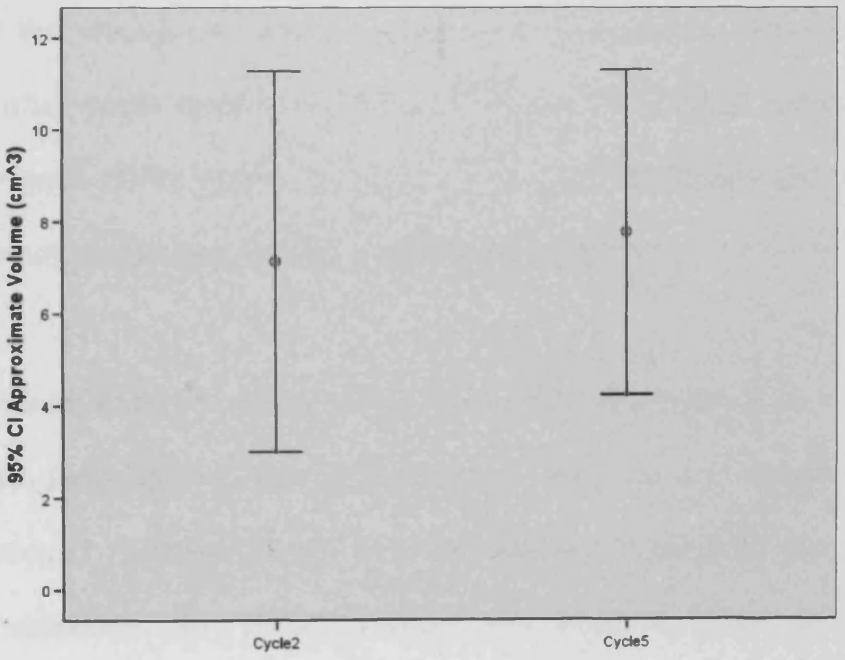


Figure 5.5 The average approximate volume of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for seven healthy volunteers, whilst using cycles 2 and 5.

The three graphs above (figures 5.3 – 5.5) demonstrate the average of the distal venous results obtained from the seven healthy volunteers for cycles 2 and 5 with the 3-chamber thigh cuff. It can be seen from figures 5.3 – 5.5 that cycle 5 produces a greater peak velocity and approximate volume of distal venous blood flow; however, cycle 2 produces a greater duration of distal venous blood flow following deflation of the compression cuff. Cycle 2 comprises three deflations, since each chamber empties independently; therefore the results above for flow duration represent the sum of the results obtained for each of the three chamber deflations. In cycle 5, chambers one and two deflate simultaneously, whilst chamber three deflates with chamber one inflated; hence, in cycle 5, a result is obtained for the simultaneous deflation of chambers one and two only. This explains why cycle 2 has produced a greater average duration of distal venous blood flow following the deflation of the chambers, when results were not always obtained for this cycle. It is also worth mentioning the size of the error bars that have been obtained for each of the cycles. In figures 5.3 – 5.5, the error bars for cycle 2 are considerably larger than those obtained for cycle 5.

A question which arises from these initial results is why there is an absence of hyperaemias during the compression period when venous return is clearly being improved? Arterial blood flow is always subjected to increased peripheral resistance during compression with cycle 5, since at least one chamber is always inflated; and perhaps the 5 second deflation period within cycle 2 is too short to allow a distal hyperaemia to ensue. However, the

sequential action of the three chambers is such that venous return is improved even when the arterial supply is not.

It was decided to adapt Cycle 5 in order to allow the arterial hyperaemias to occur during the compression sequence by splitting the regime into two minutes of compression and two minutes without compression. Therefore, there were six cycles of compression and then two minutes deflation. The theory behind this regime was that during compression venous return was being enhanced, and then the deflation period would allow the arterial hyperaemia to arise.

This sequence was examined on the same seven volunteers to determine whether or not any improvement was observed. The distal arterial response obtained with the adapted sequence of cycle 5 was significantly improved as compared with the original response demonstrated in figure 5.1. The following figure 5.6 demonstrates the average response obtained from the seven healthy volunteers. The TAM blood flow velocity was recorded every 5 seconds throughout a test which comprised 180 seconds of resting followed by five repetitions of the two minute on and off sequence, and then a further 60 seconds of resting.

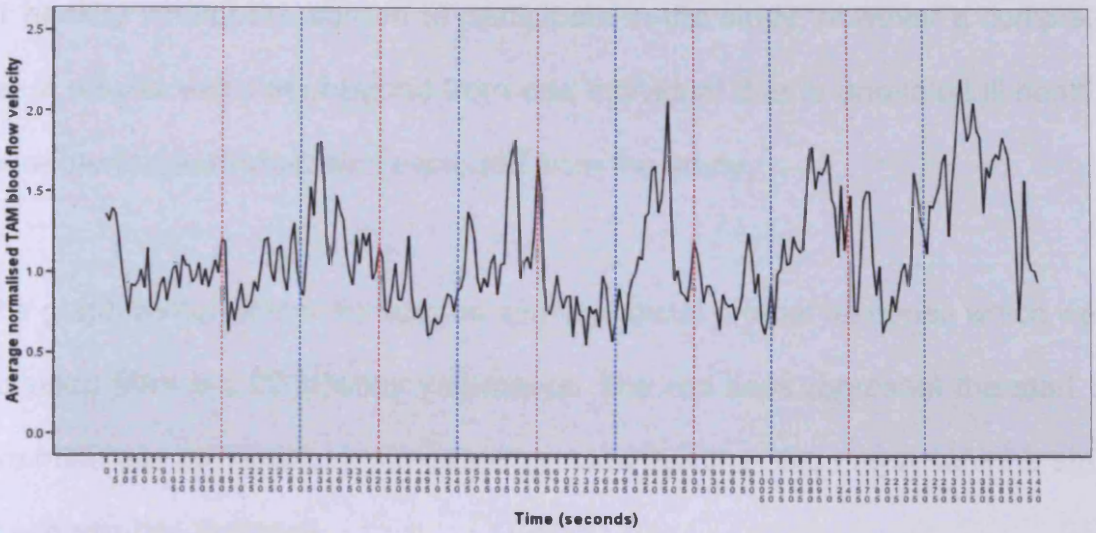


Figure 5.6 The average of the normalised distal arterial blood flow response obtained from seven healthy volunteers for the adapted sequence of cycle 5 and the 3-chamber thigh compression cuff. The grey lines represent the start and end of each two minute compression period.

The red lines in figure 5.6 represent the start of each 2 minute compression period and the blue lines represent the start of each 2 minute deflation period. As can be seen from figure 5.6, blood flow decreases during the 2 minute compression period, which is followed by a large hyperaemic response when the cuff deflates.

The investigations on healthy volunteers were continued using the two minute on and off sequence of cycle 5 for the distal arterial studies. Cycle 2 was no longer examined on the volunteers for distal arterial results as it was considered that cycle 5 produced a significantly greater distal response. The venous studies examined both cycles 2 and 5 for a distal effect.

21 healthy volunteers agreed to participate in the study, however a complete set of results was not obtained from one individual due to unrelated ill health; therefore this individual was excluded from the study.

The graph below demonstrates the average distal arterial response which was obtained from the 20 healthy volunteers. The red lines represent the start of two minutes / six cycles of compression, and the blue lines represent the start of two minutes deflation.

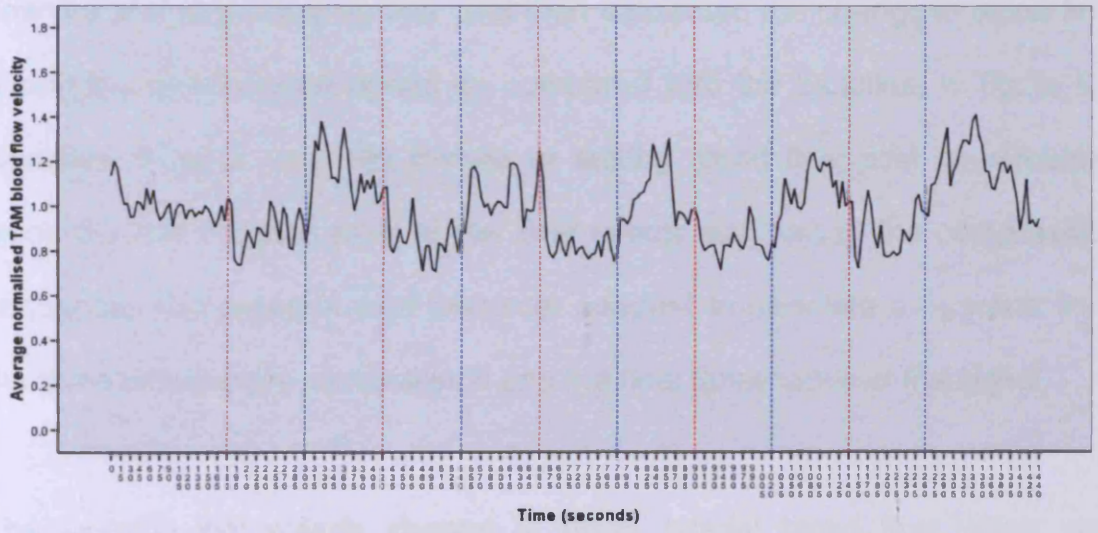


Figure 5.7 The average of the normalised distal arterial blood flow response obtained from 20 healthy volunteers for the adapted two minute on and off sequence of cycle 5 with the 3-chamber thigh cuff.

The first 180 seconds of figure 5.7 demonstrate a normalised baseline blood flow velocity of approximately 1. There is a slight peak at the very beginning of the graph which is probably an indication that the test was started a little bit prematurely, and the volunteer's blood flow had not relaxed enough. During

compression (following a red line), blood flow velocity decreases, as previously demonstrated in figures 5.1 and 5.6. When the cuff is completely deflated (following a blue line), a hyperaemia ensues. The hyperaemia persists throughout the 2 minutes whilst the cuff is deflated.

In order to calculate the percentage change in distal arterial blood flow which arises during the two minute on and off sequence of cycle 5, the computer program which had been used previously needed to be altered. Previously, the program extrapolated a baseline from the three minutes of resting blood flow pre and post compression, and then calculated the change in blood flow during the compression period as compared with the baseline. In figure 5.7 however, there is only one minute of resting blood flow post compression since the two minutes prior to the final minute are part of the compression sequence. The program was therefore adapted to calculate a baseline from the three minutes pre compression and the final 30 seconds of the signal.

The average percentage change in distal arterial blood flow which was obtained for the twenty volunteers was calculated to be -1.20%. This result implies that distal arterial blood flow has decreased during the compression period as compared with the resting periods. However, the results produced by the program must be interpreted carefully. The hypothetical baseline which is 'drawn' through the compression period can be highly skewed dependant upon the mean blood flow velocities calculated from the resting periods pre and post compression. In this case in particular, two of the final three minutes are part of the compression sequence, and the hyperaemic response occurs

in these two minutes; therefore blood flow velocity may be very high in the final minute in comparison with blood flow pre compression, and a highly skewed baseline will have been obtained. The protocol did not allow sufficient time for the blood flow to return to a true baseline, and so the calculated value does not signify a real reduction in flow.

The table below provides general information on the group of healthy individuals who participated in the study.

	Male	Female	Total
Total	10	10	20
Smoker	1	0	1
Age group:			
18 – 25 yrs	5	6	11
26 – 35 yrs	2	1	3
36 – 45 yrs	3	0	3
46 – 55 yrs	0	3	3
BMI:			
Underweight: <18.5	0	0	0
Normal: 18.5-24.9	8	7	15
Overweight: 25-29.9	2	3	5
Obesity: > 30	0	0	0
History of ...			
Vascular Disease	0	0	0
Cardiovascular Disease	0	0	0
Diabetes	0	0	0
Medications:			
Contraceptive pill	0	6	6
Other	0	3	3

Table 5.1 Information gathered from the 20 healthy volunteers who participated in the study.

There were 10 male healthy volunteers and 10 female healthy volunteers within the group, and 11 volunteers age 25 and under and 9 volunteers age over 25 years. Additional comparisons were performed of the distal arterial response for gender and age group.

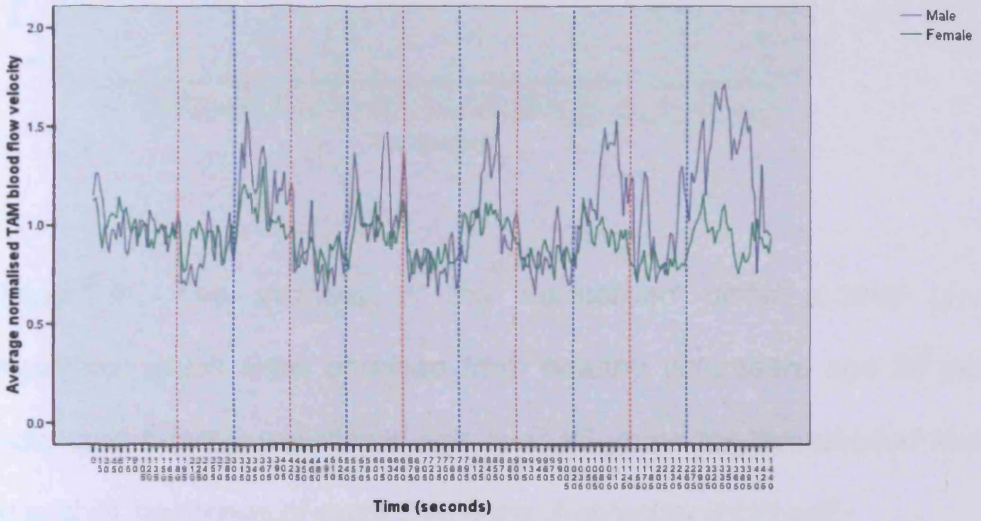


Figure 5.8 The average of the normalised distal arterial blood flow responses which were obtained from 10 healthy male volunteers and for 10 healthy female volunteers for the adapted two minute on and off sequence of cycle 5 with the 3-chamber thigh cuff.

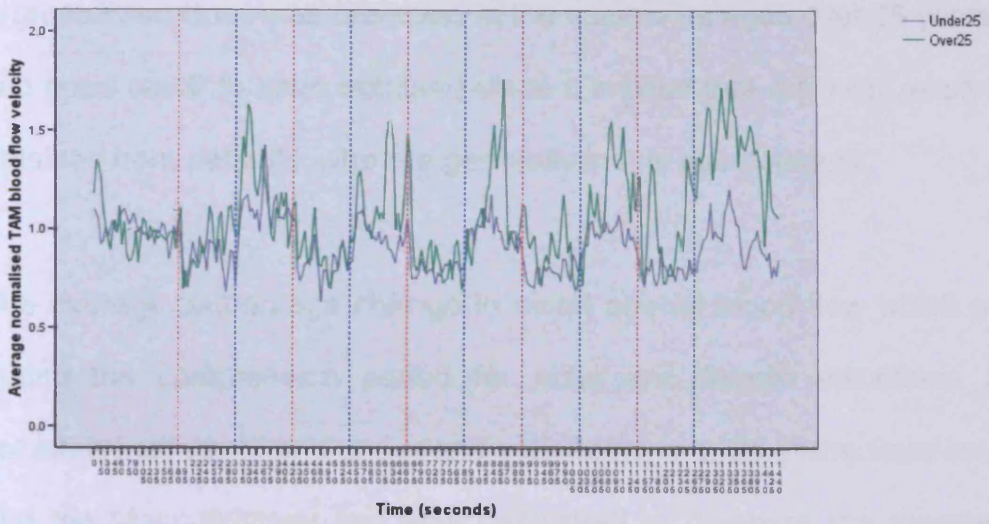


Figure 5.9 The average of the normalised distal arterial blood flow responses which were obtained from healthy volunteers age 25 years and under and healthy volunteers age over 25 years for the adapted two minute on and off sequence of cycle 5 with the 3-chamber thigh cuff.

Figures 5.8 and 5.9 demonstrate that the hyperaemic response is greater in the male volunteers than in the female volunteers, and in the volunteers age over 25 years as compared with the volunteers age 25 years and under, even though the amount by which the blood flow decreases during compression appears to be similar for each comparison. It is difficult to explain why a greater response should have been obtained in the male volunteers, perhaps with further experiments on a larger group of healthy volunteers the difference between the male and female volunteers would have reduced, and a similar response would be seen in both groups.

A greater response was observed in the volunteers aged over 25 years, which is a good result to have obtained since it implies that a similar result may be obtained from patients, who are generally in this age category.

The average percentage change in distal arterial blood flow which occurred during the compression period for male and female volunteers and for volunteers 25 years and under and volunteers over 25 years were calculated, and the Mann-Whitney test was performed to compare the averages. The Mann-Whitney test was chosen as the non-parametric equivalent to the independent samples T-test.

Even though the mean percentage change in distal arterial blood flow for the male volunteers (M = 0.17%, SD = 22.22%) was greater than the percentage change in distal arterial blood flow for the female volunteers (M = -2.56%, SD = 8.40%); a Mann-Whitney U test failed to show significance: U = 48.0; exact p = 0.912 (two-tailed).

Figure 5.9 clearly demonstrates that the volunteers over 25 years of age produce a greater distal arterial response than the volunteers age 25 years and under. However, the mean percentage change in distal arterial blood flow for the volunteers over 25 years (M = -2.17%, SD = 21.49%) has been found to be less than the mean percentage change in distal arterial blood flow for the volunteers age 25 years and under (M = -0.40%, SD = 11.86%). The discrepancy in the result produced is due to the computer program being applied to data which does not have an adequate period of post compression

resting blood flow. A Mann – Whitney U test however, failed to show a significant difference: U = 38.0; exact p = 0.412 (two-tailed). It would seem therefore, that the most accurate results are demonstrated in the graphs (figures 5.7 – 5.9).

Figures 5.10 - 5.12 demonstrate the results obtained from the distal venous studies where cycles 2 and 5 were compared on 20 healthy volunteers.

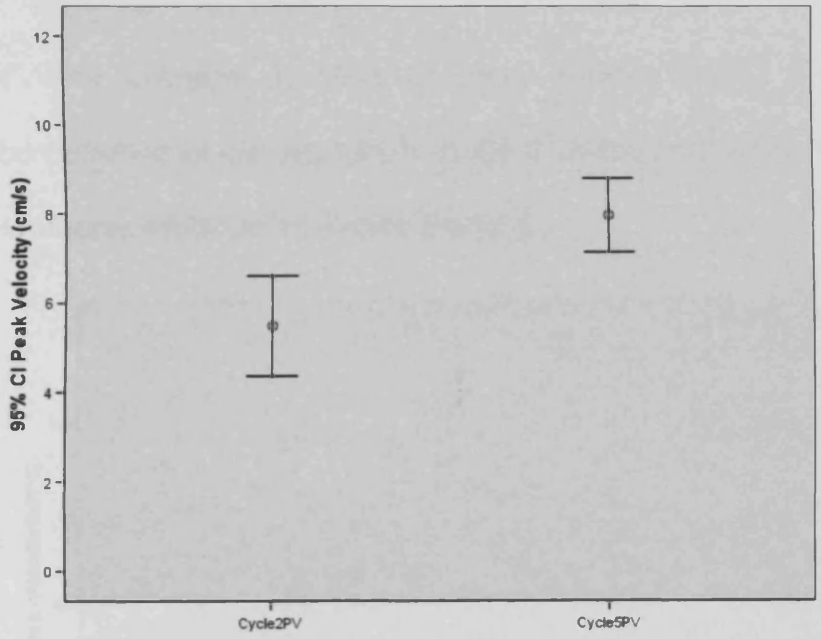


Figure 5.10 The average peak velocity of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for twenty healthy volunteers, whilst using cycles 2 and 5.

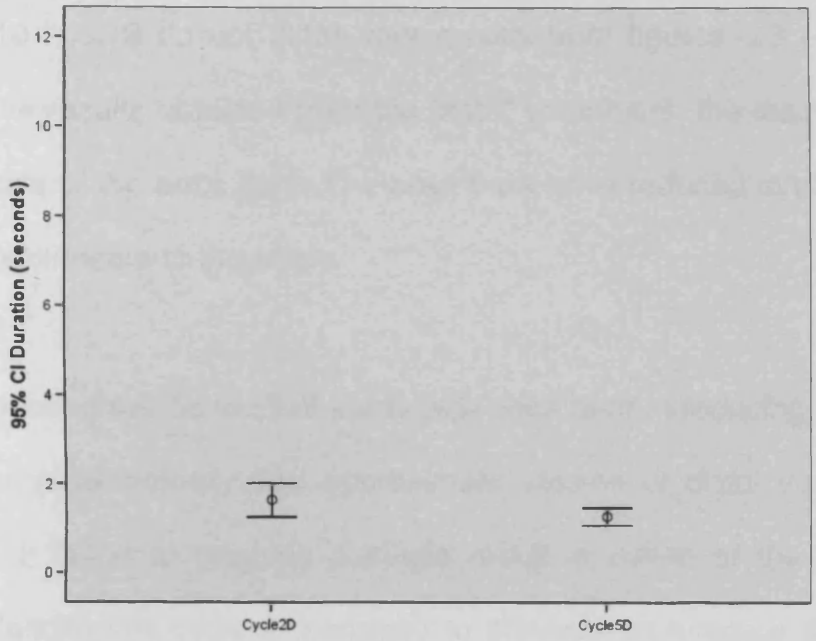


Figure 5.11 The average duration of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for twenty healthy volunteers, whilst using cycles 2 and 5.

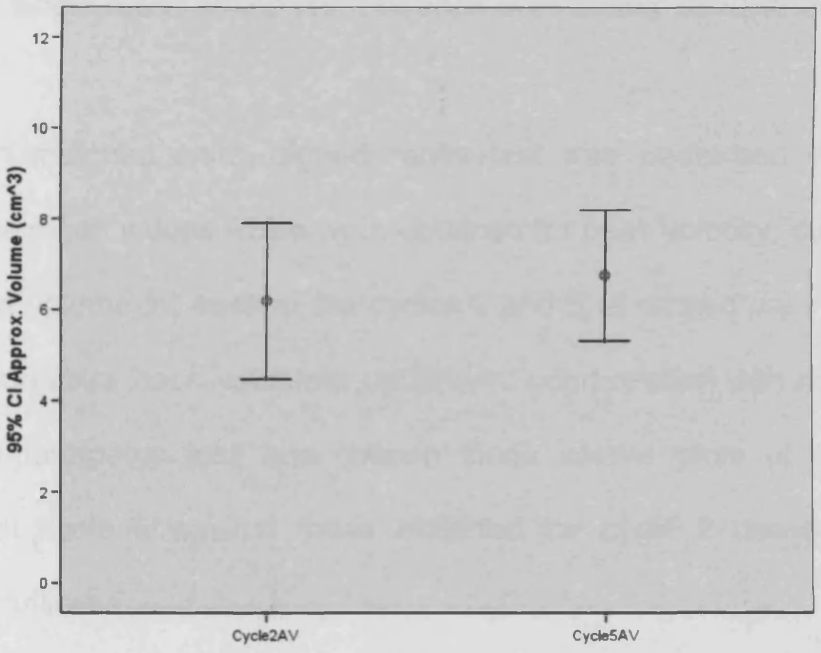


Figure 5.12 The average approximate volume of distal venous blood flow obtained following the deflation of the chambers in the 3-chamber thigh cuff, for twenty healthy volunteers, whilst using cycles 2 and 5.

Figures 5.10 – 5.12 do not differ very greatly from figures 5.3 – 5.5 which represent the results obtained from the first 7 volunteers, the main difference being the size of the error bars. The error bars have reduced in size with the addition of volunteers to the study.

Cycle 5 produced results in all of the twenty volunteers, producing on average the greatest peak velocity and approximate volume of distal venous blood flow; cycle 2 failed to produce a single result in seven of the volunteers, however, despite this cycle 2 managed to produce on average the greatest duration of distal venous blood flow. The reason behind this, as previously mentioned, is due to cycle 2 producing multiple results for each cycle as a consequence of the sequential deflation of the three chambers, whilst cycle 5 produces a single result as the first two chambers deflate simultaneously.

A Wilcoxon matched pairs, signed ranks test was performed in order to compare the mean values which were obtained for peak velocity, duration and approximate volume for each of the cycles 2 and 5. A related pairs t test was decided upon since each volunteer underwent compression with both cycles, and a non-parametric test was chosen since scatter plots of the results obtained for cycle 5 against those obtained for cycle 2 demonstrated a number of outliers.

The Wilcoxon matched pairs, signed ranks test showed that the difference between the peak velocity which was obtained for cycle 5 (M = 7.971 cm/s, SD = 5.690 cm/s) and the peak velocity which was obtained for cycle 2 (M =

5.487 cm/s, SD = 7.891) was significant beyond the 0.05 level: exact p = 0.024 (two-tailed). The difference between the duration of venous blood flow which was obtained for cycle 5 (M = 1.268 s, SD = 1.392 s) and the duration of venous blood flow which was obtained for cycle 2 (M = 1.638 s, SD = 2.706 s) was not significant beyond the 0.05 level: exact p = 0.956 (two-tailed); and similarly, the difference between the approximate volume of distal venous blood flow which was obtained for cycle 5 (M = 6.761 cm^3, SD = 9.933 cm^3) and the approximate volume of distal venous blood flow which was obtained for cycle 2 (M = 6.195 cm^3, SD = 11.888 cm^3) was not significant at the 0.05 level: exact p = 0.245 (two-tailed).

In summary, cycle 5 produces a significantly greater peak velocity of distal venous blood flow during compression than cycle 2; however the duration and approximate volume of distal venous blood flow produced by each of the cycles are not significantly different. Other factors to consider are that cycle 5 always produced a result in the volunteers whilst cycle 2 did not, and that cycle 5 produced a greater distal arterial blood flow response than cycle 2.

The following bar chart compares the results which were obtained for the volume of distal venous blood flow emptied during 600 seconds of compression for cycles 2 and 5.

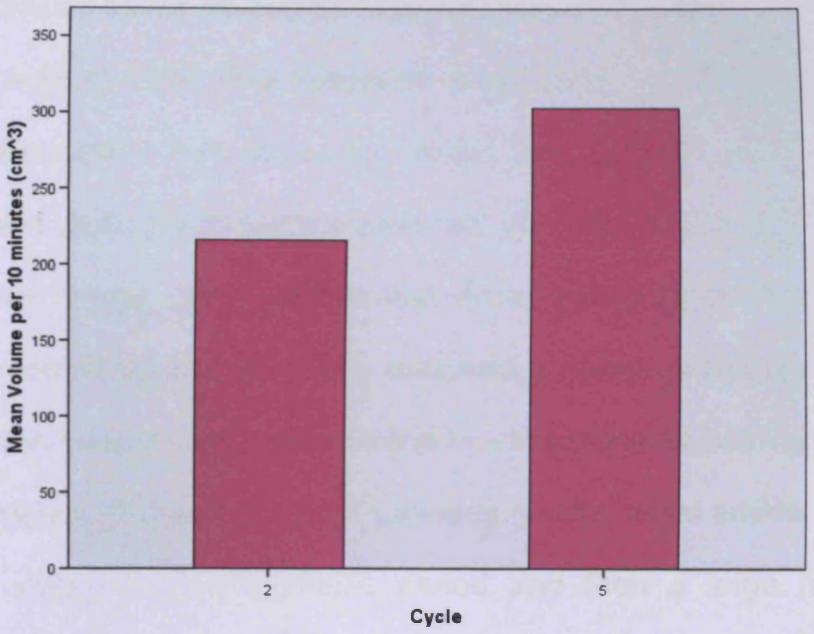


Figure 5.13 A bar graph to compare the volume of distal venous blood emptied during 600 seconds of compression for cycles 2 and 5 with the 3-chamber thigh cuff.

Figure 5.13 demonstrates that cycle 5 empties a greater volume of venous blood from the distal circulation during 600 seconds of compression than cycle 2; 303 cm^3 per 600 seconds as compared with 216 cm^3 per 600 seconds respectively.

5.4 Conclusions for Investigations with Healthy Volunteers

The distal arterial blood flow response which has been obtained with the healthy volunteers differs from that which was obtained with the single volunteer who participated in the preliminary investigations. In the preliminary investigations, it was demonstrated that distal arterial blood flow increased during the compression period, and resumed a normal blood flow following the end of the compression period. Initial investigations on healthy volunteers were in complete disagreement with previous results; distal arterial blood flow decreased during the compression period and then a large hyperaemic response was observed following the completion of ten cycles of compression. Cycles 2 and 5 are both very rapid cycles, with single cycle times of 25 and 20 seconds respectively, and whilst cycle 2 does include 5 seconds of complete deflation within each cycle; cycle 5 involves at least one chamber always being inflated. Therefore, the composition of each of these cycles could be such that the arterial blood flow is subjected to a prolonged increase in peripheral resistance, which prevents the occurrence of a hyperaemic response during the compression period.

Following the adaptation of cycle 5 to a sequence which involved 2 minutes of compression or 6 cycles, followed by 2 minutes without compression; testing on healthy volunteers revealed that a hyperaemic response was obtained during the deflation period which extended throughout the 2 minutes without compression, whilst distal arterial blood flow decreased during the 2 minutes of compression. However, from figure 5.7 it would appear that the increase in blood flow which arises during the deflation period was greater than the

decrease in blood flow which occurred during the compression period, therefore producing an overall net increase in distal arterial blood flow during the five repetitions of the 2 minute on and off sequence.

It was also demonstrated in the graphs (figures 5.8 and 5.9) that the distal arterial response which was obtained from 10 healthy male volunteers was greater than that which was obtained for 10 healthy female volunteers, and that the distal arterial response in volunteers over the age of 25 years was greater than that for volunteers of 25 years and under. It can be concluded therefore that the greatest response was seen in the older male volunteers. However, obtaining a greater response in the older volunteers is a significant result since in general patients with leg ulcers tend to be in this age category.

A comparison of the distal venous blood flow responses which were obtained for cycles 2 and 5 revealed that cycle 5 produced a significantly greater peak velocity following the deflation of the chambers. Even though the difference between the duration, and the approximate volume of distal venous blood flow was not significant, the fact that cycle 5 always produced a result in each of the volunteers and that cycle 5 produced the greatest improvement in venous return over 600 seconds corroborates the conclusion that cycle 5 produces the optimal distal venous response with the 3-chamber thigh cuff.

It was found during the experiments on healthy volunteers that the 3-chamber thigh cuff had a tendency to slip down the leg as the cycle was progressing. This was thought to be as a result of the lining of the cuff which was quite

smooth. To prevent the cuff slipping, a new cuff was manufactured from a non slip fabric.

The next objective of the research was to investigate the effects of compression on patients with leg ulcers of varying aetiologies. It was decided as a result of the investigations on healthy volunteers, that investigations would examine the 3-chamber thigh compression garment with cycle 5 within a 2 minute on and off sequence, at a pressure of 60mmHg.

Chapter 6: Leg Ulcer Patients

6.1 Introduction

It was concluded in chapter 5 that the optimal compression system for enhancing the distal blood flow in healthy volunteers was the 3-chamber thigh garment with cycle 5 within a 2 minute on and off sequence, at a pressure of 60mmHg. In this chapter this system was investigated on patients with leg ulcers of different causes for distal arterial and venous responses, to determine whether a similar or perhaps an even greater response could be achieved as compared with the healthy volunteers.

6.2 Methods

6.2.1 Variables

The 3-chamber thigh cuff system was investigated on a number of patients with leg ulcers of arterial, venous, diabetic, mixed or other causes. The patient exclusion criteria were as follows:

- absence of vascular pathology;
- congestive heart failure;
- pulmonary oedema;
- known or suspected deep vein thrombosis (DVT) or phlebitis;
- any local condition in which the garments would interfere, such as gangrene, untreated/infected wounds, recent skin grafts, or dermatitis;
- inability to give informed consent;
- dementia.

6.2.2 Data Acquisition

Patients were recruited from West Wales General Hospital in Carmarthen, by the Vascular Surgeon Mr Locker, and the Tissue Viability Nurse Mrs James. Ethical approval had been obtained to carry out the research on patients, from the Dyfed Powys Local Research Ethics Committee. Those patients who met the inclusion and exclusion criteria were provided with an information sheet and asked to participate in the study. If the patient agreed to participate, a consent form was signed and an appointment was made for the patient to return to the hospital to partake in the investigations.

A duplex scan would have been performed prior to the patient participating in the study, by the medical physicist Dr N. Pugh; so that the vascular pathology of the patient was known, and also therefore, the cause of the ulceration.

The patient was asked to lie on the scanning couch and to remove their shoes and socks. The experimental procedure was explained to the patient prior to commencing. The 3-chamber thigh cuff was placed around the thigh of the patient, over their trousers, and Doppler ultrasound was used to locate the dorsalis pedis artery and posterior tibial vein in the patients ulcerated leg. It was not always possible to locate these two particular blood vessels dependant upon the location and severity of the patient's vascular disease, and so Doppler signals were attempted from other distal blood vessels. If, for example, an arterial signal was not possible, due to the severity of the arterial disease, venous results were obtained and the arterial experiment was abandoned.

Initially, three Flowpac pumps were used to inflate the 3-chamber thigh cuff as in previous studies; however, a single pump capable of inflating and deflating the three chambers in the specific action of cycle 5 within a 2 minute on and off sequence had been produced by Huntleigh Healthcare Ltd, and therefore some of the patients who participated in the study used the new pump, a modified version of the the Flowtron AC300-R (see chapter 2).

The tests proceeded as with the healthy volunteers. The arterial study involved recording the TAM blood flow velocity (see chapter 3.2.2) every 5 seconds throughout a test which comprised 180 seconds of resting followed by five repetitions of cycle 5 within a 2 minute on and off sequence, followed by a further 60 seconds of resting. The venous study involved recording the peak velocity and duration of distal venous blood flow following the simultaneous deflation of chambers one and two. This was repeated ten times. Photoplethysmography signals were also recorded for 10 minutes.

6.2.3 Data Analysis

The arterial results were normalised and averaged together and plotted as a line graph in SPSS. Additional graphs were plotted which compared the results obtained from the male and female volunteers, from different ulcer aetiologies and age groups.

The percentage change in distal arterial blood flow which occurred during the compression period as compared with resting blood flow pre and post compression was calculated using the computer program written in Turbo

Pascal, as in chapter 5. Non-parametric tests were performed to compare the differences between the results which were obtained for male and female volunteers, ulcers of different aetiologies and age groups.

Ten results were obtained for each volunteer for the peak velocity and the duration of distal venous blood flow following the simultaneous deflation of chambers one and two within each cycle. An approximate volume of distal venous blood moved per cycle was calculated by multiplying the duration of venous blood flow by the average maximum velocity of blood flow (TAM velocity).

The arterial and venous results which were obtained from the patient studies were also compared with those results obtained from the studies with healthy volunteers.

PPG signals were recorded for each volunteer; however, it was not possible to average the signals together. After the PPG system had calibrated, the three Flowpac pumps were started in succession in the sequence of cycle 5; however, as the pumps were started manually, there was no guarantee that the pumps were functioning at exactly the same timings for each patient. In addition, after the PPG system had calibrated, it started recording immediately, and the time at which the first pump was started after the PPG system started recording varied for each patient. Due to these reasons it was not possible to average the signals together.

6.3 Results and Discussion

6.3.1 Arterial Study

15 patients were recruited to participate in the study; however, one patient was excluded as the cuff would not fit the leg. Data was therefore collected from 14 patients with varying ulcer aetiologies.

Of the 14 patients who participated, only 7 produced results in the arterial study. The arterial study involved locating a pulsatile distal arterial signal for the QVL 120 Doppler system to be capable of calculating the TAM (time average maximum) blood flow velocity. The QVL system calculates the TAM velocity by identifying three consecutive cardiac pulses and averaging the maximum velocity envelope; however, in many of the participants, the distal arterial blood flow signal was very weak due to the degree of disease present, and therefore it was not possible to obtain the TAM blood flow velocities.

The data from the 7 patients producing a complete set of arterial results was normalised and averaged together, and plotted as a graph. The results are demonstrated in figure 6.1. The red lines correspond to the start of 2 minutes compression, while the blue lines represent the start of 2 minutes rest.

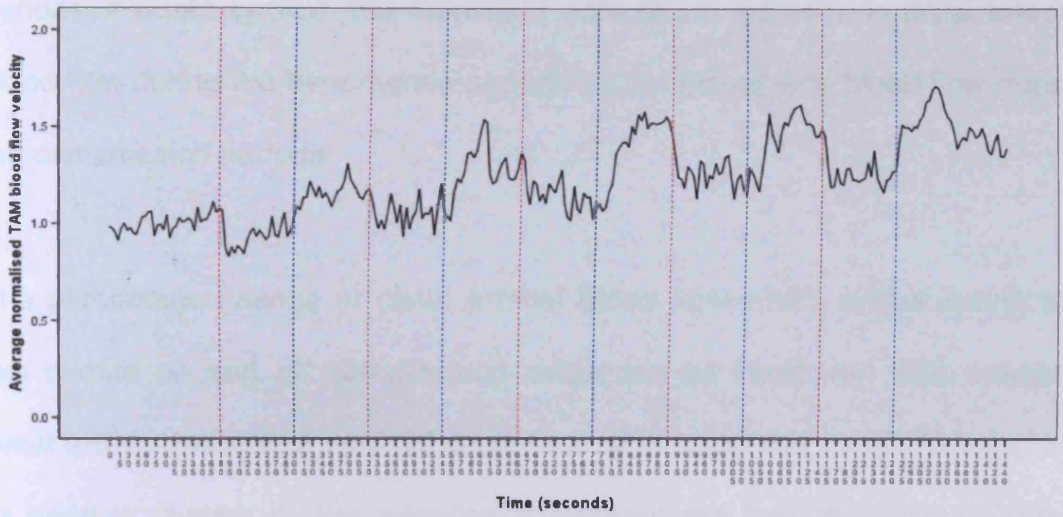


Figure 6.1 The average of the normalised distal arterial blood flow response obtained from 7 patients with ulcers of differing aetiologies, during compression with the 3 chamber thigh cuff, using cycle 5 within a 2 minute on and off sequence and a pressure of 60mmHg.

This graph displays a very similar trend to figure 5.7, which represents the average normalised distal arterial blood flow response obtained from 20 healthy volunteers. The distal arterial blood flow decreases during the compression periods, followed by a hyperaemia when compression is released. A Wilcoxon signed ranks test was performed to compare the patients' average distal arterial blood flow during the compression periods with the average hyperaemic blood flow arising during the resting periods. The test showed that the difference between the patients' average normalised distal arterial blood flow during the compression period (M = 1.135993028, SD = 0.14760281) and during the hyperaemic period (M = 1.358141807, SD = 0.182939295) was significant beyond the .01 level: exact $p < .005$ (two-tailed). From the mean values calculated during the compression and hyperaemic

periods, it would appear that there is a 20% (2 s.f) increase in distal arterial blood flow during the hyperaemic periods as compared with blood flow during the compression periods.

The percentage change in distal arterial blood flow which arises during the two minute on and off compression sequence as compared with baseline distal arterial blood flow was calculated using the adapted computer program as used in chapter 5. The baseline is extrapolated from the data collected during the three minutes prior to the commencement of the compression sequence, and the final 30 seconds of the signal. The average percentage change in the patients' distal arterial blood flow was calculated to be 4.76%; which implies that there is an overall net increase in distal arterial blood flow during the treatment period as compared with baseline distal arterial blood flow, even though blood flow decreases during each two minutes of compression. As previously mentioned, the results produced by this program should be interpreted with care; however, it is evident from figure 6.1 that distal arterial blood flow is improving with treatment progression, and hence the result calculated by the computer program substantiates the findings displayed in the graph.

Figure 6.2 compares the results obtained from the patients with those obtained from the healthy volunteers.

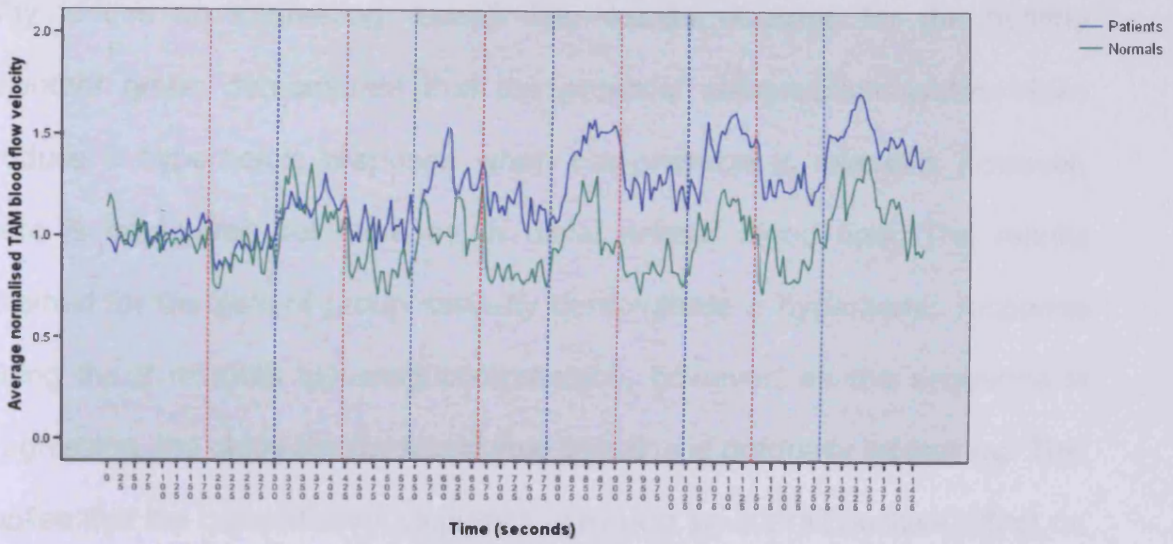


Figure 6.2 A comparison of the average normalised distal arterial blood flow response which was obtained from 20 healthy volunteers and 7 patients with leg ulcers of differing aetiologies, as a consequence of compressing the limb proximally with the 3 chamber thigh cuff, using cycle 5 within a 2 minute on and off sequence.

In figure 6.2, both graphs demonstrate a decrease in distal arterial blood flow during the 2 minutes of compression and an increase during the 2 minutes rest; a hyperaemia occurring in response to the release of compression. The hyperaemic responses appear to be of a comparable size and duration, as also do the reductions in blood flow which occur during compression. There is however one interesting difference between the results obtained from the two different groups of participants. Initially the two graphs seem to be overlapping, whilst as time progresses the graphs begin to diverge; the results for the healthy volunteer group remain level, whilst the results for the patient group are gradually rising, there being an overall upwards trend.

Why is this an interesting result? The results obtained for the healthy volunteer group demonstrate that the proximal compression system does produce a hyperaemic response when compression is released; however, there is no overall net increase in distal arterial blood flow. The results obtained for the patient group similarly demonstrate a hyperaemic response during the 2 minutes following compression, however, as the sequence is progressing, the distal arterial blood flow baseline is gradually increasing. This implies that the compression sequence is having an overall positive effect on distal arterial blood flow in patients, increasing the distal supply of blood to the tissues. It is possible that the same effect is not demonstrated in the results obtained from the healthy volunteers as they could already have optimal arterial blood flow, as compared with the patients who could be subject to reduced blood flow, and therefore there is 'room for improvement'.

A Mann-Whitney U test demonstrated that the difference between the overall results obtained for the patient group (M = 1.224454561, SD = 0.205154431) and those obtained for the healthy volunteer group (M = 0.985320978, SD = 0.154852673) was significant beyond the .01 level: exact $p < .005$ (two-tailed).

The following table (table 6.1) provides information on the patients who participated in the study.

Patient	Gender	Ulcer	Age	Smoker
1*	M	Diabetic	39	No
2*	M	SLE	60	No
3	M	Mixed	77	No
4*	M	Venous	75	No
5*	F	Venous	72	Yes
6	F	Arterial	69	No
7	M	Diabetic	81	No
8*	M	Arterial	78	No
9	F	Arterial	82	history of
10	M	Mixed	67	history of
11*	F	Venous	73	No
12	M	Arterial	72	No
13*	F	SLE	73	No
14	M	Arterial	73	No

Table 6.1 Information on those patients who participated in the study. Patients marked with an asterisk produced complete arterial results. SLE is an acronym for Systemic Lupus Erythematosus.

The data in table 6.1 is summarised in table 6.2.

	Male	Female	Total
Total	9	5	14
Smoker:			
Current	0	1	1
History of	1	1	2
Ulcer Aetiology:			
Arterial	3	2	5
Venous	1	2	3
Mixed	2	0	2
Diabetic	2	0	2
SLE	1	1	2
Age Group:			
≤ 60 yrs	2	0	2
61 – 70 yrs	1	1	2
71 – 80 yrs	5	3	8
81 – 90 yrs	1	1	2

Table 6.2 A summary of the patients who participated in the study.

The graphs below compare the results which were obtained from different groups of patients; gender, ulcer type and age.

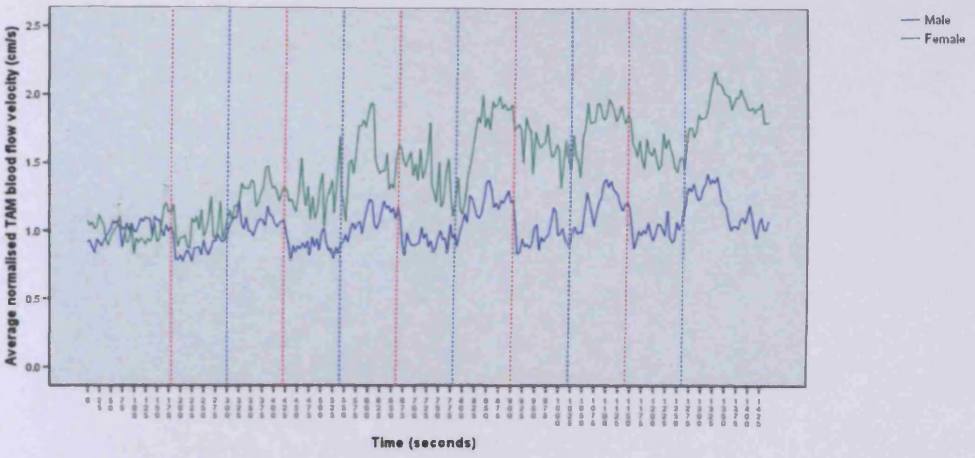


Figure 6.3 A comparison of the average normalised TAM blood flow velocities obtained from male and female patients with leg ulcers of varying aetiologies, whilst receiving compression with the 3-chamber thigh cuff, using cycle 5 within a 2 minute on and off sequence and a pressure of 60mmHg.

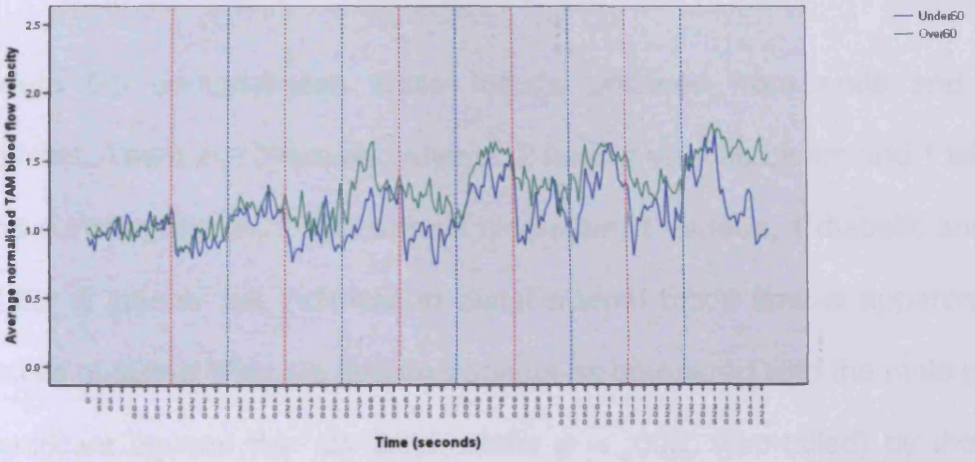


Figure 6.4 A comparison of the average normalised TAM blood flow velocities obtained from patients with leg ulceration of varying aetiologies of age 60 years and under, and over 60 years, whilst receiving compression with the 3-chamber thigh cuff, using cycle 5 within a 2 minute on and off sequence, and a pressure of 60mmHg.

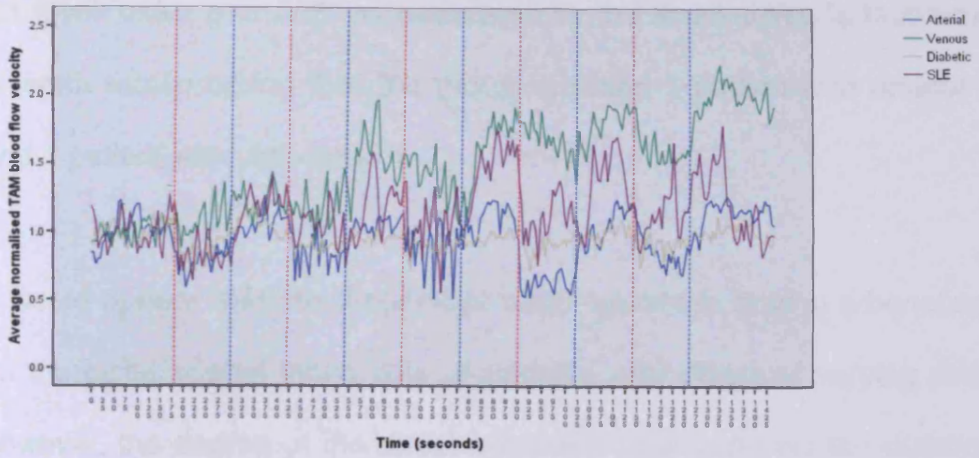


Figure 6.5 A comparison of the average normalised TAM blood flow velocities obtained from patients with leg ulcers of arterial, venous, diabetic and SLE ulcers, whilst receiving compression with the 3-chamber thigh cuff, using cycle 5 within a 2 minute on and off sequence, and a pressure of 60mmHg.

Figure 6.3 demonstrates those results obtained from male and female patients. There are 3 female patients, 2 having venous ulcers and 1 with SLE, and 4 male patients, 1 with arterial ulceration, 1 venous, 1 diabetic and 1 with SLE. A greater net increase in distal arterial blood flow is apparent in the results obtained from the female patients as compared with the male patients; significant beyond the .01 level: exact $p < .005$, (two-tailed) by the Mann-Whitney U test. This difference is likely to be as a result of ulcer aetiology, rather than gender, as demonstrated in figure 6.5. It can be seen that patients with venous pathology produce the greatest distal arterial response (possibly since there is no arterial disease), followed by patients with SLE, arterial disease and finally diabetes. The difference between the distal arterial responses obtained for the varying ulcer aetiologies are significant beyond the

.01 level: exact $p < .005$, as calculated by the Kruskal-Wallis test; however, it is worth remembering that the group included 1 patient with arterial disease and 1 patient with diabetes.

It would appear that the 3-chamber thigh system is having a beneficial effect on the distal arterial blood flow of patients with ulcers of varying aetiologies; however, the degree of the distal response observed over the duration of the study, depends upon the degree of arterial pathology.

6.3.2 Venous Study

Studies were also conducted to determine the effect of the 3-chamber thigh system on distal venous blood flow in patients with leg ulceration of varying aetiologies. 13 out of the 14 patients who participated in the study produced a complete set of venous results. It was not possible to locate a distal venous signal in one of the patients with venous disease. The patient had had a left leg below knee amputation many years ago and was suffering from circumferential venous ulceration in the right leg. The extent of the venous disease prevented a distal venous signal being located.

As with the healthy volunteers, accelerated distal venous blood flow was observed following the simultaneous deflation of the first and second chambers of the 3-chamber thigh cuff. 10 measurements of the peak velocity and duration of distal venous blood flow were recorded for each of the patients. The results were entered into SPSS, and comparisons were performed with those results which had been obtained from the healthy

volunteers. Figures 6.6 and 6.7 display the results obtained for patients and healthy volunteers for peak distal venous blood flow velocity and duration of distal venous blood flow following the simultaneous deflation of the first and second chambers.

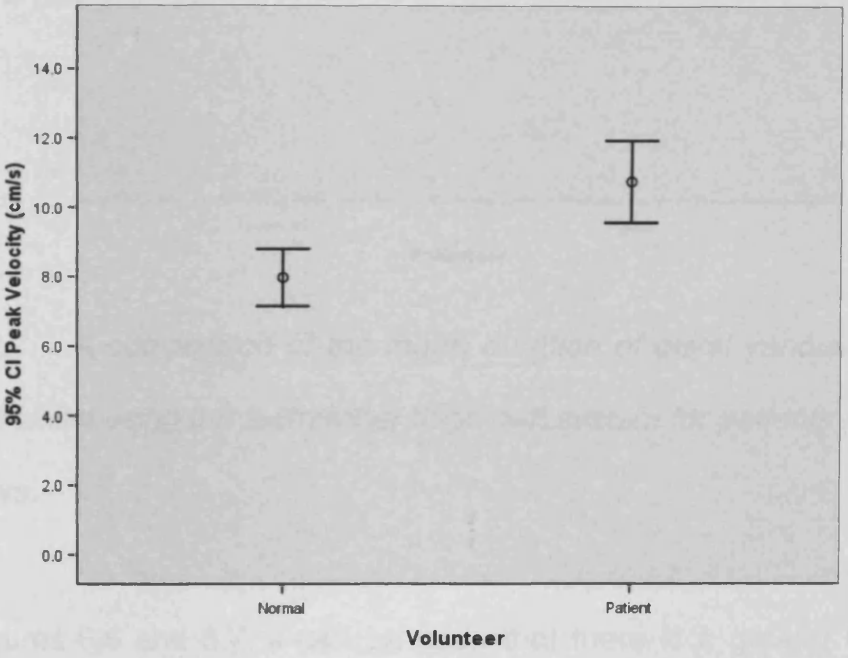


Figure 6.6 A comparison of the mean peak distal venous blood flow velocities obtained whilst using the 3-chamber thigh cuff system for patients and healthy volunteers.

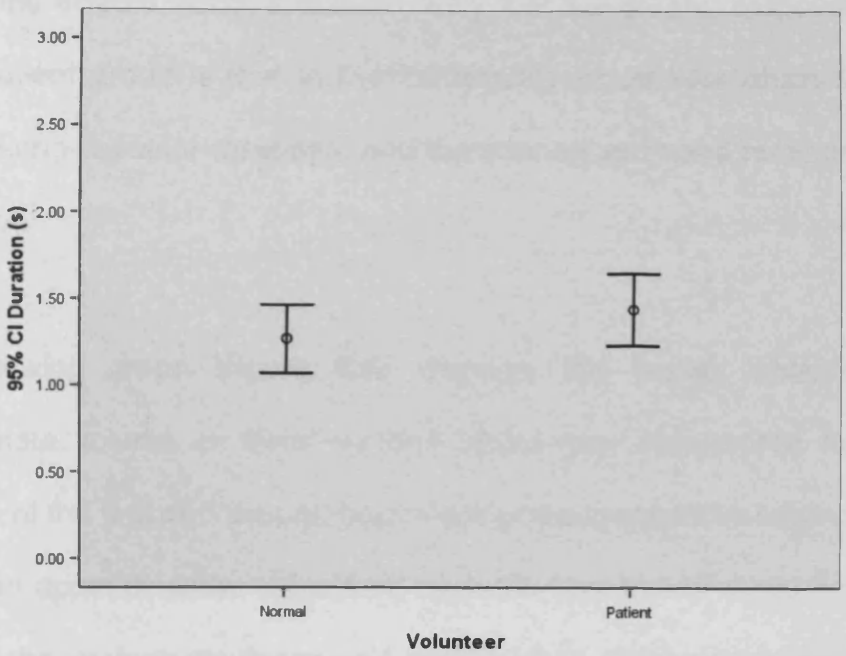


Figure 6.7 A comparison of the mean duration of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for patients and healthy volunteers.

From figures 6.6 and 6.7, it can be seen that there is a greater increase in distal venous blood flow in the patient group as compared with the healthy volunteer group. The Mann-Whitney U test showed that the difference between the mean peak distal venous blood flow velocity for the patient group (M = 10.754 cm/s; SD = 7.0843 cm/s) and for the healthy volunteer group (M = 7.971 cm/s; SD = 5.9367 cm/s) was significant beyond the .01 level: exact $p < .005$ (two-tailed); and similarly, the difference between the mean duration of distal venous blood flow for the patient group (M = 1.4431 s; SD = 1.25256 s) and for the healthy volunteer group (M = 1.2684 s; SD = 1.42048 s) was significant beyond the .01 level: exact $p = 0.001$ (two-tailed).

As with the arterial study, it is quite likely that the greater response observed in the patient group is due to the inadequate blood flow which results from their differing vascular diseases, and the consequent need for improved blood circulation.

The following graph (figure 6.8) displays the results obtained for the approximate volume of distal venous blood flow accelerated following the deflation of the first and second chambers of the 3-chamber thigh cuff system. This is an approximation, calculated from the duration of distal venous blood flow and the average maximum velocity (TAM) of distal venous blood flow.

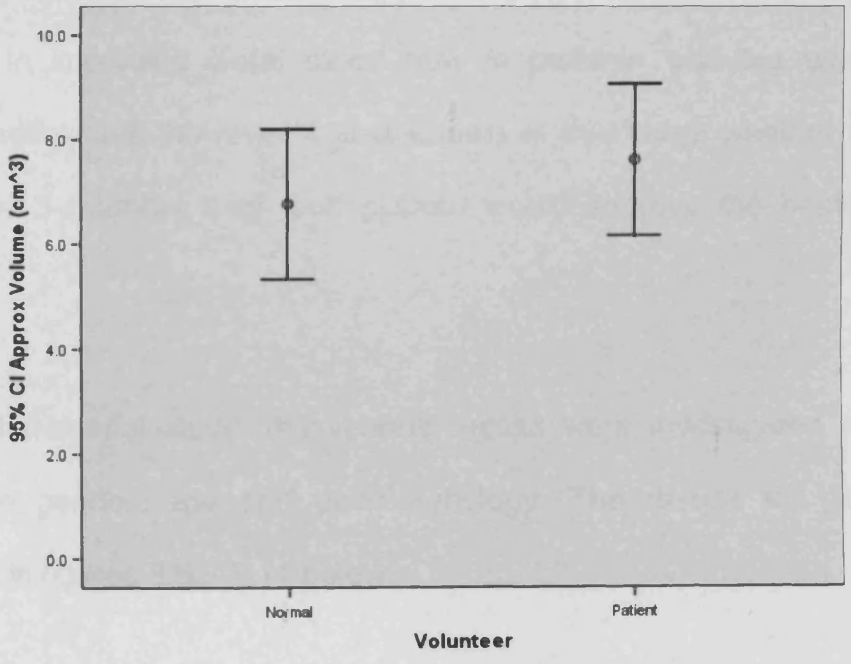


Figure 6.8 A comparison of the mean approximate volume of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for patients and healthy volunteers.

The graph demonstrates that there is a greater improvement in the approximate volume of distal venous blood flow in the patient group as compared with the healthy volunteers; which is confirmed by a Mann-Whitney U test showing that the difference between the patient group (M = 7.61007 cm^3; SD = 8.695838 cm^3) and the healthy volunteers group (M = 6.76105 cm^3; SD = 10.325796 cm^3) is significant beyond the .05 level: exact p = 0.026 (two-tailed).

Therefore, there is a significant improvement in the distal venous blood flow response associated with the use of the 3-chamber thigh cuff system in patients with circulatory disorders, as compared with the healthy volunteers. This is an excellent result, seemingly satisfying one of the objectives of the research in improving distal blood flow in patients with leg ulceration of differing aetiologies; however it is unknown at this stage whether long term use of the 3-chamber thigh cuff system would improve the healing of the ulcer.

As with the arterial study, the venous results were investigated for effects relating to gender, age and ulcer aetiology. The results for gender are displayed in figures 6.9 – 6.11 below.

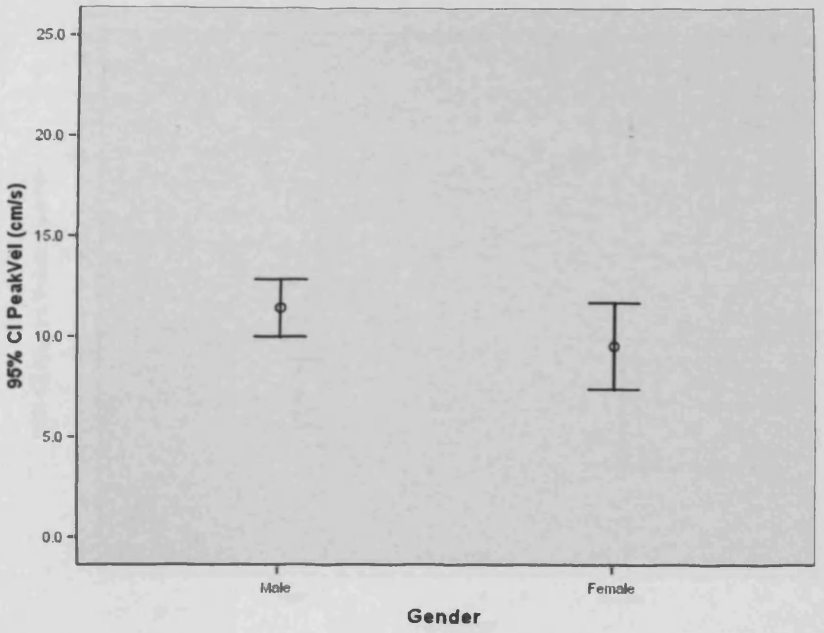


Figure 6.9 The mean peak distal venous blood flow velocity obtained whilst using the 3-chamber thigh cuff system for male and female patients with leg ulcers of varying aetiologies.

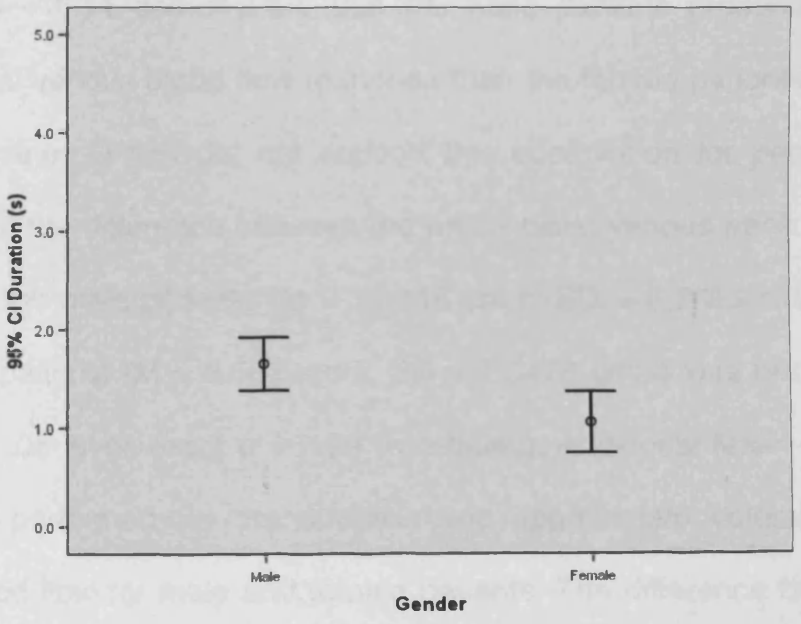


Figure 6.10 The mean duration of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for male and female patients with leg ulcers of varying aetiologies.

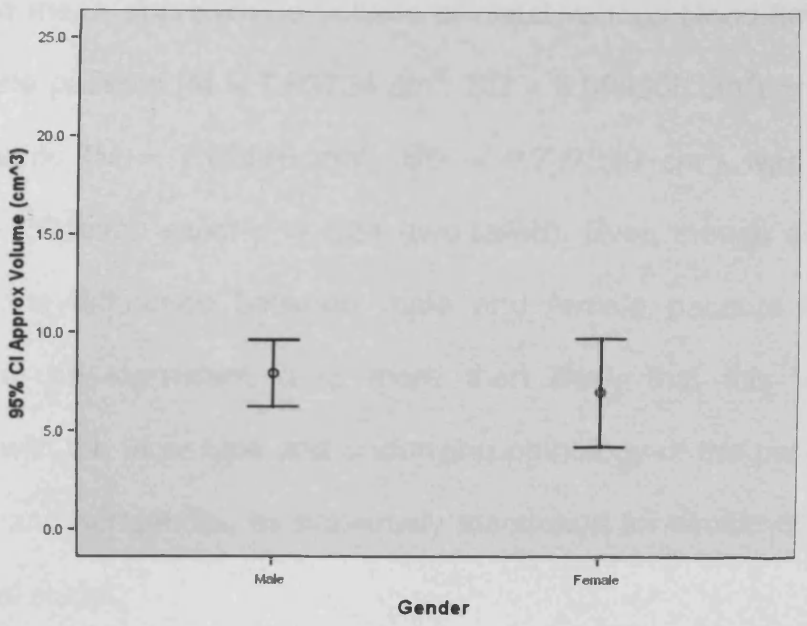


Figure 6.11 The mean approximate volume of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for male and female patients with ulcers of varying aetiologies.

Figures 6.9 – 6.11 demonstrate that the male patients produce a slightly greater distal venous blood flow response than the female patients; however, a Mann-Whitney U test did not support this observation for peak velocity, showing that the difference between the mean distal venous peak blood flow velocity for the male patients (M = 11.416 cm/s; SD = 6.7658 cm/s) and for the female patients (M = 9.562 cm/s; SD = 7.5478 cm/s) was not significant beyond the .05 level: exact p = .199 (two-tailed). Additional Mann-Whitney U tests were performed for the duration and approximate volume of distal venous blood flow for male and female patients. The difference between the mean duration of distal venous blood flow for male patients (M = 1.6552 s; SD = 1.29117 s) and the female patients (M = 1.0614 s; SD = 1.09143 s) was significant beyond the .01 level: exact p < .005 (two-tailed); and the difference

between the mean approximate volume of distal venous blood flow obtained from the male patients (M = 7.93724 cm^3; SD = 8.099008 cm^3) and from the female patients (M = 7.02116 cm^3; SD = 9.737379 cm^3) was significant beyond the .05 level: exact p = .024 (two-tailed). Even though some of the results for the difference between male and female patients have been calculated to be significant, it is more than likely that this variation is associated with the ulcer type and underlying pathology of the patients within each group and not gender, as previously mentioned for similar comparisons in the arterial study.

The following three graphs (figures 6.12 – 6.14) demonstrate the results obtained for the comparison of results obtained from different age groups.

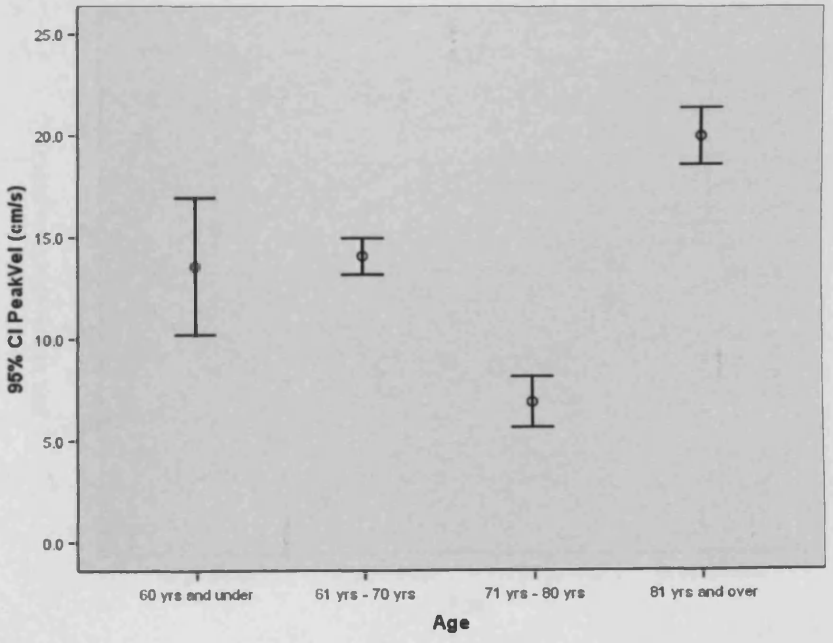


Figure 6.12 A comparison of the mean peak distal venous blood flow velocity obtained using the 3-chamber thigh cuff system for leg ulcer patients of different age groups.

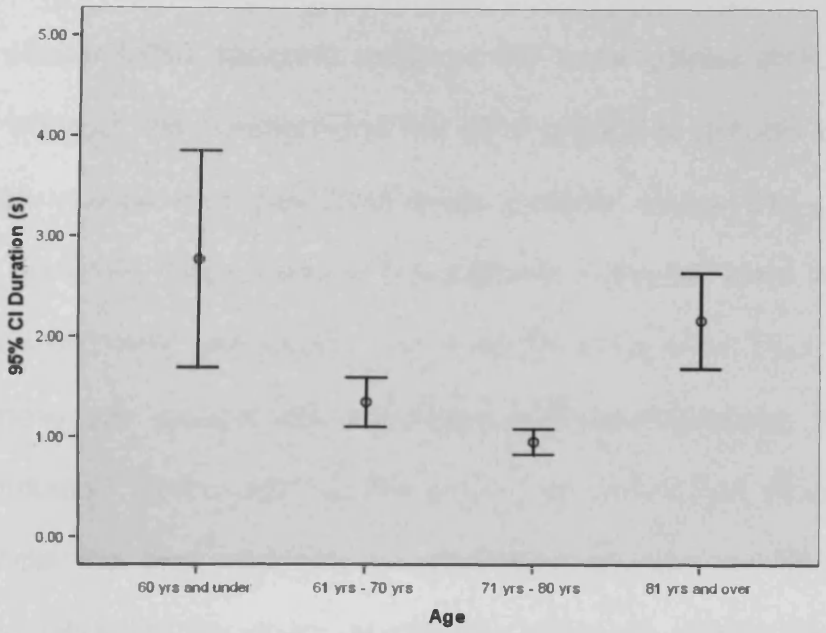


Figure 6.13 A comparison of the mean duration of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for leg ulcer patients of different age groups.

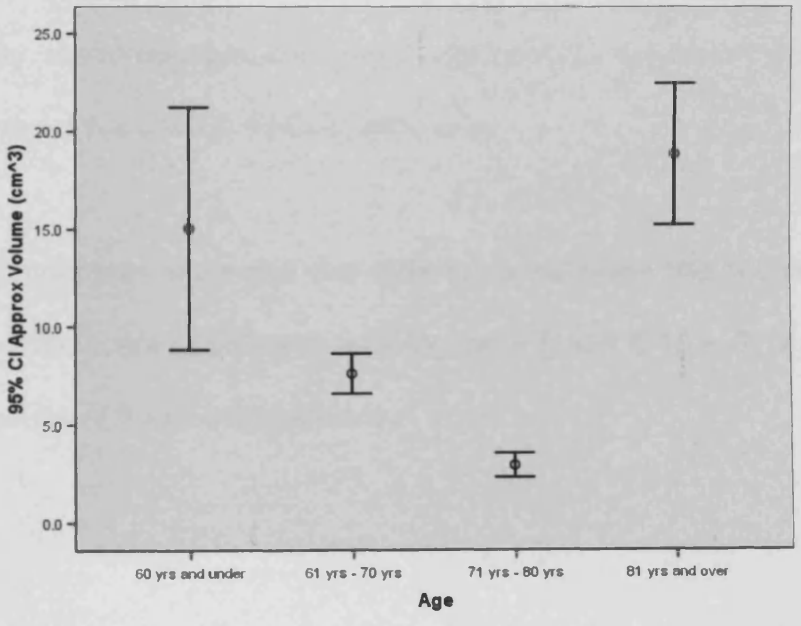


Figure 6.14 A comparison of the mean approximate volume of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for leg ulcer patients of different age groups.

There is a similar trend apparent amongst the three graphs above (figures 6.12-6.14), whereby the younger and the older groups of patients produce a greater distal venous response than those patients in the 61 – 80 years categories. However, there are only two patients in the 60 years and under, and 81 years and over categories, and in addition, the error bars are much larger for these age groups; any significant difference between the results which is attributed to the age of the patient is considered to be slightly dubious, whilst the true variance is considered to be, as with previous comparisons, related to the variety of vascular diseases present amongst the patients.

A Kruskal – Wallis test demonstrated that there was a significant difference between the results obtained for patients of different age groups for mean peak velocity, mean duration and mean approximate volume of distal venous blood flow: exact $p < .005$ in each comparison.

The final comparison examines the difference between the results obtained for patients with ulcers of different aetiologies. Figures 6.15 – 6.17 display the graphical results of these comparisons.

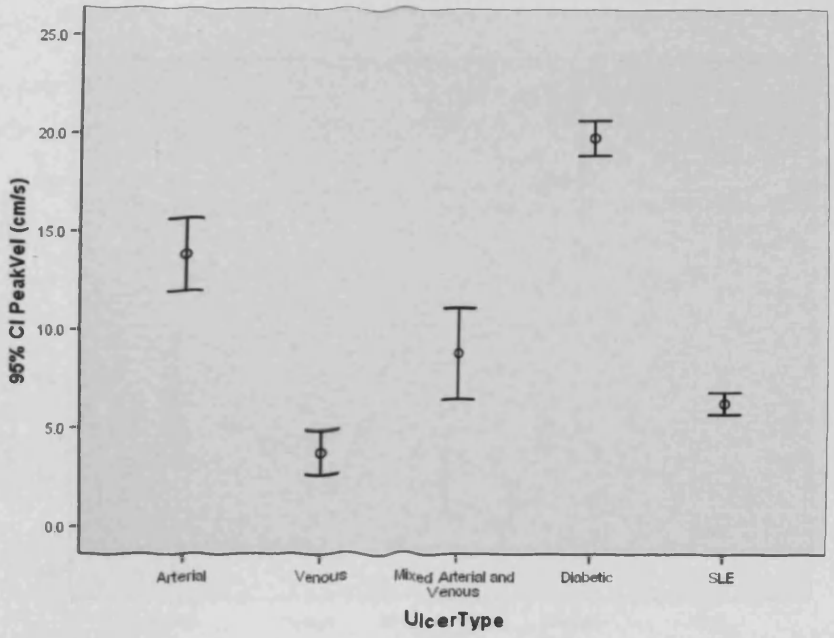


Figure 6.15 A comparison of the mean peak distal venous blood flow velocities obtained whilst using the 3-chamber thigh cuff system for patients with leg ulcers of different aetiologies.

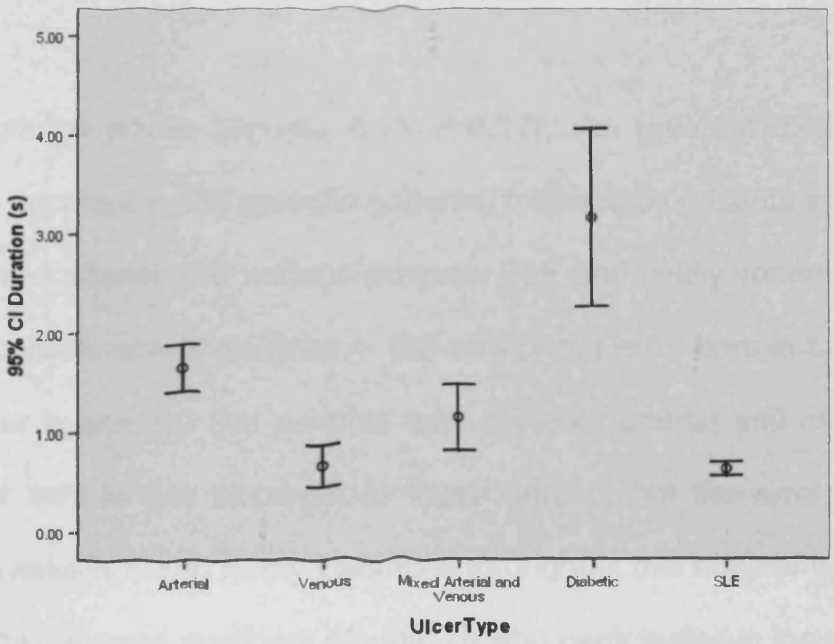


Figure 6.16 A comparison of the mean duration of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for patients with leg ulcers of different aetiologies.

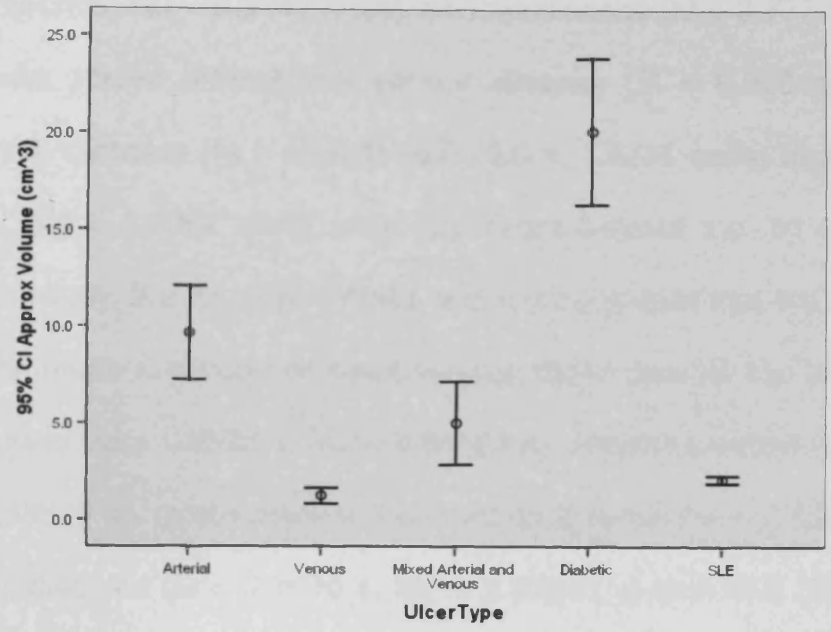


Figure 6.17 A comparison of the mean approximate volume of distal venous blood flow obtained whilst using the 3-chamber thigh cuff system for patients with leg ulcers of different aetiologies.

From the graphs above (figures 6.15 – 6.17), the greatest distal venous response is apparent in the diabetic patients, followed by patients with arterial disease, mixed arterial and venous disease, SLE and finally venous disease. There is a considerable difference in the size of the error bars in the graphs, being greater in size for the patients with diabetic, arterial and mixed ulcer causes. Not only is this apparent in these graphs, but the error bars and standard deviations are in many instances throughout this chapter quite large. This is due to the small numbers of patients who participated in the study; it is hoped that with greater repetition of the tests, the error bars would reduce in size. A Kruskal Wallis test showed that the differences between the mean peak velocities of distal venous blood flow for the patients with arterial disease

(M = 13.838 cm/s; SD = 6.5047 cm/s), venous disease (M = 3.777 cm/s; SD = 3.0144 cm/s), mixed arterial and venous disease (M = 8.830 cm/s; SD = 5.0016 cm/s), diabetes (M = 19.870 cm/s; SD = 1.9271 cm/s) and SLE (M = 6.315cm/s; SD = 1.1962 cm/s) were significant beyond the .01 level: exact $p < .005$. Similarly, the Kruskal – Wallis test demonstrated that the differences between the mean durations of distal venous blood flow for the patients with arterial disease (M = 1.6576 s; SD = 0.84093 s), venous disease (M = 0.6720 s; SD = 0.55579 s), mixed arterial and venous disease (M = 1.1525 s; SD = 0.70914 s), diabetes (M = 3.1670 s; SD = 1.92001 s) and SLE (M = 0.6305; SD = 0.14515 s) were also significant beyond the .01 level: exact $p < .005$; as were the differences between the mean approximate volumes of distal venous blood flow for patients with arterial disease (M = 9.66548 cm^3; SD = 8.465911 cm^3), venous disease (M = 1.23960 cm^3; SD = 1.084768 cm^3), mixed arterial and venous disease (M = 5.01255 cm^3; SD = 4.652516 cm^3), diabetes (M = 20.13485 cm^3; SD = 8.085907 cm^3) and SLE (M = 2.10000 cm^3; SD = 0.397222 cm^3): exact $p < .005$.

Different degrees of distal blood flow response are to be expected amongst patients with different vascular conditions; it is of no surprise that those patients without any venous disease should produce a more pronounced distal venous response than patients with significant venous pathology, and similarly with the arterial study, the greatest distal arterial response was detected in patients with no signs of arterial disease, but with venous disorders. What is of importance is that a distal arterial and venous response was identified in patients with each of the different vascular diseases

addressed in the study. The objective of the research was to optimise an intermittent pneumatic compression technique for the improvement of vascular inflow and outflow proximal to the site of a leg ulcer of varying cause; therefore, from the results demonstrated in this chapter, it can be seen that the 3-chamber thigh cuff system does improve the distal arterial and venous blood flows in the legs of patients with leg ulcers of arterial, venous, diabetic, SLE and mixed aetiologies; the ultimate intention is that with long term use of the system an improvement in the healing of the ulcer will transpire.

PPG (photoplethysmography) signals were recorded from each of the patients, however; it was not possible to average the signals together as the start times varied. Examples of the signals obtained are shown in figures 6.18 and 6.19.

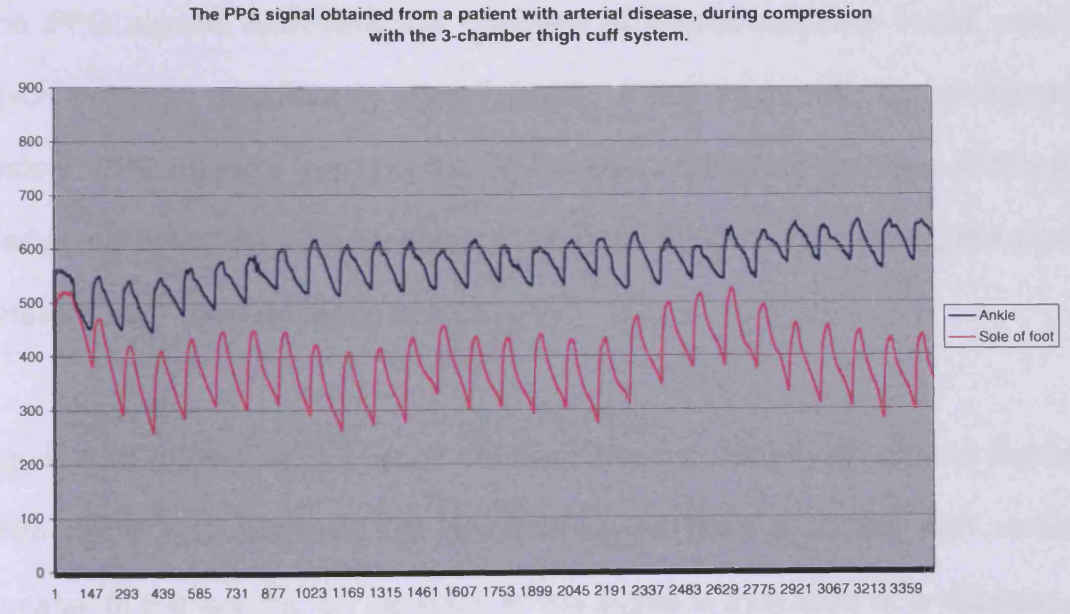


Figure 6.18 The PPG signal associated with the use of the 3-chamber thigh cuff system, from a patient with arterial disease.

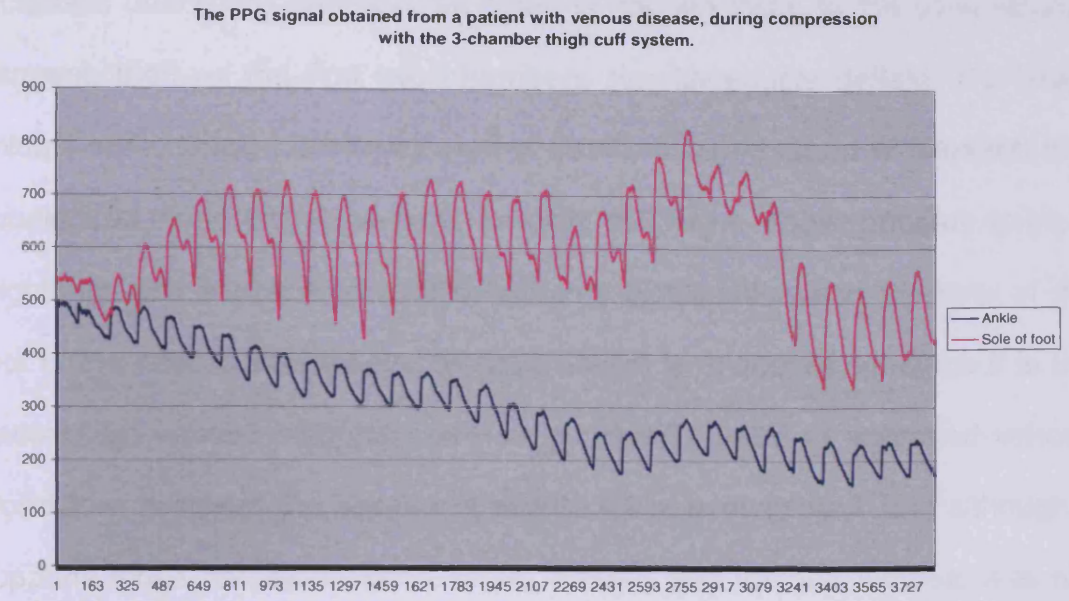


Figure 6.19 The PPG signal associated with the use of the 3-chamber thigh cuff system, from a patient with venous disease.

The PPG signals represent the changes in microcirculatory blood volume which occur in response to compression of the thigh with the 3-chamber system. PPG sensors were placed on the sole of the foot and also above the medial malleolus; the pink and blue lines in the figures representing the signal obtained from each location respectively.

Figure 6.18 represents the result obtained from a patient with arterial disease while figure 6.19 displays the result obtained from a patient with venous disease. In the graphs, an increase in the signal is indicative of a decease in microcirculatory blood volume, whilst a decrease in the signal represents an increase in microcirculatory blood volume. The shape of both signals, from each location are very similar; microcirculatory blood volume gradually

increases during compression, as blood is trapped distal to the compression garment, then as the first two chambers simultaneously deflate, the blood volume immediately decreases as the distally trapped blood is released and accelerated along the veins back towards the heart. There appears to be a slightly greater variation in microcirculatory blood volume in the sole of the foot of the patient with venous disease, which is encouraging, since it is the patient with venous pathology who is in greatest need of improved venous blood flow; however, this result represents a single individual, and although it supports those results obtained in the arterial and venous studies, it is not representative of the group as a whole.

6.4 Conclusions for Investigations with Patients

This chapter has examined the distal blood flow response associated with the use of the 3-chamber thigh cuff system in patients with leg ulcers of different causes. The results have been very encouraging; it would appear that the use of the 3-chamber thigh cuff system does instigate an improvement in distal blood flow in patients with leg ulcers. The distal arterial response comprises a reduction in blood flow during the two minutes of compression, which is followed by a hyperaemic response during the two minutes of rest. In this way, the distal arterial response obtained in the patient group was identical to that observed in the healthy volunteer group; however, an overall rising trend was also apparent in the distal arterial response recorded from the patients, whereby the baseline seemed to be increasing with the progression of the sequence, signifying a gradually increasing supply of blood to the distal tissues. This difference was attributed to the patients' deficient blood flow associated with their different vascular diseases, and their subsequent need for improved blood flow, as opposed to normal blood flow in the healthy volunteers. The distal venous blood flow response was similar to the response demonstrated in the healthy volunteers, accelerated venous return following the simultaneous deflation of the first two chambers of the cuff, however, the average response recorded from the patient group was greater than the average response recorded from the healthy volunteer group, possibly for similar reasons to those proposed for the difference between the arterial studies.

Patient recruitment proved to be a challenging aspect of the research. Patients with leg ulceration tend to be elderly; in this study, the mean patient age was 71 years (to the nearest year). It was found that patients did not want to make separate journeys to the hospital to participate in the study due to their age and consequent reduced mobility, and also due to the weather during the winter months; however, due to a lack of available rooms at the hospital, it was not possible to conduct the study at the time of their initial appointment with the vascular surgeon. Another factor which excluded a number of patients was the size of the cuff. According to the tissue viability nurse at WWGH, there were a number of leg ulcer patients eligible to participate in the study who were prevented from doing so due to the size of the cuff. The cuff being used in the study allowed for a range of limb circumferences; however, it would not fit those patients who were overweight / obese.

Due to the limited number of patients recruited from WWGH, additional research sites were included in the study. Prince Philip Hospital in Llanelli contributed some patients to the study, as also did Saundersfoot Medical Health Centre. Apart from the problems encountered with recruitment, the patient study did not pose any other major difficulties.

The patient study is the culmination of the work which preceded in the other chapters. Extensive preliminary investigations on a single healthy volunteer provided insight into the effects of altering the pressure, inflation and deflation durations and cuff design of intermittent pneumatic compression on the distal

haemodynamics of the individual. A new cuff design resulted from these initial experiments, which was tested firstly on a group of healthy volunteers, and finally on the target users; the leg ulcer patients of this chapter.

Going back to chapter 1 and the research proposals, it would appear that the objectives have been satisfied, in so far as a proximal intermittent pneumatic compression technique has been optimised for simultaneously improving distal arterial and venous blood flows in patients with leg ulcers. There were two new aspects to this research, which have never been addressed prior to this study; namely, the use of thigh only compression for improving distal blood flow, and the use of a single compression technique for simultaneously improving distal arterial and venous blood flows, each of which have been demonstrated through the studies completed to be successful in achieving their aims. It would appear that proximal compression could be implemented as a viable alternative in those instances where whole leg or calf compression is not possible, and distal arterial and venous blood flows can both be improved using a single intermittent pneumatic compression system.

The implications of the results which have been achieved are very encouraging. A system capable of improving both distal arterial and venous blood flows, which therefore would be applicable to the majority of patients with chronic non-healing leg ulcers; which is easy for the patient to use; does not require the ulcer to be covered, minimising discomfort and therefore aiding patient compliance; and has the potential to improve the healing of chronic leg ulcers with long term use. When asked, patients recruited in this study

assured that the system was very comfortable, whilst the sequential action of the cycle was 'therapeutic'.

In order to complete the research, a small number of case studies were carried out to investigate the long term use of the 3-chamber thigh cuff system, the effects on ulcer healing and the practicalities of using the system in the home environment. The case studies are described in the next and final chapter.

Chapter 7: The Home Study

7.1 Introduction

In previous chapters, the distal haemodynamic effects of various compression garments and operating regimes have been investigated in order to determine the optimal compression system for enhancing distal blood flow, ultimately for treating and managing chronic leg ulcers. It was determined that the 3-chamber compression garments produced a greater distal response than the uniform compression garments. A decision then had to be made as to which of the three chamber garments should be further investigated on healthy volunteers and patients; the 3-chamber thigh garment produced a greater distal arterial response whilst the 3-chamber whole leg garment produced a greater distal venous response. It was concluded that the 3-chamber thigh garment would be more agreeable to the patient, as it would not interfere with the wound site, since leg ulceration is generally below the knee; and the 3-chamber thigh garment would also be easier for the patient to use in the home environment. The 3-chamber thigh garment was therefore investigated on a group of healthy volunteers, comparing the effects of two different cycles. Cycle 5 was demonstrated to be the optimal compression sequence; however, due to a decrease in distal arterial blood flow arising during compression and a hyperaemia occurring when compression ended, the cycle was adapted slightly to allow for the hyperaemic response to occur. Cycle 5 was consequently operated within a 2 minute on and off sequence. This final compression regime was investigated for distal arterial and venous effects on

a number of healthy volunteers, and a group of patients with leg ulcers of different causes, where improved distal circulation was observed during the studies. It now remains to be determined whether any clinical benefits are achievable as a consequence of using the 3-chamber thigh cuff system over an extended period of time. Therefore, a home study was proposed which would involve patients taking a 3-chamber thigh cuff system home with them for daily use over approximately 3 months, in order to assess the clinical benefits of the compression system and also to assess the practicalities of using the compression system in the home environment.

7.2 Equipment

Previously, the 3-chamber thigh cuff has been operated with three Flowpac pumps, one pump per chamber. It was not deemed practical for patients to take three Flowpac pumps home with them as they are not only bulky and heavy, but their use would require the patient to accurately start the pumps at the specific timings of cycle 5.

A new pump was developed by Huntleigh Healthcare which allowed the 3-chamber thigh cuff to be operated by a single pump, and which only required the patient to press start and stop. The pump, an adapted Flowtron AC300-R, performed the compression sequence of cycle 5, as described in chapter 2.

7.3 The Case Studies

7.3.1 Introduction

Although a number of patients were identified to be suitable to participate in the home study, consent was difficult to obtain. Agreeing to participate did involve a high level of commitment on the patients' part, and therefore perhaps for further trials with the system, some form of incentive might be required. However, two patients did consent to take a 3-chamber thigh cuff system home with them for the 3 month period.

Ethical approval had been obtained to conduct the trial, from the Dyfed Powys Local Research Ethics Committee.

7.3.2 Case Study 1

The first patient was recruited from WWGH by the Tissue Viability Nurse. The details of the study were explained to the patient, and a consent form was signed. The patient was male, aged 77, and was a non-smoker of average height and weight. From here on the patient will be referred to as Mr H.

The patient presented with an ulcer on the right foot of uncertain aetiology. It was suggested that the ulcer could have been caused as a result of both arterial and venous pathologies. Mr H described 'excruciating' pain after getting out of bed.

A duplex scan of the right leg, performed a week prior to start of the study demonstrated a 'short segment CFA (common femoral artery) occlusion, very diseased SFA (superficial femoral artery)', whilst examination of the veins revealed 'gross SFJ / I (sapheno-femoral junction incompetence) only'. ABPI of the right leg was 0.55.

Mr H was not eligible for reconstructive surgery due to a previous mitral valve replacement. The mechanical mitral valve has a tendency to cause blood clots, which could lead to a stroke if they are dislodged and travel in the circulation; it is therefore necessary for Mr H to take warfarin on a regular basis in order to prevent the occurrence of a clot. For Mr H to have arterial reconstructive surgery he would have to stop taking the warfarin and take heparin, increasing the risk of a stroke.

Mr H was willing to try anything that could help heal the ulcer and relieve the unbearable pain that he was experiencing. He was therefore provided with a cuff and pump, an instruction sheet and contact telephone numbers and shown how to use the equipment. Pictures were taken of his ulcer for comparative purposes.

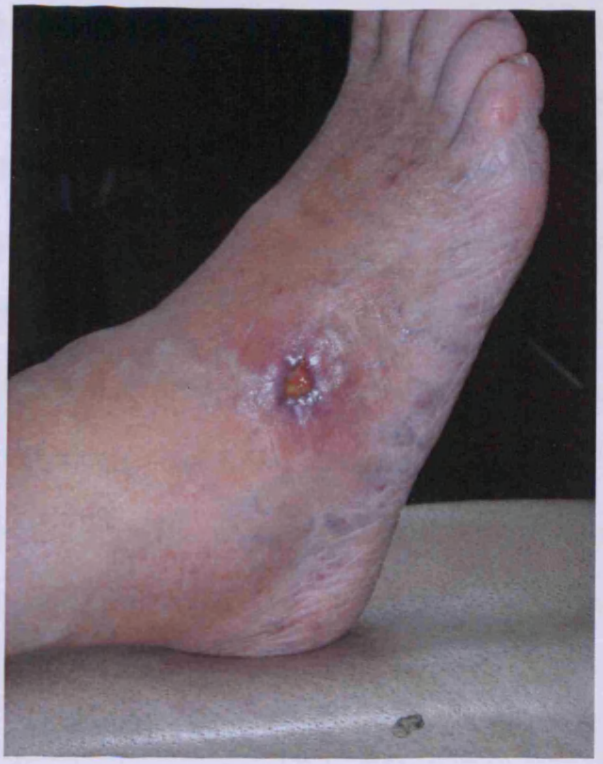


Figure 7.1 Ulcer of mixed aetiology of Mr H. at the start of the home study.

A week later a phone call was made to Mr H to check on his progress. Mr H was happy with the equipment and had been using it daily for the last week. He had been using the pump for approximately 3 hours every day during the first week, which was not as long as he would have liked but he had been very busy. He was hoping to be able to increase the amount of usage over the next few weeks. He noted that he had not encountered any difference in his ulcer or pain level as yet, and queried when it might be expected to notice a change. He was informed that it was difficult to know when to first expect a change, but that maybe after a few more weeks he may start to encounter an improvement. Mr H appeared very committed to the study, and was hopeful that using the system would reduce his pain.

About a month later a phone call was received from Mr H to say that he had not been doing very well with the system. After the first conversation, he had continued to use the cuff and pump, until his foot started swelling. He stopped using the equipment, and the other foot also became swollen. It took a long time for the swelling to reduce. The swelling was not considered to be as a result of the compression system since it was present in both legs; therefore, it was likely to be as a result of infection, or related to his pre-existing heart condition. Once he felt that he was ready to recommence compression, he developed shingles, and was quite unwell. At the time of the conversation he was beginning to recover, and was hopeful that he would be able to slowly start compression again within a weeks' time.

At the completion of the 3 month period, Mr H was contacted to organise an appointment for returning the equipment and to see whether he had had any success with the treatment. Mr H had not used the equipment since the first few weeks of the study. He had experienced many complications with his ulcer, related to the type of dressing used, and he was suffering with the level of pain he was experiencing. He had met with Mr Locker, and even though there were considerable risks, they were considering surgical intervention.

Even though Mr H was enthusiastic and committed about the study, it would seem that the complexity of his existing medical conditions and the pain he was experiencing did not make him the ideal candidate to participate in the home study.

7.3.3 Case Study 2

The second patient was recruited by the District Nurses at Saundersfoot Medical Health Centre. She had previously participated in the Patient study discussed in chapter 6.

Mrs A was 73 years of age, and a non-smoker of average height and weight. She had been diagnosed with Systemic Lupus Erythematosus (SLE) in 1989, polymyalgia rheumatica in 2000, having a Thompson hemiarthroplasty of the left hip in 2000, and a further left girdlestone arthrodiesis in 2003; she suffered a transient ischaemic attack (TIA) in 2004, and was diagnosed with ischaemic heart disease in 2006. She was also hypertensive, but was taking medication to control this.

Mrs A first developed a varicose ulcer in 1973. It was treated with Bactigras dressings and Scherisorb until 1991; she was fitted for support stockings and found to be allergic to Ichthopaste dressings in 1993. The ulcer did not heal completely until November 1993. The ulcer returned in March 1996 and was infected. Granuflex was used to dress the ulcer, which was painful and produced a large amount of discharge. The ulcer was healing well by July 1996, however, it recurred once more in August 1997 and was again infected. The ulcer was applied with Intrasite gel and a Tegaderm dressing for the remainder of 1997. In September 1998, Mrs A was referred to a wound care specialist. The ulcer recurred again in 1999, and on this occasion, 3 and 4 layer bandaging was used until the ulcer was almost healed in early 2000. Mrs A developed phlebitis later in 2000, and a recurrence of the ulcer. She

continued to wear support stockings, and have her ulcer dressed until the present day.

The pictures in figures 7.2 and 7.3 demonstrate Mrs A's ulcer at the start of the home study.

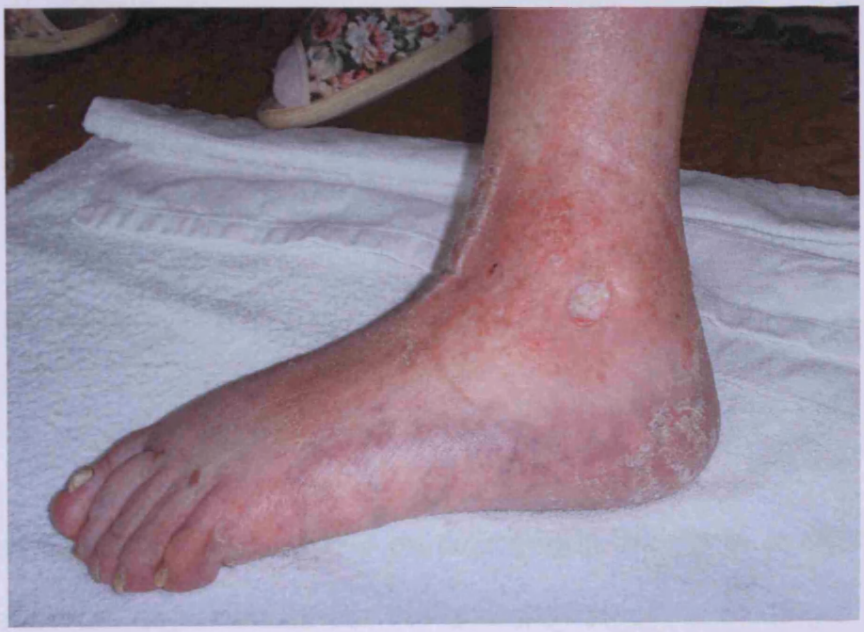


Figure 7.2 Venous / SLE ulcer of Mrs A at the commencement of the home study.

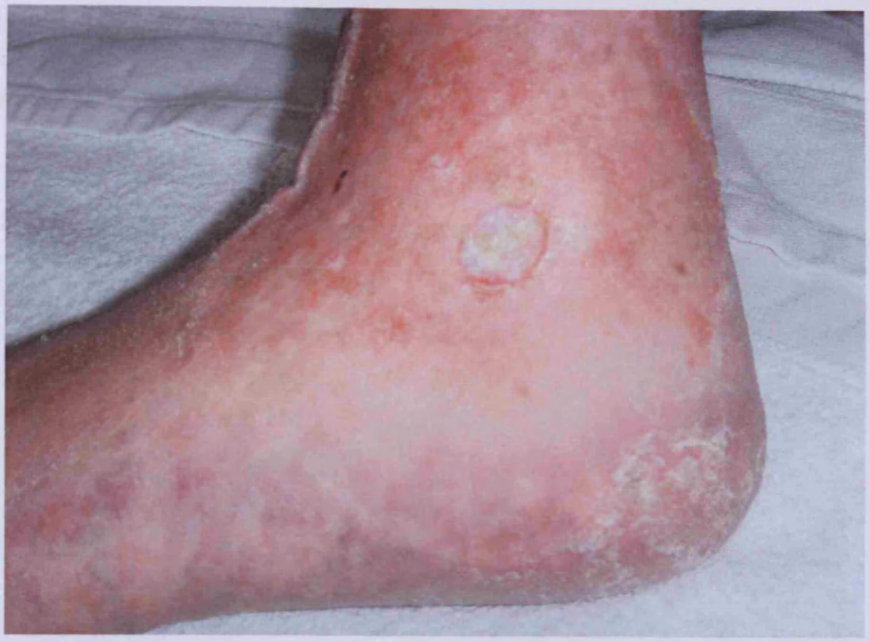


Figure 7.3 Venous / SLE ulcer of Mrs A at the commencement of the home study.

Mrs A was very enthusiastic about participating in the home study. She used her system most days throughout the 3 month study, excluding a period of about a week to ten days when she was in hospital for an unrelated surgical procedure. She used the system every evening, going to bed earlier than normal and putting the cuff on for two hours whilst reading or listening to the radio. She would set an alarm to go off after 2 hours to ensure she did not fall asleep with the cuff still going.

Mrs A did not encounter any problems with the equipment; she found it easy to use and very comfortable, and was encouraged when she could see that her ulcer was improving.

The following pictures demonstrate the progress her ulcer had made after 2 months using the system.

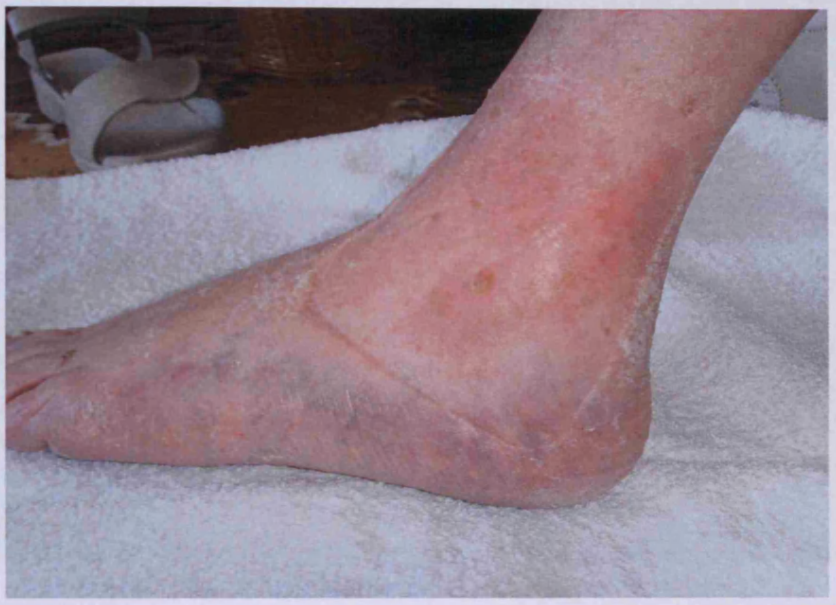


Figure 7.4 Almost healed ulcer of Mrs A, 2 months following the start of the study.

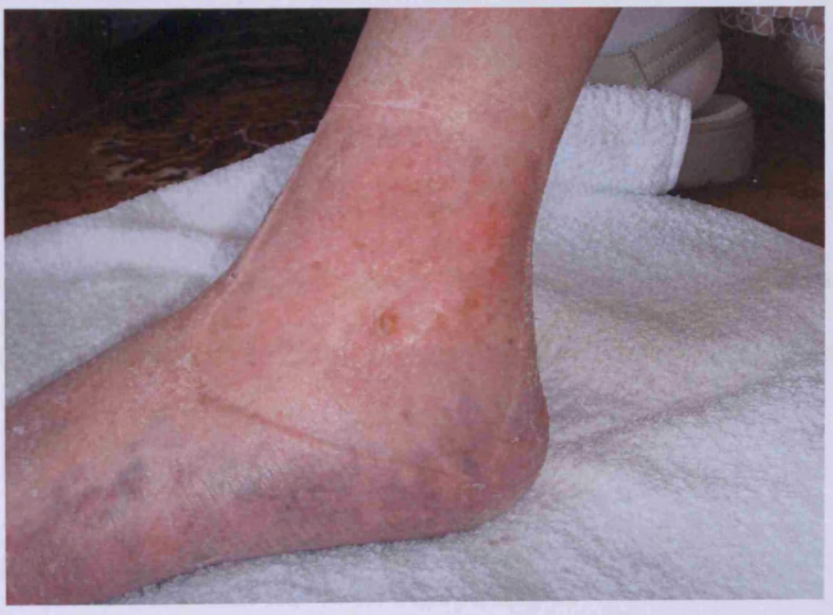


Figure 7.5 Almost healed ulcer of Mrs A, 2 months following the start of the study.

At the end of the 3 month period, her ulcer had completely healed.

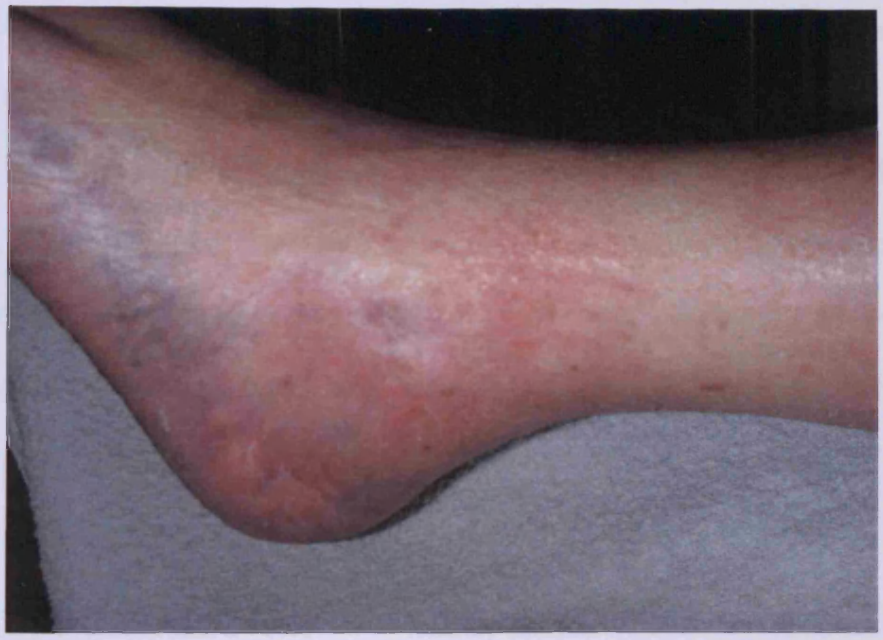


Figure 7.6 Mrs A's completely healed ulcer at the end of the 3 month study.

Mrs A was extremely pleased that her ulcer had healed; having suffered with recurrent ulceration for many years, she was delighted that her ulcer had improved within such a short period of time. She enquired whether she would be able to use the system again should her ulcer recur in the future. She was very grateful that she had been given the opportunity to participate in the study, and was surprised that other patients had not been keen to partake.

7.1 Conclusion

A home study was conducted in order to investigate the clinical effects of the 3-chamber thigh cuff system, and to assess the practicalities of using the system in the home environment. It was aimed to enrol a small group of patients to participate in the home study; however, due to a shortfall in ulcer patients, and the level of commitment required of the patient, only two patients were recruited. The first patient had other medical conditions which caused him a great deal of pain, and prevented him from using the system consistently. He used the system enthusiastically at the start of the trial; however, once pre-existing and complicating medical conditions became involved, use of the system came to an end. Therefore, of the two patients recruited, only one used the equipment routinely throughout the 3 month trial. The second patient used the system for 2 hours every day (excluding a period in hospital for a non-related surgical procedure), and improvement in the healing of the ulcer was noticeable early in the trial, complete healing having been achieved by the end of the 3 months.

The result obtained with Mrs A was very encouraging. However, since it is a single result, its significance is questionable. The study would need to be repeated on a larger group of ulcer patients in order to determine whether the ulcer healed as a consequence of using the 3-chamber thigh cuff system.

The purpose of the home study was also to assess the practicalities of using the system in the home environment. Both patients found the system easy to

use, easy to transport and comfortable. Neither patient had any problems or difficulties with the system itself.

Although a positive result was obtained from the home study for both clinical effects and the practicalities of using the system, the significance of the results cannot be relied upon due to the number of participants involved. Further research is required to support the outcome of this study.

Conclusions and Future Research

The aim of this research was to determine whether or not intermittent pneumatic compression (IPC) produced a distal blood flow response, and dependant upon the presence of a distal effect, whether compression could be used as a viable treatment option for chronic non-healing leg ulcers of different aetiologies. Previous research has always investigated the proximal effects of intermittent pneumatic compression, so this element of the project was completely new.

Investigations demonstrated that there was a distal blood flow response associated with IPC. When the compression cuff deflated, a distal arterial hyperaemia was detected. Even though distal arterial blood flow decreased during compression, the size of the hyperaemia was such that there was an overall increase in distal arterial blood flow. At the same instant, when the cuff deflated, a volume of distal venous blood was accelerated back towards the heart, indicative of a distally trapped volume of blood being released.

The size of the distal response was found to vary dependant upon the type of compression cuff, a greater effect being observed with the 3-chamber cuffs as compared with the uniform cuffs. However, a distal response was obtained with thigh only compression, which in itself is a good result. Thigh only compression has never been investigated as a method for improving blood flow; the results of this study seem to imply that thigh only compression could potentially be used as

a means of improving the distal circulation in those patients who are not suitable for whole leg or calf compression.

Another new aspect of this research examined the potential of improving both distal arterial and venous blood flows using a single compression sequence. It was established that a rest period was required within the compression sequence for a distal arterial hyperaemia to ensue, whilst improved distal venous blood flow occurred within a fairly rapid sequential compression cycle. The final result was a 20 second sequential cycle which was operated within a 2 minute on and off sequence; thereby improving distal venous blood flow during the 2 minutes of compression, and allowing a distal arterial hyperaemia to transpire during the 2 minutes rest.

The final product; a 3-chamber thigh compression cuff, with the afore mentioned compression sequence, operated by a modified Flowpress AC300-R pump was investigated on a group of patients with ulcers of varying aetiologies. The results were very encouraging, revealing that use of the system over a short period of time produced a net increase in distal arterial blood flow, and an improvement in distal venous return. However, the number of patients who participated in the study was small; 14 in total, and only 7 produced distal arterial results, therefore further investigations would be required to substantiate the findings. Nevertheless, the implications of these results suggest the potential of the system, which, in addition to improving the distal circulation of patients with

vascular pathologies, and consequently having the potential to enhance ulcer healing, is also simple to use, lightweight and easily transportable, comfortable and inexpensive.

It was hoped to conduct a small number of case studies as an insight into the clinical results of the new system, and also to determine the practicalities of using the system in the home environment. However, it proved very difficult to recruit patients into the 3 month study, possibly due to the amount of commitment involved. Of the two patients who consented to participate in the study, only one used the system on a regular basis and consequently produced any results. The lady with SLE (Systemic Lupus Erythematosus) and a long standing varicose ulcer used the pump for on average 2 hours daily for 3 months, and noticed almost immediate results. By the end of the study, her ulcer had practically healed. Even though this is only a single result, it leads the way for further long term trials of the system.

This research has demonstrated the potential of using proximal compression for improving the distal haemodynamics in patients with leg ulcers related to circulatory disorders, and has also generated a new product which appears to be capable of achieving these results. It is hoped that this study is the preliminary stage of a future trial, which is aimed at confirming the beneficial results which were achieved in the case study.

Appendix

Method used for normalising the results obtained from the distal arterial studies

1. The results obtained for the first 180 seconds of the study were averaged together by totalling the TAM velocities, and dividing by the number of results that were recorded during the 180 second time period.

2. The entire data set was then divided by this pre-compression average, in order to obtain a set of results that were normalised, or relative to unity.

3. The purpose of normalising the results was to enable comparison between data sets, and the ability to average data sets together.

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