2009-08-01

The Tromped, a Means of Prophylaxis for Flight Related Deep Vein Thrombosis

Carolyn Collins
Technological University Dublin

THE TROMPED, A MEANS OF PROPHYLAXIS FOR FLIGHT RELATED DEEP VEIN THROMBOSIS

Submitted for the Award of Doctor of Philosophy to the Dublin Institute of Technology

August, 2009.

Carolyn Collins BSc (Hons)

School of Mechanical and Transport Engineering

Supervisors: Dr. David Kennedy
Dr. Steve Jerrams

ABSTRACT.

The process of blood flow in the leg, against gravity and towards the heart is instigated by compression of the veins in the foot. Contraction of the calf muscles results in an ejection volume (EV) of blood towards the heart, completing the process.

Research studies have shown an association between flight travel and deep vein thrombosis (DVT). Stasis of blood flow can lead to the development of thrombus formation. Deep Vein Thrombosis occurs in situations where people are immobile for long periods of time, whether this is a result of ill health or travel on land or in the air. This alteration in venous haemodynamics may contribute to the development of DVT.

A novel prototype design of an in-flight exercise device to stimulate blood flow in the seated position was designed and developed. It consisted of a foot pedal attached to a base by a hinge mechanism and a spring. Four test set-ups, 1 to 4, of differing resistance were evaluated. Calf muscle pump function was assessed by the technique of Air Plethysmogrpahy (APG) in ten healthy volunteers. Ejection Volume Fractions (EVF) and Residual Volume Fractions (RVF) were determined in the standing position (control) and compared to those achieved in the seated position, by compression of the four pedals. The normal EVF is greater than or equal to 60%. It is the volume of blood ejected towards the heart when a participant stood on their tip-toes for five seconds. The normal residual volume (RV), the amount of blood remaining in the veins after exercise, is less than or equal to 35% and is an ideal indicator toward the prevention of venous stasis. Two devices (test set-up 2 and 3) achieved comparable EVF and RVF values to those achieved by the tiptoe control manoeuvre. As Test set-up 3 was more user friendly, its spring parameters were used in the subsequent device designs, namely demonstrator A (DA) and demonstrator B (DB). These prototypes were more streamlined versions designed with the shape of a foot in mind. They had differing dimensions meaning the springs would be positioned differently in relation to the foot.

An assessment was conducted to determine if a significant difference existed between the two. DA produced more efficient results and so was used in the follow up study, conducted in Beaumont Hospital, Dublin. The aim of which was to determine if any of the in-flight exercises (advocated by airlines) conducted in the seated position were efficient at creating venous return. This study consisted of two parts. Volunteers first conducted the standard APG assessment, followed by walking, DA and three foot exercises in the seated position. The second part of the study was conducted in the same sequence however participants wore Mediven® Travel Compression Stockings. DA in the seated position was effective at creating venous return however the in-flight exercises did not achieve the required EVF of greater than 60 percent.

The concept of the Tromped was integrated into an aircraft footrest. An assessment was conducted with 18 volunteers, six obese, six healthy individuals and with six women taking the contraceptive pill. The four footrest prototypes were compared to tiptoe (control) in the standing position and DA used in an aircraft seat. This seat had an incline of approximately 40mm from the front to the rear of the cushion and differed from previous assessments which were conducted in situ on a level examination couch. Neither of these footrests achieved the required EVF or RVF values. DA was only efficient in the obese group. Further research is recommended, particularly in redesigning the ergonomics of an aircraft seat to specifically enhance venous return in the seated position.

DECLARATION

I certify that this thesis which I now submit for examination for the award of PhD, is entirely my own work and has not been taken from the work of others, save and to the extent that such work has been cited and acknowledged within the text of my work.

This thesis was prepared according to the regulations for postgraduate studies by research of the Dublin Institute of Technology and has not been submitted in whole or in part for an award in any other Institute or University.

The work reported on in this thesis conforms to the principles and requirements of the Institute's guidelines for ethics in research.

The Institute has permission to keep, to lend or to copy this thesis in whole or in part, on condition that any such use of the material of the thesis be duly acknowledged.

Signature _____ Date _____

Candidate

ACKNOWLEGEMENTS

To my special parents, words cannot express how much I love you both. Thank you for all your support and belief in me through all the tears and all the good times. My darling brother Alan, thank you for all your contributions to this research, for all your words of encouragement, your hugs and for answering my prayers. I miss those hugs and I wish you were here to see me complete this!

Emrah hersey için çok teşekkur ederim, seni çok seviyorum canim kocam benim. Ölene kadar beraber, sőz birtanem!

A special thanks to Thomas Corrigan, for all his encouragement, suggestions, proof reading and red marks!

To both my supervisors; Dr. David Kennedy and Dr. Steve Jerrams, thank you for your guidance and assistance through out the last few years. I especially wish to thank you for your patience, kind words and your moral support in times gone by.

A special word of thanks to Professor David Bouchier-Hayes, MCh, FRCS, FRCSI, FACS, the Professor and Chairman, Department of Surgery, the Royal College of Surgeons Ireland, Beaumont Hospital (now retired) for answering my letter and introducing me to Dr Fitzgerald. Also for all your assistance with the medical paper, it is such a pleasure to have written a peer reviewed paper with you.

Doctor Patricia Fitzgerald, Director of the Non-Invasive Vascular Unit, Beaumont Hospital. You have been the most amazing mentor, teacher and friend to me, thank you so much for all your energy, encouragement and guidance.

A special thanks to Frank Dunne, Alan Buckley, Ciaran Smith and John Kelleher, whom produced the Tromped prototypes with enthusiasm in their own free time.

Many thanks to Seamus Green for assessing the spring parameters by a simple harmonic test, Michael Hall, for your enlightenment on springs. Also a special thanks to Lufthansa Technik Airmotive Ireland for assessing my spring parameters with the Chatillion Digital Force Gauge. Thanks to Aisling Kelleher for your funky autocad diagram of the Tromped Footrest and runners and to Leslie Smith for your fabulous diagrams of Option I and IV!

Finally to all who volunteered to take part in the Tromped Assessments, it could not have been done without you all. If I have forgotten anyone I am extremely sorry.

Table of Contents

LIST OF FIGURES

List of Tables.

List of Publications

i. Collins, C., Fitzgerald, P., Kennedy, D. M., Corrigan, T., Jerrams, S., Bouchier-Hayes, D. J. **The Tromped: A Solution for Flight-Related Deep Vein Thrombosis?** Angiology 2008 59: 72-76.

ii. Collins, C., Kennedy, D. M., Jerrams, S., Corrigan, T. (2006). "The Tromped, an in-flight exercise device to prevent Flight Related Deep Vein Thrombosis". Second International Conference on Reasearch in Air Transportation, June 24-28 2006. pp. 259-64.

iii. C. Collins, D. M. Kennedy, T. Corrigan and S. Jerrams. "Mechanical and medical investigations determining the efficiency of an in-flight deep vein thrombosis prophylactic device". International Conference on Materials-Energy-Design, MED06

iv. C. Collins, D.M. Kennedy and T. Corrigan "Exercise work-out 30,000 feet above land." The Engineers Journal. Vol. 59:1 January/February 2005.

v. Collins C (2005) "Stop all the clots by steps, A DIT research student has developed a device to stop the blood clots thought to be caused by long-haul flights". The Irish Times by Dwan, B., p.17, Thursday December 8, 2005.

vi. C. Collins, D.M. Kennedy and T. Corrigan. "Design and development of a novel device to prevent flight related Deep Vein Thrombosis". MATRIB'04 Conference in Vela Luka, Croatia June 2004 23-25.

vii.

Awards.

Kelly Rodgers Award for a novel device "The Tromped", presented by the Irish Royal Aeronautical Society, May 2002.

GLOSSARY OF TERMS.

Activated Protein C - destroys Fva and FVIIIa. It is activated by thrombin when it is bound to thrombomodulin.

Acute – of an illness, coming rapidly to a crisis (rapid onset of pain).

Air Plethysmography – a technique used to determine relative volume changes in the lower limbs in response to postural alterations and muscular exercise

Anatomy is the study of body structure and the relationships among body parts,

Anterior – at or nearer the front.

Antithrombin is any substance that inhibits or prevents the effects of thrombin in such a way that the blood does not coagulate. A deficiency of antithrombin results in recurrent thrombosis

Antithrombin III (AT III) is a protein which stimulates the removal of blood clots in the blood system. Conditions that may have an association with a low value of At III include liver disease and disseminated intravascular coagulation (DIC).

Arteriole(s) - the smallest arteries and site of variable resistance in the circulatory system.

Artery(ies) - blood vessels that carry blood away from the heart.

Asymptomatic – displaying no signs or symptoms

Atria – each of the two upper cavities of the heart

Blood pressure – is the force or pressure which the blood exerts on the walls of the artery in which it is contained**.**

Bones – are organs, they make up the skeleton in vertebrates.

Bone – in a different context is the hard whitish tissue from which bones are made

Bronchi – major air passageways of the lungs which spread out from the trachea (windpipe)**.**

Capillaries – fine branching blood vessels which form a network between the arteries and the veins**.**

Cephalad – in the direction towards the heart

Chronic – a long duration or frequent recurrence.

Demonstrator A – the first prototype device of the Tromped assessed by Air Plethysmography

Demonstrator B – the second prototype device of the Tromped assessed by Air Plethysmography

Diastole – widening of the chambers of the heart between two contractions when the chambers fill with blood

Dorsi flexion – moving the distal foot up

Dyspnea – difficulty breathing.

Degrees of freedom – this phrase is used to describe the number of values in the final calculation of a statistic that are free to vary.

Diaphragm – the flat dome shaped muscle below the lungs that controls breathing.

Endothelium (Endothelial Cells) - are involved in both the pathology of venous thrombosis and they contain antithrombotic substances to aid their dissolution

ECM (extracellular matrix) – non-living chemical substances located between connective tissue cells

Evertor - turns a limb outward

Factor – general name given to signal molecules when first found.

Factor I, Fibrinogen – a soluble plasma protein

Factor II, Prothrombin – a protein which is synthesised by the liver

Factor III, Tissue Thromboplastin initiates the extrinsic pathway by reacting with Factor VII and calcium to form factor VIIa

Factor IV, Calcium is an element taken in through the diet that is essential for a variety of bodily functions such as neurotransmission, muscle contraction and proper heart functions as well as clotting of the blood

Factor V, Proaccelerin - has the ability to function as both a procoagulant and an anticoagulant. It is synthesised in the liver. FV circulates in free form in plasma and is present in α-granules of platelets. FV platelets account for approximately 25 percent of the total amount of FV in the blood and are secreted due to platelet activation during coagulation.

Factor Va is a labile plasma glycoprotein which accelerates the conversion of prothrombin to thrombin in blood coagulation (Bergquist *et al.,* 1994), by forming a complex with Fxa, phospholipids and calcium. Activated coagulation factor V (Fva) is a necessary cofactor to activated factor X (Fxa).

Factor VI has the same function as activated Factor V

Factor VII is a stable plasma protein which is affected by tissue thromboplastin to form factor VIIa in the extrinsic pathway of blood coagulation. Factor VII is a vitamin K dependent clotting factor. The clotting activity of Factor VII is reduced by warfarin

Factor VIIa catalyses the activation of factor X to factor Xa

Factor VIII, Antihemophilic factor. A congenital deficiency in the amount of Factor VIII resulting in classic haemophilia (more prone to bleeding)

Factor IX, Christmas Factor, it is a plasma thromboplastin component, a stable blood coagulation factor acting in the intrinsic pathway. Its activated form Xa, forms a complex with FVIII and calcium on platelet Factor 3 to Fx and Fxa. It is antihemophilic factor B.

Factor X, Stuart Power Factor, is a stable glycoprotein blood coagulation factor that can be activated to factor Xa by both intrinsic and extrinsic pathways. A deficiency

of Factor X, known as Stuart –Prower factor deficiency may lead to a systemic coagulation disorder.

Factor Xa is an activated form of factor X, which catalyses the conversion of prothrombin to thrombin.

Factor XI, Plasmin thromboplastin antecedent – plasma protein synthesized in the liver

Factor XII, Hageman Factor – plasma protein required for intrinsic stage 1

Factor XIII, Fibrin-stabilising factor - Activation of FXIII by thrombin.

Fascia – is a connective tissue which covers the body by forming a sheet of tissue under the skin it also surrounds muscles and muscle groups

Fibrin is an insoluble protein formed from fibrinogen by the proteolytic (spitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides) action of thrombin during normal clotting of the blood. Fibrin forms the essential portion of the blood.

Fibrinolysis – solubilisation of fibrin in blood clots

Fibrosis – this occurs when fibrous tissue is formed for healing purposes if there is loss of tissue or the cells destroyed do not regenerate e.g. following chronic inflammation

Heart – the hollow muscular organ in the chest that pumps the blood around the body.

Haemoglobin – oxygen carrying pigment of red blood cells

Hemoptysis – coughing up of blood from the respiratory tract

Hemostasis – process of keeping blood within the blood vessels by repairing breaks without compromising the fluidity of blood.

Hypoxia – insufficient oxygen reaching the tissues of the body

Incidence – the frequency with which cases are identified. Incidence is commonly measured in new cases per 1,000 (or 100,000) of population at risk per year.

Intermittent claudication - presents with pain during walking due to arterial insufficiency which is produced during the walking process.

Interstitial – found in or relating to small spaces within something.

Lateral – relating to the side or sides

Lung – each of the pair of organs within the ribcage of humans and most vertebrates, into which air is drawn in breathing.

Medial – situated in the middle (midline).

Mediastinum – region between the pleural sacs.

Morbidity – relating to or indicating disease

Mortality of a disease - the probability that death will be the end result

Muscle – the tissue of an animal body which has the ability to contract, in response to a stimulus.

Nitric Oxide (NO) is produced within EC, it inhibites the adhesion and aggregation of platelets

Oedema – the accumulation of fluid in the interstitial place.

Onset – the time of appearance of the first symptoms of a condition, prior to seeking diagnosis.

Pathology is the study of the functional and structural changes that occur in cells and tissues as a result of direct damage by or reaction to a wide variety of events.

Pericardium – the membrane enclosing the heart

Perforating Veins - The function of a perforating vein is to form a connection between the superficial and deep systems

Peripheral resistance - resistance to blood flow created by (primarily) the arterioles.

Peurperium is a period of about 6 weeks following childbirth when the reproductive organs are returning to their normal state

Physiology is the study of the body's function and how it works.

Placebo is used as a control substance when conducting pharmacological studies to determine the efficiency of a new or potential product.

Plantar flexion – moving the distal foot down (e.g. rising the heel off the ground and placing weight on the ball of the foot)

Plasma – A cellular fluid in which blood cells are suspended.

Plasmin – it is an enzyme that breaks down fibrin, and is derived from the breakdown of circulating plasminogen

Platelets bind to damaged endothelium cells and subendothelium cells, to aid thrombosis development.

Posterior – at or nearer the rear.

Prophylaxis – intended to prevent disease

Protein C is a vitamin K dependent protein in plasma that inhibits the formation of a clot

Protein C deficiency results in thrombotic disease and excess platelets with recurrent thrombophlebitis (inflammation of the vein that occurs when a clot forms)

Protein S inhibits blood clotting by serving as a cofactor for activated Protein C

Protein S deficiency is a disorder which leads to decreased levels of plasma protein S associated with the onset of venous thrombosis and PE.

Pulmonary – An adjective meaning "to do with the lungs"

Resolution - signs of inflammation

Respiratory System - supplies oxygen to cells and releases carbon dioxide

Saphenofemoral junction – junction where the saphenous (superficial vein) drains into the deep system (femoral vein)

Sequelae - conditions resulting from a disease or injury

Systole – contraction of the chambers of the heart to drive blood into the Aorta and Pulmonary Artery.

Thorax – the part of the body between the neck and the abdomen

Thrombin – a plasma protein that converts fibrinogen into fibrin . It is produced from prothrombin by the action of the extrinsic system (tissue factor and Phospholipids) or by the intrinsic system (contact of blood with a foreign surface).

Thrombomodulin is produced within EC and is a natural anticoagulant.

Thrombophilia - a hereditary or acquired predisposition to develop blood clots

Thromboplastin is a plasma substance that converts prothrombin to thrombin

Tissue Factor (TF) or tissue thromboplastin is released from endothelial cells, tissue cells, platelets and monocytes, TF activates Factor IX.

Tissue Factor Pathway Inhibitor (TFPI) is produced by endothelial cells and it inhibits TF, VIIa and Xa.

Trachae – The portion of the respiratory tract located in the neck (also called the windpipe).

Ventilation – movement of air between the atmosphere and the lungs.

Ventricles – each of the two larger and lower cavities of the heart

Veins – any of the tubes forming part of the circulation system by which blood is carried from all parts of the body towards the heart.

"**Vitamin K** is a cofactor necessary for the production not only of blood clotting factors but also for proteins necessary in the formation of bone" (Kumar & Clark, 2002, p.233). Vitamin K deficiency results in an increase in prothrombin time and haemorrhage.

ABBREVIATIONS

AGTW	aircraft gross take-off weight
AHU	Aviation Health Unit
AHWG	Aviation Health Working Group
APC	Activated Protein C
APCR	Activated Protein C Resistance
APG	Air Plethysmograph®
AT	Anterior Tibial (vein)
ATIII	Antithrombin III
ATM	Atmosphere
CAA	Civil Aviation Authority
CFR	Code of Federal Regulations
CI	Confidence Interval
CMD	Calf muscle pump dysfunction
CMPF	Calf muscle pump function
CNC	Computer Numerical Control
CO_2	Carbon Dioxide
CT	Computed Tomography
CVD	Chronic Venous Disease
CVI	Chronic Venous Insufficiency
DVT	Deep Vein Thrombosis
EASA	European Aviation Safety Agency
EV	Ejection Volume
EVF	Ejection Volume Fraction
FAR	Federal Aviation Requirements
FDP	Fibrin Degradation Products
FIII	tissue thromboplastin
FIX	plasma protein
FRDVT	Flight Related Deep Vein Thrombosis
FRPE	Flight related pulmonary embolus
FV	Factor V
FVIII	Factor VIII

FVL	Factor V Leiden
FVLM	Factor V Leiden Mutation
GECS	Graduated Elastic Compression Stockings
HRT	Hormone Replacement Therapy
IATA	International Aviation Transport Association
ICU	Intensive Care Unit
LMWH	Low Molecular Weight Heparin
LSV	Long Saphenous Vein
NO	Nitric Oxide
OC	Oral Contraceptive
PAD	Peripheral Arterial Disease
P_aO_2	Partial arterial pressure of oxygen
PC	Protein C
PE	Pulmonary Embolism
PEP	Pulmonary Embolism Prevention
PLS	Post thrombotic Leg Syndrome
PO_2	Partial pressure of oxygen
PS	Protein S
PSI	Pounds per square inch
PT	Peroneal Tibial (vein)
PVD	Peripheral Venous Disease
RBC	Red Blood Cells
RV	Residual Volume
RVF	Residual Volume Fraction
SIGN	Scottish Intercollegiate Guidelines Network
SPJ	Saphenopopliteal junction
SSV	Short Saphenous Vein
SVPT	Supine venous pump function
SVT	Superficial Venous Thrombosis
TF	Tissue Factor
TFPI	Tissue Factor Pathway Inhibitor
TT	Tissue Thromboplastin
UK	Urokinase

VFI	Venous Filling Index
VTE	Venous Thromboembolism
VTED	Venous Thromboembolism Disease
VV	Venous Volume
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION AND BACKGROUND

1.0. Introduction

An association between air travel and the development of deep vein thrombosis (DVT) is well documented (Belcaro *et al.,* 2001a; Belcaro *et al.,* 2001b; Scurr *et al.,* 2001; Belcaro *et al.,* 2002; Cesarone *et al.,* 2003a; Schreijer *et al.,* 2006). DVT is the formation of thrombus, coagulated blood, in a deep vein. Thrombus formation can result from multiple factors however DVT as a result of venous stasis is the focus of this study. Venous stasis (stagnation of blood resulting in poor circulation) can affect the deep veins, particularly in situations where people are seated for long periods in cramped conditions such as during air travel. When a DVT occurs as a result of air travel this is referred to as flight related deep vein thrombosis (FRDVT). At its worst, DVT can result in death by pulmonary embolism (PE). This occurs when a section of the thrombus, known as an embolus, breaks off from its site of formation and travels into the lungs where it can cause an obstruction which can be fatal.

Recommendations to minimise the risks of FRDVT include exercises and the use of devices to improve flow of blood from the leg veins while seated. With this concept in mind, the main hypothesis of this work was that it should be possible to develop a foot pump that is capable of mimicking the venous haemodynamics of walking whilst in the seated position. Hence the device would prevent blood pooling in the veins of the lower limbs and the formation of DVT. The device advocated is termed “The Tromped” and was first produced in prototype form. The necessary parameters required to ensure sufficient venous return were initially established (Collins, 2002-2003). The principle

was to exercise each lower limb whilst seated by means of two spring loaded foot pedals. This form of exercise activates adequate blood flow to prevent venous stasis. The Tromped design was then modified for use on board an aircraft.

1.1. Aims and Objectives

1.1.1 Research Aims

The aims of this research were to:

a) Develop a device to aid in the prevention FRDVT;

b) Haemodynamically assess the efficiency of this device.

1.1.2. Research Objectives

To realise these aims the objectives of this research were to produce research data, conclusions and recommendations that:

i. outline the causes and effects of DVT and FRDVT;

ii. describe the symptoms of this disorder and those people whom are most likely to be affected;

iii. Review current medical research on DVT and FRDVT in the context of aviation derived pathology;

iv. Highlight the measures that can aid in prevention;

v. Develop and evaluate the Tromped as an in-flight exercise device.

1.2. Ethical Issue

The research was conducted in accordance with the Declaration of Helsinki (1964), (refer to http://www.wma.net/e/policy/pdf/17c.pdf).

Ethics approval was sought from the (Medical Research) Ethics Committee in Beaumont Hospital, Dublin. Approval to conduct the assessment (refer to section 7.1) was granted and obtained in December 2006 (Appendix A). Ethics approval was also sought from the Dublin Institute of Technology (DIT) to conduct the study entitled "The Tromped Footrest Experiment". This study was carried out in DIT Bolton Street (section 8.1). Ethics approval was granted and obtained in September 2006 (refer to Appendix B).

1.3. Outcomes of this research

The planned aims of this research were to:

i. prove the Tromped was as efficient or better than other methods designed to prevent FRDVT;

ii. establish a collaboration between the Dublin Institute of Technology (DIT) and the Non-Invasive Vascular Unit, Beaumont Hospital to address and solve the problem of FRDVT;

iii. carry out haemodynamic assessments of the exercise machines efficiency at all levels of redesign and manufacture;

iv. use of the Tromped on board a commercial aircraft and so be compliant with the requirements of European Aviation Safety Agency (EASA), Certification Specifications For Large Aeroplanes, CS-25 and the Codes of Federal Aviation Requirements for Large Aeroplanes, (CFR, 25);

v. offer conclusions and recommendations that will be of benefit to the airlines and other bodies concerning FRDVT.

1.4. Limitations

The limitations of this body of research were as follows:

i. The true incidence of DVT and FRDVT is unknown;

ii. The lack of aviation industry acceptance of the issue and co-operation to conduct an in-flight assessment of the Tromped;

iii. The lack of objective documentation surrounding the efficiency of mechanical devices and exercises recommended in FRDVT prophylaxis has the potential to undermine the design of an efficient form of prophylaxis

1.5. Method of approach

The research work undertaken in this programme required theoretical and experimental routes to be followed (Figure 1.1). The former was necessary to determine the contributing factors of FRDVT so that criteria could be established to aid the design of an in-flight medical device. The latter is new knowledge established in relation to FRDVT.

1.6. Case Studies.

This research has been conducted in an attempt to alleviate the real problem of FRDVT. Development of thrombi during flight can affect passengers' health but also can be fatal. Piet Fourie, was travelling from Los Angelus to Johannesburg with Virgin Atlantic Christmas Eve, 2002. The woman in the seat in front of him reclined her seat and she also had a box positioned under her seat so Piet did not have adequate leg room. When he tried to walk at the back of the plane, people were sleeping on the floor. As a result Piet developed a thrombus on that flight ("Man develops blood clot….", 2003). In the year 2000, Emma Christofferson travelled from Sydney to Heathrow Airport. Upon arrival at the airport she was pronounced dead at 28 years old. The cause of death was established

as a flight related pulmonary embolism (PE) (Eklöf *et al.*, 2005). A more in-depth description FRDVT and the associated dangers are provided in Chapter four.

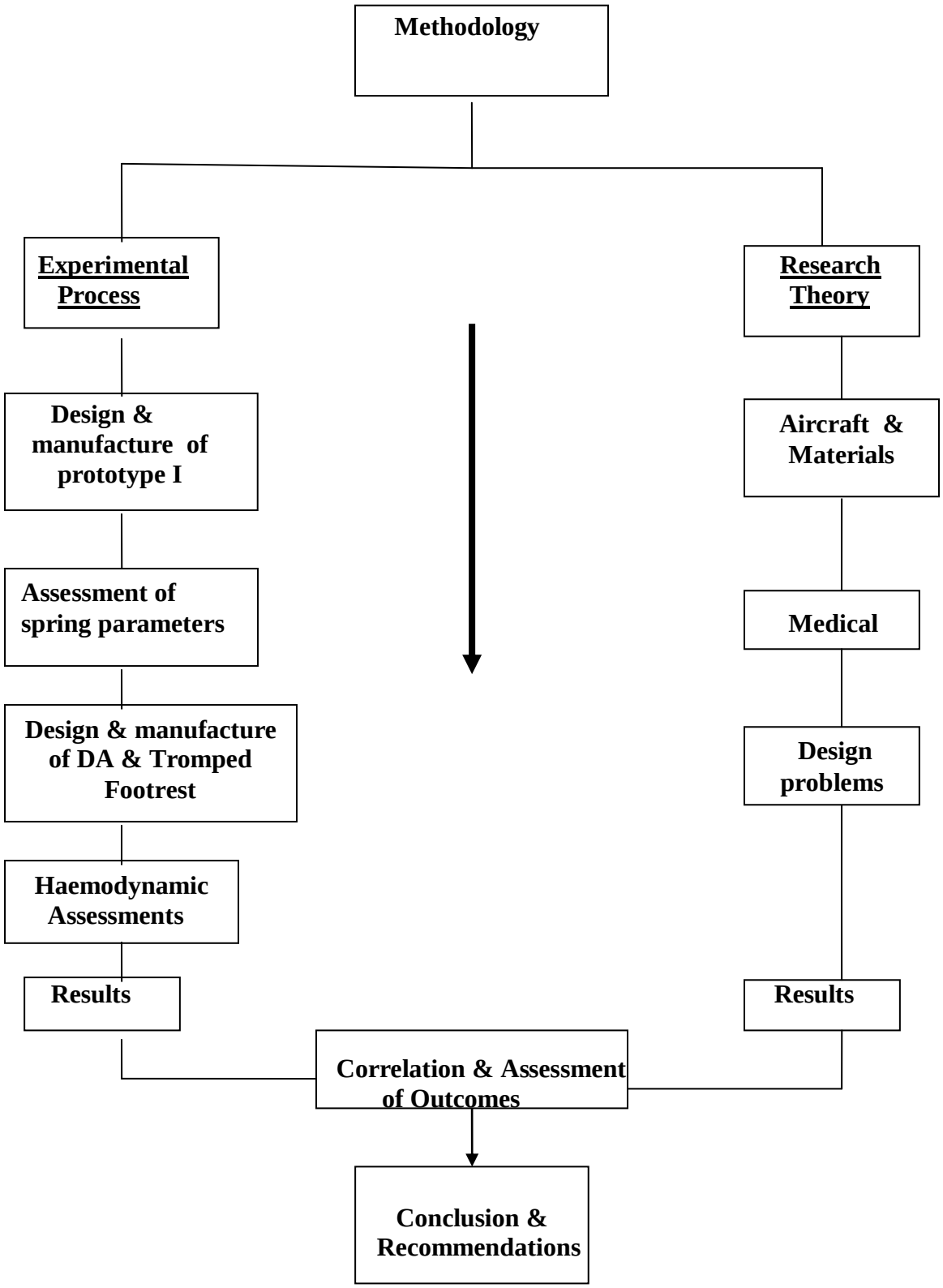


Figure 1.1 Flowchart of Research Plan

Chapter two introduces the human vasculature system and the constituents of blood and the anatomy and physiology of which are outlined in conjunction with a brief description of the skeletal and musculature system directly affecting venous return. An understanding of these factors and how they are linked was a prerequisite in understanding how to attempt prevention of both DVT and FRDVT by developing a form of prophylaxis. In chapter three the pathology of DVT, PE and VTE are explained, as are the associated inherited and environmental risk factors. Current practices of both diagnosing and treating this syndrome were identified. A literature review of FRDVT was also undertaken. The incidence of DVT and contributing factors associated with this flight related syndrome are investigated in conjunction with current forms of prophylaxis. Chapter four encompasses the methods, techniques and equipment used to conduct this research. The development and production of a novel form of prophylaxis is described in chapter five; to be precise, how the initial test piece "demonstrator A" progressed and developed into the final in-flight prototype the Tromped footrest. The final prototype was designed for use on board a commercial aircraft. Each device was produced and their associated design constraints were discussed.

Chapter six describes how two demonstrator devices were haemodynamically assessed (with different springs) in the seated position on a level examination couch. Chapter seven haemodynamically considered Mediven® travel compression stockings, exercises the airlines advocate and Demonstrator A. The natural progression of this research was to haemodynamically assess the Tromped footrest when used, seated in a commercial aircraft seat. This assessment is outlined in chapter eight. Finally, research conclusions are offered in chapter nine.

CHAPTER 2

ANATOMY AND PHYSIOLOGY OF

THE VASCULAR SYSTEM

2.0. Introduction

The human body is made up of living cells that require oxygen and nutrients to maintain life ("Jeppesen, 2002). It consists of a skeletal structure, muscle tissues and Fibres and a vascular system which transports blood flow to and from all the main organs. Blood is transported to the organs by the arterial system (the arteries) and from the organs by the venous system (the veins) (Solomon *et al.*, 1990, Monkhouse, 2001). The heart and the respiratory system will be briefly discussed, as both of these systems are interrelated with the vascular system. The cardiovascular system includes the heart, blood and blood vessels (Solomon *et al.*, 1990; Monkhouse, 2001). The respiratory system consists of the air passageway and the lungs. The skeletal and muscular systems function together as a single entity to allow limb and body movement to occur. The bones act as levers which transmit the mechanical forces generated by muscles as they contract (Solomon *et al.*, 1990). Venous return in the lower limbs (towards the heart) is affected by the calf muscle pump function, requiring an explanation and description of the muscles in the lower limb. This research is mainly concerned with venous return from the lower extremities and the pathology of venous thrombosis.

2.1. The function and constituents of Blood

Two fluids flow through the body, blood and lymph. Blood carries oxygen (O_2) and food to the cells, and carries carbon dioxide (CO_2) from the cells. The interstitial fluid known as lymph, flows towards the heart, carrying water and waste into the venous system

(Belcaro *et al.,* 1995). Living cells require materials to survive and to perform functions required to maintain life (Bullock, 1996). In the human body, this is accomplished by blood transporting oxygen, nutrients, hormones and waste products (Bullock, 1996). Blood consists of red blood cells (RBCs) or erythrocytes, (Underwood, 2004), white blood cells (WBCs) or leukocytes and platelets all circulating in a straw like coloured liquid known as plasma (Bullock, 1996). Plasma can be broken down into 92 percent water, seven percent protein and less than one percent of nutrients, respiratory gases, hormones and ions (Solomon *et al.,* 1990).

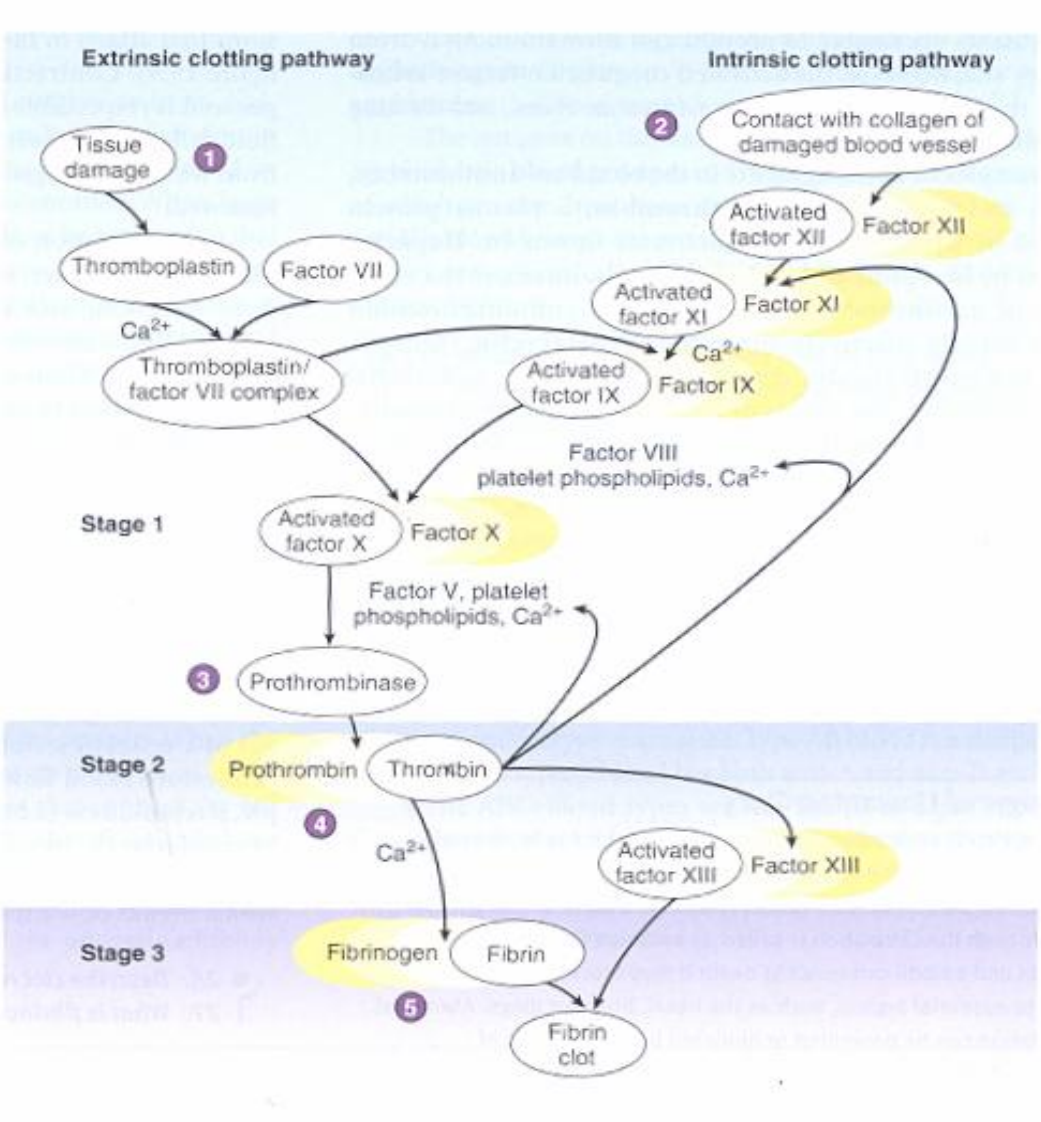
RBCs are rich in haemoglobin, which transmits oxygen from the lungs to the cells and carbon dioxide from the cells to the lungs (Radomski and Radomski, 2000; Underwood, 2004). Within the lungs, hemoglobin unites with oxygen, which it later releases in the tissues (Bullock, 1996). Normal circulating blood volume contributes eight per cent of the total body weight (Solomon *et al.,* 1990; Bullock, 1996). WBCs defend against infection and platelets are responsible for blood clotting (Solomon *et al.,* 1990; Underwood, 2004).

The proteins in plasma can be broken down into three subgroups namely; albumins, globulins and fibrinogen. Albumins account for 55 percent of plasma proteins and globulins 38 percent. These are necessary to sustain blood volume. Fibrinogen makes up the remaining seven per cent and it, in conjunction with the other plasma proteins, initiates the clotting process. Fibrinogen (Factor I), has two purposes, to aggregate platelets and to form fibrin, a necessary constituent of thrombi (Bullock, 1996; Krupski, 1997; Kumar and Clarke, 2002).

Platelets are also known as thrombocytes and are formed in the bone marrow (Bullock, 1996). Their main function is to halt bleeding (haemostasis) as they physically move into the damaged area of the vessel, plugging it and releasing chemicals which will then

initiate the coagulation process (Solomon *et al.,* 1990; Underwood, 2004). Platelets adhere to damaged endothelium (the lining of the blood vessel) or to the resultant exposed sub-endothelial tissue (Radomski and Radomski, 2000; Woolf *et al.,* 2002). Platelets range in size from two micrometers (μm) to four μm in diameter. They remain in the venous circulation for seven to ten days before the phagocytes in the spleen removes them from the system (Krupski, 1997; Radomski and Radomski, 2000). They are contractible and adhesive cells (Underwood, 2004) and "…they interact with the blood vessel wall, other platelets, and the coagulation proteins" (Krupski, 1997, p. 261). The presence of fibrinogen and calcium is necessary for platelet - platelet interaction. Plasma fibrinogen is enough to allow aggregation, in its absence; platelets can release fibrinogen to support the occurrence of aggregation (Krupski, 1997). Aggregation is the adhesion of platelets to other platelets to form a mass of cells, which are known as fibrinogen bridges (Woolf *et al.*, 2002). Activated platelets promote thrombin generation, because they have negatively charged phospholipids on their surface which accelerate coagulation factor activation. Platelets aid the activation of prothrombin by Factor Xa and Factor X by Factor IXa –VIIa complex (Woolf *et al.*, 2002). Thrombin also causes platelet activation (Krupski, 1997; Labelle and Kitchens, 2005) and will convert soluble fibrinogen to insoluble fibrin, activating clot formation (Labelle & Kitchens, 2005).

Ten plasma proteins, namely prothrombin, FIX, FX, FXI, FXIII, (Hirsh, 1990), FV, FVIII, FVII, FVIIa and fibrinogen with one tissue protein, known as subendothelial tissue factor, all play a part in the pathology of clot formation (Figure 2.1) (Butenas and Mann, 2002; Crowther and Kelton, 2003).



Source: Seeley *et al.*, (2006, p.665)

Figure 2.1. The Coagulation Cascade

2.2. The Human Heart

2.2.1. Anatomy of the Heart

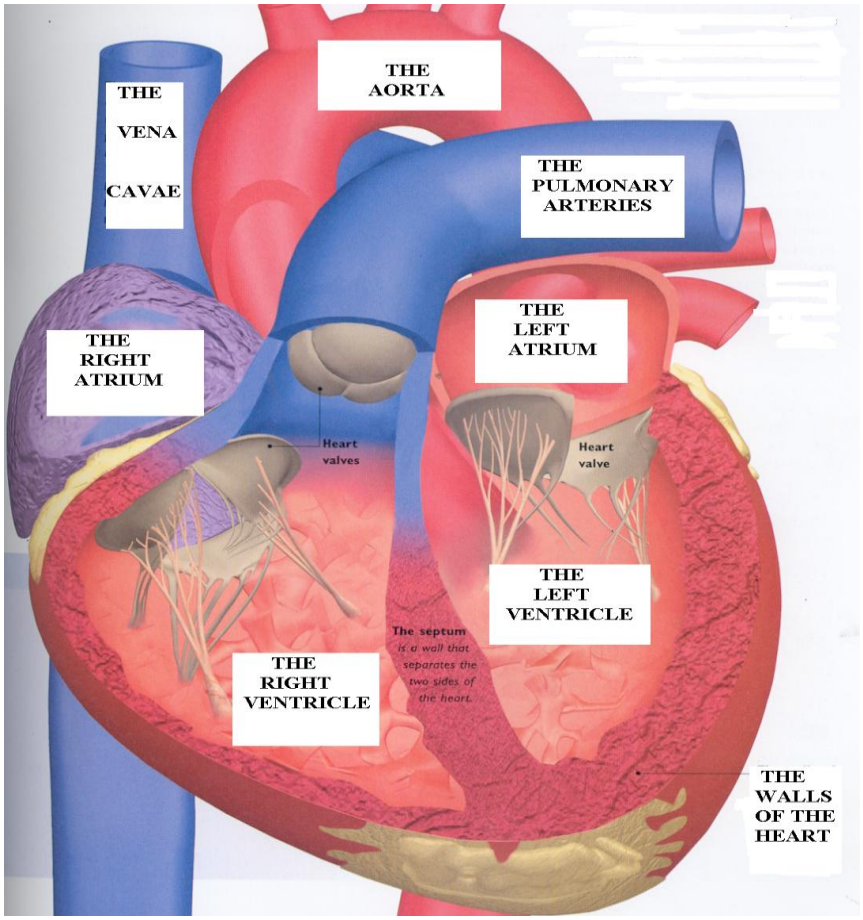
The purpose of the human heart is to maintain life. This is achieved by the continuous circulation of blood through the body, which is driven by contraction of the heart muscle (Strandness and Sumner 1975; Solomon *et al.*, 1990). The heart has the power to drive

the blood to all the body organs and lower extremities and also helps to return it to itself (Menzoain *et al.,* 1997). It forces more than 5 litres per min (l/min) of blood through the body per day. The heart beats more than 40 million times a year, the purpose of which is to supply the tissues of the body with a consistent supply of nutrients and to permit the excretion of waste products from the tissues and blood stream (Damjanov, 2002; Kumar *et al.,* 2005). The heart is found in the thorax (chest) region of the body (Monkhouse, 2001). It is contained within a protective sac named the pericardium which is located between the two lungs, in an area named the mediastinum (Solomon *et al.,* 1990; Monkhouse, 2001; Damjanov, 2002). "The heart is a four-chambered hollow, muscular organ that has a conical shape" (Solomon *et al.,* 1990, p.670). The chambers are the right and left atria and the right and left ventricules (Figure 2.2) (Osman *et al.,* 1973, p.128; Strandring, 2005).

2.2.2. Physiology of the Heart

The heart has a natural pacemaker, known as the sinoatrial node, responsible for generating electrical impulses which stimulate contraction of the heart (Sims, 2000).

The right atrium receives blood from the superior and inferior vena cava (from the upper and lower body), which is depleted of its oxygen by the body's tissues (Strandring, 2005). Blood passes into the right ventricle where it is pumped into the lungs via the pulmonary trunk, here the blood is re-oxygenated before it is passed into the left atrium by the pulmonary veins. Blood is then pumped into the aorta by the contracting action of the left ventricle. The aorta returns the blood into the systemic system (Osman *et al.,* 1973; Solomon *et al.,,* 1990; Monkhouse, 2001).



Source: Sims (2000).

Figure 2.2. The Heart.

The heart usually pumps at a constant force. Blood flows from the aorta (the largest of the arteries) towards arteries which gradually become smaller. Blood flow moves from the arteries to the arterioles then to the capillaries and finally the veins (Osman *et al.*, 1973).

2.3. The Human Lungs

2.3.1. Anatomy of the Lungs

The lungs are located within the chest cavity on either side of the heart, enclosed by the pleura, chest wall, respiratory muscles and diaphragm. The purpose of the lungs is to

supply adequate volume of oxygen to the body at all times by the exchange of gases between inspired air and blood. The lungs branch out from the trachea (windpipe). The right lung bud is divided into three branches (bronchi) and the left lung bud, which is the smaller of the two, is divided into two main bronchi. There are three lobes on the right, upper, middle and lower and two on the left (Kumar *et al.*, 2004; Monkhouse, 2001). The right and left bronchi then subdivide into what are called lobar bronchi which then go on to separate into terminal bronchioles, (Figure 2.3) (Bullock, 1996; Monkhouse, 2001). These terminal bronchioles branch into the respiratory bronchioles which contain alveolar ducts and alveoli, which is where the exchange of gases occurs (Bullock, 1996; "Jeppesen", 2002).

2.3.2. Physiology of the Lungs

The ventilation process is the transfer of oxygen from the atmosphere through the trachea and bronchial tree (lungs) to the alveoli (Goldhaber and Elliot, 2003; Colbert, 2004). When an individual breathes in air, the diaphragm descends and the pressure in the thoracic area reduces and the volume of the lungs increases. Pressure also reduces along the walls of the right atrium, to allow it to fill up with blood, from the main draining veins of the body (superior and inferior vena cava).

There are four stages in the transportation of oxygen from atmosphere to the body cells:

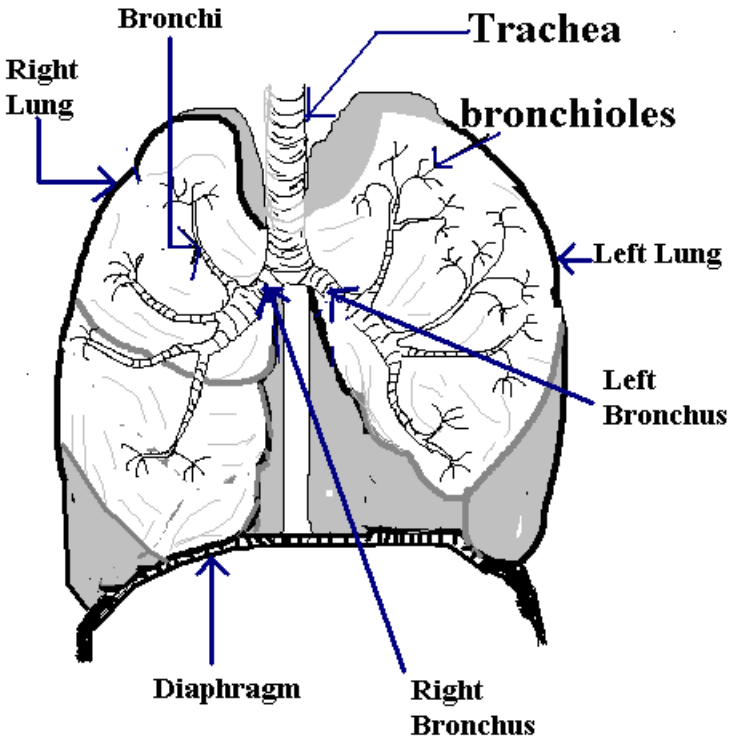
i. Ventilation process: oxygen flows from the atmosphere through the trachea and bronchial tree to the alveoli;

ii. In the alveoli oxygen comes in contact with the alveolar capillary walls and passes to the blood. This is known as pulmonary diffusion;

iii. Oxygen is then carried by the blood from the lungs, to the heart where it is pumped via the arteries to the tissues;

iv. The oxygen diffuses from the tissue capillaries to the sites of utilisation of oxygen.

(Goldhaber and Elliot, 2003; Colbert, 2004).



Source: Bullock, 1996

Figure 2.3 The Lungs.

2.4. Skeletal and muscular systems

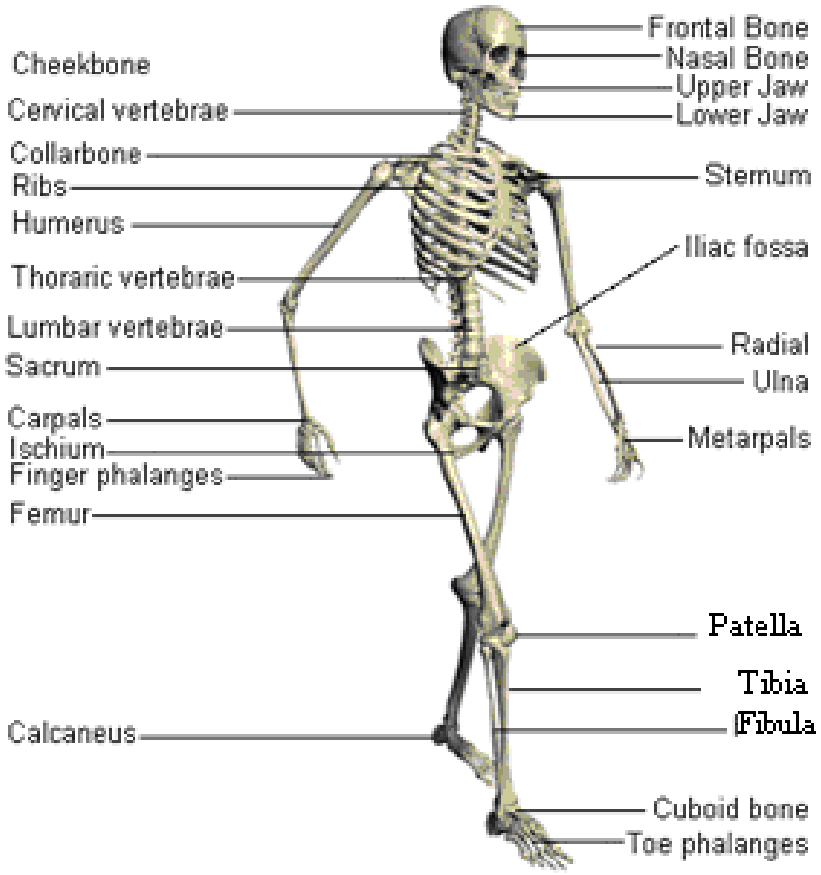
"Muscles produce movements at joints by pulling on the bones to which they are attached." (Tyldesley and Grieve, 1989, p.36). The skeletal and muscular systems of the lower limb are important factors in venous return. Commonly used nomenclature for anatomical structures include the following: anterior ~ to the front; medial ~ the midline; lateral ~ away from the midline and finally posterior ~ to the rear (Monkhouse, 2001).

2.4.1. Bones of the lower extremity

2.4.1.1. Anatomy

"The bones of the lower extremity consist of those of the pelvic girdle, of the thigh, of the leg, and of the foot" (Pickering and Howden, 1977).

The skeleton of the leg consists of four bones which are known as the Femur, the Patella which is the bone placed in front of the knee, the Tibia and the Fibula (Figure 2.4) (Pickering and Howden, 1977; Monkhouse, 2001). The femur (the heaviest bone in the body) is found in the thigh region. The fibula is the lateral calf bone and the tibia is the medial calf bone.



Source: Contamedia

Figure 2.4. The Human Skeleton.

2.4.1.2. Physiology

The main function of the bones of the lower limb is the transmission of weight (Moffat and Mottram, 1987). The bones function as levers and are connected by synovial joints, thus enabling mobility. Muscles attached to the bones provide the force to enable their movement (Winwood and Smith, 1985).

2.4.2. Muscles of the lower limb

Contraction of muscles within fascia collapses the vein resulting in blood moving toward the heart.

2.4.2.1. Anatomy

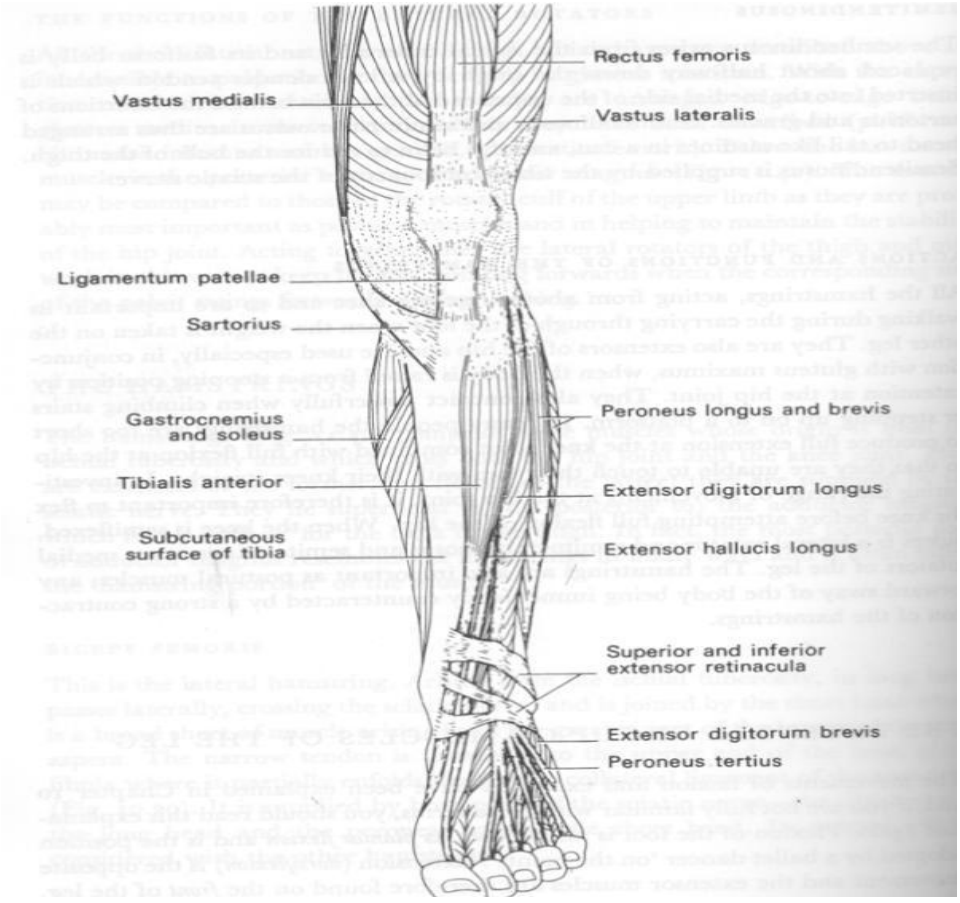
Muscle tissue is composed of cells designed to allow contraction. Muscle cells are referred to as fibres, which when contracted become shorter and thicker in size, thus facilitating movement of the body parts attached to them (Solomon *et al.*, 1990). Muscles are ensheathed by a fascia. The muscles of the leg are divided into muscular compartments by fascia (Pickering and Howden, 1977; Stranden, 2000). The most important areas for venous return are anterior and posterior compartments of the leg. Muscles allow precise movements, e.g. the calf muscles pull on the heel to raise the foot onto the toes. The line of body weight lies in front of the ankle joints. The calf muscles are required to maintain balance over the foot base (Tyldesley and Grieve, 1989). Movement of the foot is controlled by the muscles of the calf. These are traditionally described in three main groups, the anterior, posterior and fibular group (Winwood and Smith, 1985).

The anterior group consists of the Tibialis Anterior muscle, the Extensor Hallucis Longus and the Extensor Digitorum Longus and Peroneus Tertuis (as shown in Figure 2.5).

The posterior group of muscles consists of both superficial and deep layers. The superficial muscles of the posterior group include the Gastrocnemius, the Soleus and the Plantaris. A transverse section of the mid calf can be seen in Figure 2.7.

The deep muscles include the Popliteus, Tibialis Posterior (Figure 2.6) Flexor Digitorum Longus and Flexor Hallucis Longus.

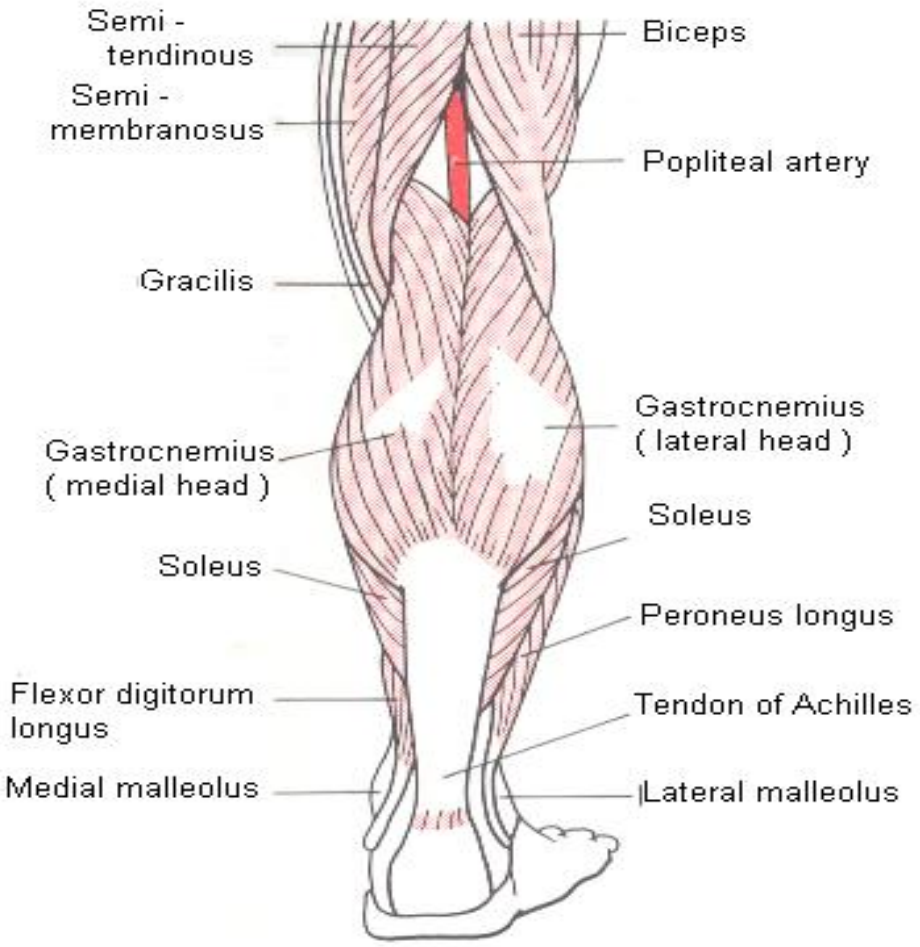
The lateral group of muscles are the Peroneus Longus and the Peroneus Brevis (Figure 2.8) (Winwood and Smith, 1985).



Source: Moffat and Mottram, 1987.

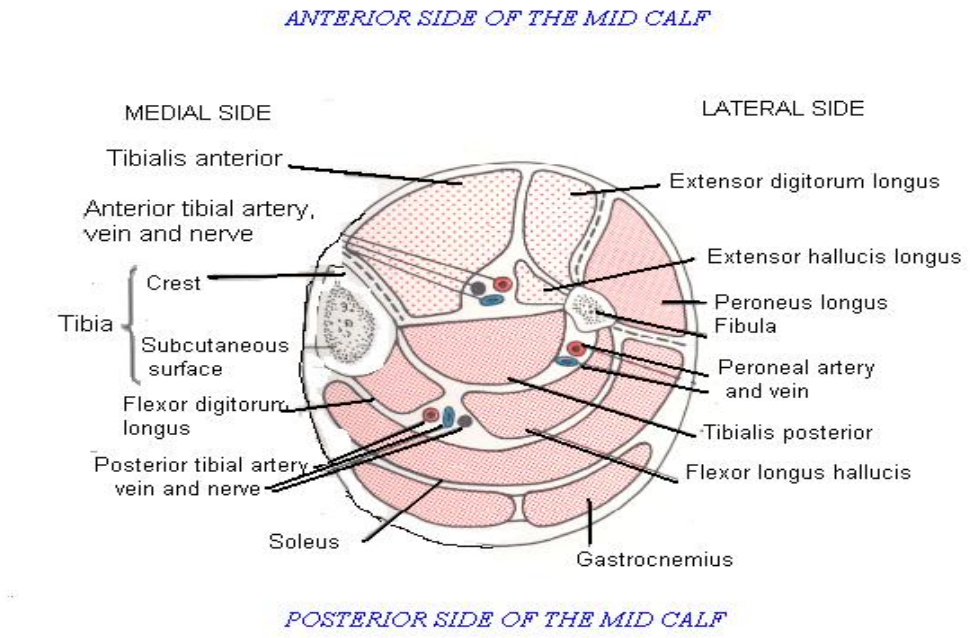
Figure 2.5. The Anterior muscles of the lower limb.

The Peroneus Longus arises from the lateral surface of the fibula. It is inserted into the lateral side of the first metatarsal and the medial cuneiform. This muscle is also a dorsiflexor and evertor of the foot and maintains the arches of the foot during walking. The Peroneus Brevis arises from the lower two-thirds of the lateral surface of the fibula. It is inserted at the base of the fifth metatarsal. It too maintains the arches of the foot and contributes to eversion (Romanes, 1986).



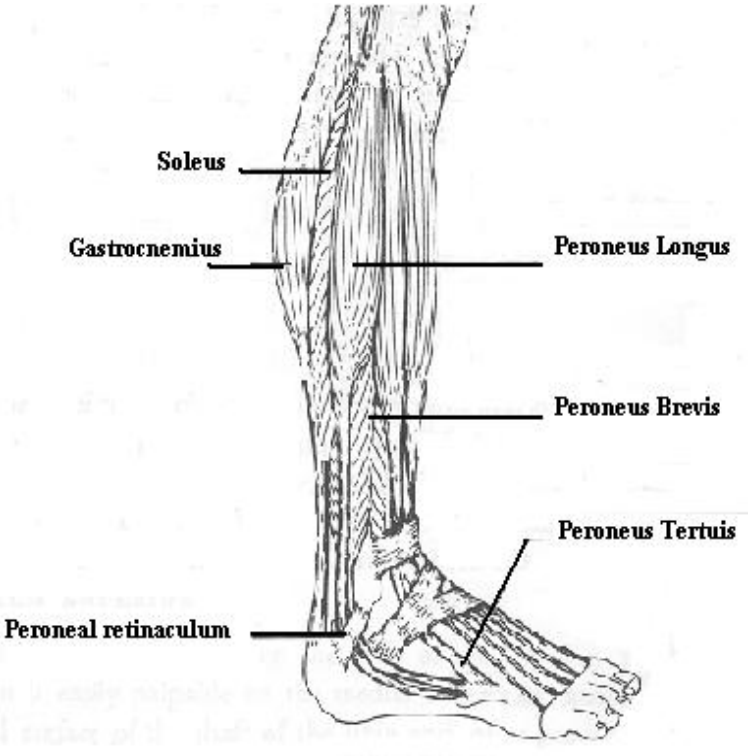
Source: Winwood and Smith, 1985

Figure 2.6. The Posterior superficial muscles of the lower limb.



Source: Winwood and Smith, 1985.

Figure 2.7. Transverse Section of the mid calf demonstrating the anterior and the posterior group of muscles.



Source: Moffat and Mottram, 1987.

Figure 2.8. The Peroneal Muscles.

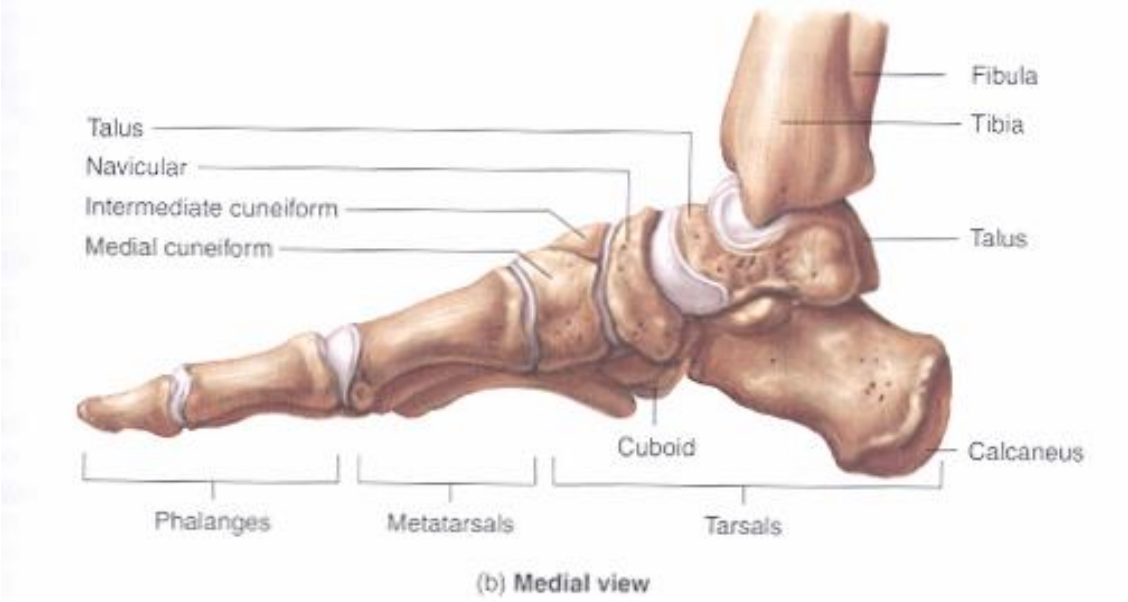
2.4.2.2. Physiology

The muscles of the calf are the primary flexors of the foot at the ankle joint. They are necessary to stand, walk and jump. It is the gastrocnemius which provides the majority of the propulsive force during walking running and jumping (Palastanga *et al.,* 1994). The soleus is one of two main plantar flexors of the ankle joint. One of its main functions is to prevent the body falling forwards during standing. Intermittent contraction of the muscle during standing aids venous return, this is known as the soleal pump as communicating vessels join both the deep and superficial venous systems which pass through its substance (Palastanga *et al.,* 1994). The main functions of the lower limbs are support in standing, swing and support in movement, transfer of the body from supine to sitting to standing and provision of sensory information via the soles of the feet from supporting surfaces such as the ground (Tyldesley and Grieve, 1989). The hamstring muscles of the thigh work with the gluteus maximus in the buttock to create propulsion for walking. When walking, the human heel comes into contact with the ground first, followed by the ball of the foot. The Gastrocnemius and the Soleus muscles (Figure 2.6) contract drawing on the Calcaneus to lift the heel off the ground (Monkhouse, 2001). Thus the term plantar flexion refers to the movement which raises the heels of the foot off the ground (Tyldesley and Grieve, 1989). As the body is supported on the raised foot the opposite leg may be carried forward. The peroneus muscles transfer the body weight to the ball of the foot. The toes flexors are used to grip the floor and thrust forwards (Solomon *et al.,* 1990; Pickering and Howden, 1977). The soleus prevents the body from falling forward. The Plantaris is an accessory to the Gastrocnemius when flexing the ankle of the free foot or bending the knee if the foot is on the ground (Pickering and Howden, 1977).

2.5. The Human Foot

2.5.1. Anatomy

The skeleton of the foot is divided into three divisions; the Tarsus, Metatarsus and the Phalanges (Pickering and Howden, 1977). The seven tarsal bones are situated in the proximal area of the foot (Figure 2.9). The calcaneus (heel bone) is the strongest bone in the foot (Seeley *et al.,* 2006). The metatarsals are the foot bones and the term phalanges, is used to describe the toes (Figure 2.9) (Solomon *et al.,* 1990). The area between the metatarsals and phalanges is known as the ball of the foot (Seeley *et al.,* 2006). The deep plantar flexors are three muscles whose tendons pass round the medial side of the ankle and enter the sole of the foot, Tibialis posterior, Flexor Digitorum Longus and Flexor Hallucis Longus.



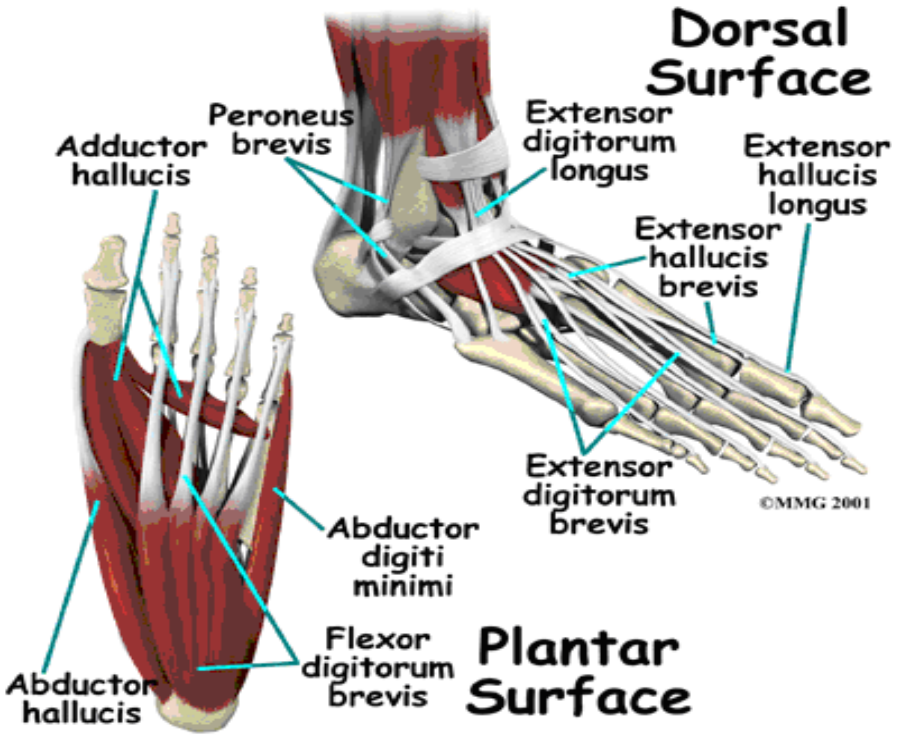
Source: (Seeley *et al.,* 2006, p. 241)

Figure 2.9. Skeleton of the Human Foot

These plantar flexors aid the calf muscles in propulsion of the ankle (Sumner, 2000). There are four ankle dorsiflexors (Figure 2.10); the Tibialis anterior, Extensor hallucis longus, Extensor digitorum longus and Peroneus tertius (Manganaris *et al.*, 2001).

2.5.2. Physiology

The muscles of the feet and the calf instigate venous return to the thigh and the pelvis area (Menzoian *et al.*, 1997). The arches of the foot "…distribute the weight of the body between the heel and the ball of the foot during standing and walking." (Seeley *et al.*, 2006, p.242). During walking, weight transfers from the tibia and the fibula to the talus bone when the foot is placed on the ground. This weight then transfers onto the calcaneus, prior to moving along the lateral arch system and into the ball of the foot (Seeley *et al.*, 2006).



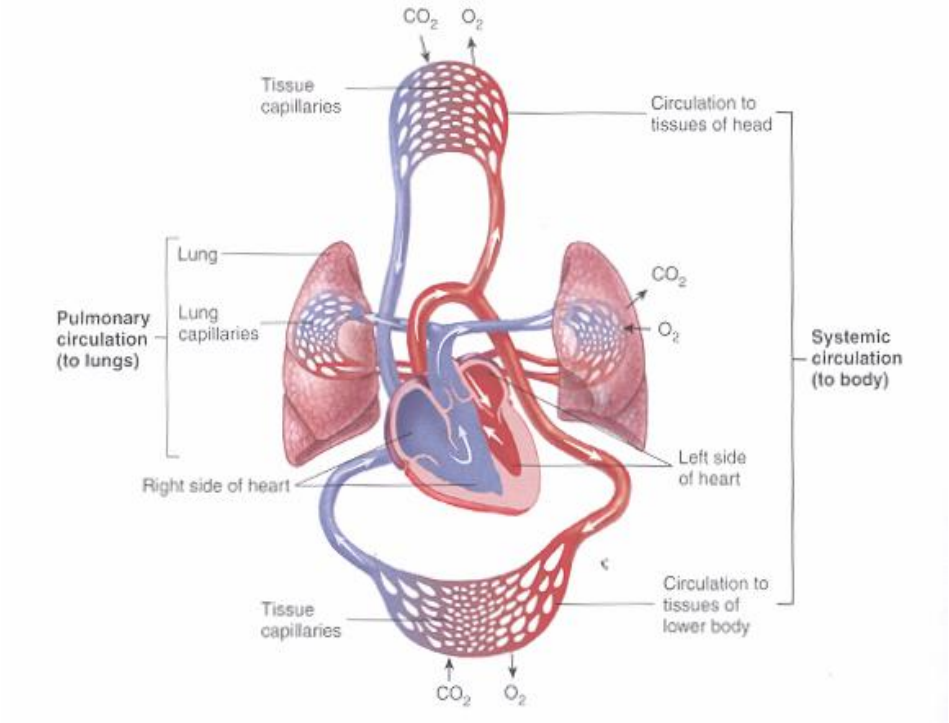
Source: Southwest Orthopaedic Surgery Specialists, PLC

Figure 2.10. Muscles of the dorsal and plantar surfaces of the foot.

The plantar plexus can be defined as "large dilated veins on the plantar aspect of the foot" (Gardner and Fox, 2001). The human foot is unique in that blood flows from the deep veins to the superficial veins" (Ricci *et al*., 1997). Compression of the plantar plexus instigates the flow of blood towards the heart (Sumner, 2000) (refer to section 2.6.2). Weight bearing, such as walking, forces blood from these veins into deep veins and superficial (Ricci *et al.*, 1997).

2.6. The Vascular System

The vascular system consists of arteries which bring blood from the heart to the organs. The blood then passes through a network of small vessels to eventually drain into the veins which bring the blood back to the lungs for oxygenation and then back to the heart (Figure 2.11).



Source: Seeley *et al.*, (2006).

Figure 2.11. The Vascular System

2.6.1. Blood Vessels

2.6.1.1. Arterial supply to the lower limbs

Arteries function by dilating and elongating with increased blood flow and narrowing at times of reduced blood flow, with structural changes occurring in the wall to make this possible (Sho *et al.*, 2004).

Blood vessel walls consist of the following three layers, (Figure 2.12):

i. The Tunica Intima which is composed of an elastic lamina, that is lined by a layer of endothleial cells which are in contact with the blood flow (Cole, 2001a);

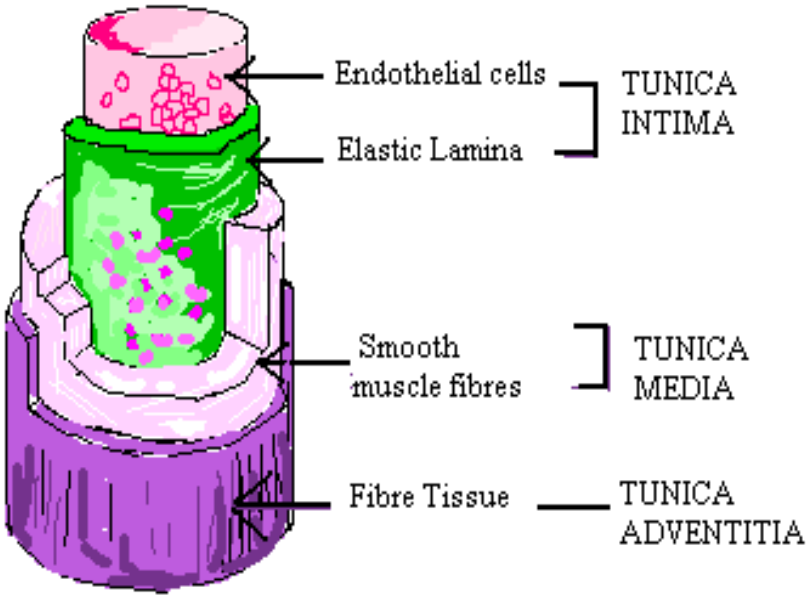
ii. The Tunica Media, which consists of smooth muscle fibres that circle the vessel, fibrous tissue and vasavorum which are blood vessels. The smooth muscle fibres regulate the blood flow of the artery by contracting or dilating (Cole, 2001a);

iii. Tunica Adventitia, which consists of an elastic lamina enclosed by fibrous tissue. The elastin fibres run longitudinally and give elasticity to the arteries (Cole, 2001a).

Arterial blood of the lower limb, originates from the Femoral Artery and its branches (Figure 2.13). The femoral artery descends into the popliteal fossa where it becomes the popliteal artery. Then descending down the leg the popliteal artery divides into the anterior, posterior tibial and peroneal arteries. The dorsalis pedis (DP) artery is the continuation of the anterior tibial (AT) artery into the anterior part of the ankle, whereas the posterior tibial (PT) artery is found in the inside hollow of the ankle bone (Monkhouse, 2001).

2.6.1.2. Arterioles

Arteries branch into smaller vessels known as arterioles, until the blood flows through tiny thin walled capillaries (Solomon *et al.*, 1990). Arterioles have medial smooth muscle cell contraction, the purpose of which is to adjust the diameter of the lumen and control the distribution of blood flow (Dobrin, 1997).



Source: (Cole, 2001a)

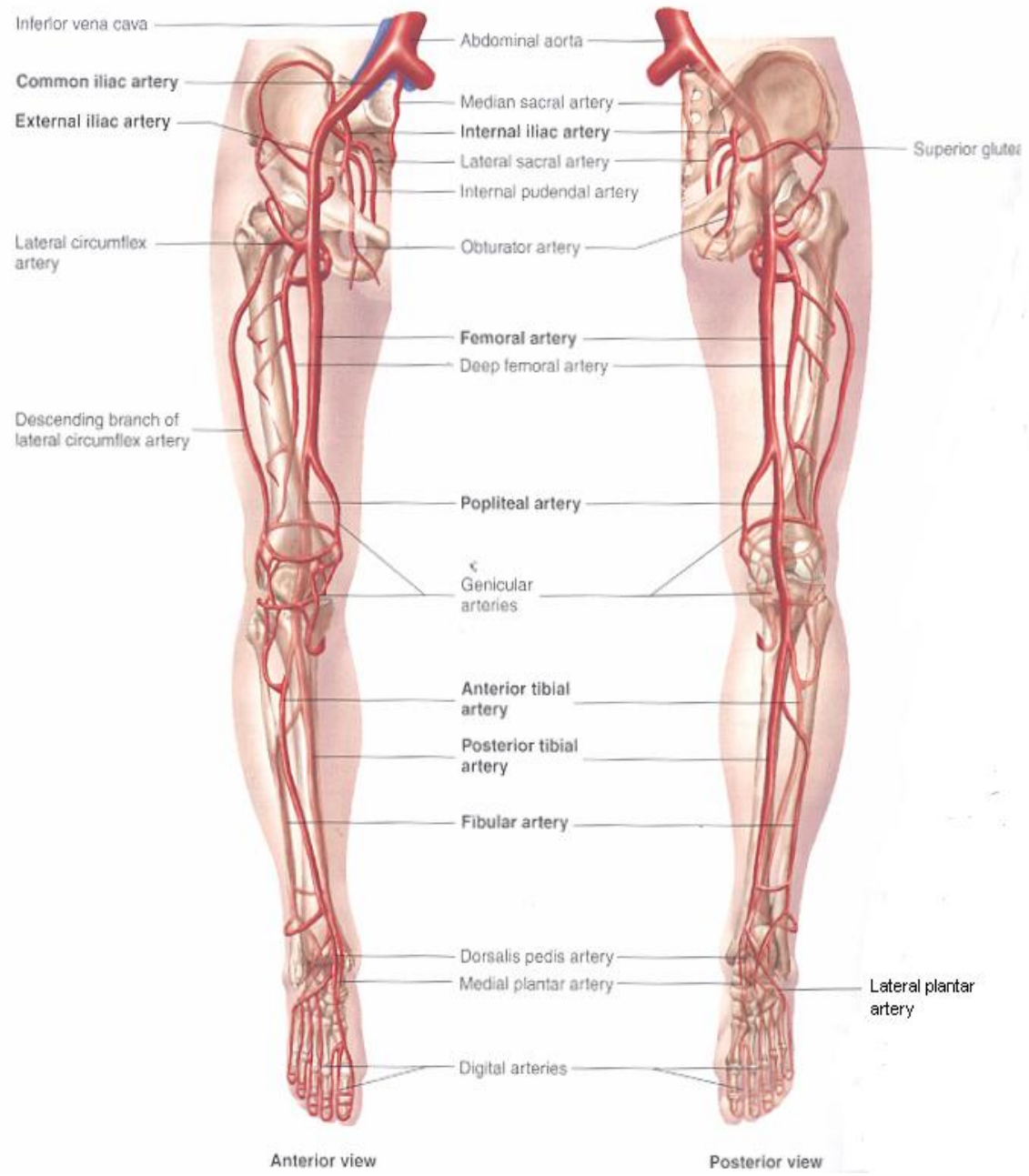
Figure 2.12. Disection of the artery walls

This contraction regulates the arterial blood pressure before directing it towards the capillaries (Strandness and Sumner, 1975).

2.6.1.3. Capillaries

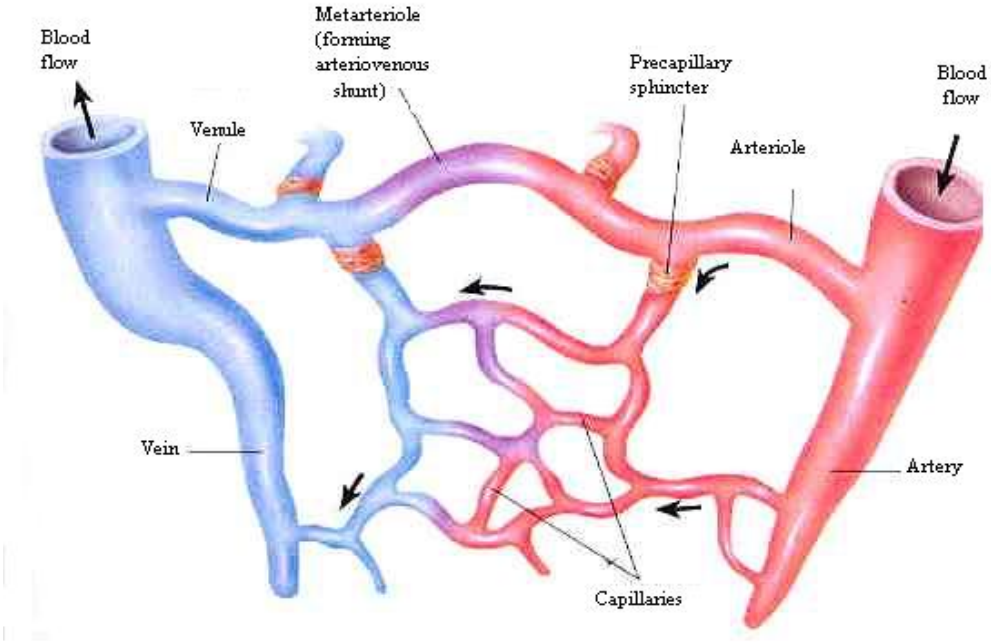
Capillaries allow the exchange of nutrients and waste products between blood and cells (Solomon *et al.*, 1990; Dobrin, 1997). They have a large cross sectional area but their walls are thin, which allows exchange of oxygen and diffusible substances between plasma and the tissues (Vander *et al.*, 1998). Blood flows from the capillaries (Figure

2.14), to postcapillary venules, to collecting venules and on into small, medium or large veins (Silverthorn, 1998).



Source: Seeley *et al.*, (2006)

Figure 2.13. Arteries of the Lower Limbs



Source: Fox (1996)

Figure 2.14. The Capillaries.

2.6.2. Venous anatomy of the lower limbs

"The function of the veins is to return blood from the peripheral capillary beds to the heart" (Tibbs, 1992). Another function of veins is to control dissipatation of heat from the core of the body, by diverting the blood flow to the superficial cutaneous veins (Belcaro *et al.,* 1995). This can be important in lower limb swelling during long haul flight.

Veins carry approximately 70 percent of the total blood volume at any one time (Belcaro *et al.,* 1995; Dobrin, 1997). Veins of the lower limbs are classified into three sets; superficial, deep and sinuses (Gray, 2001). They have different characteristics to arteries; they have thinner walls, are collapsible and contain valves which permit unidirectional flow (Tibbs, 1992).

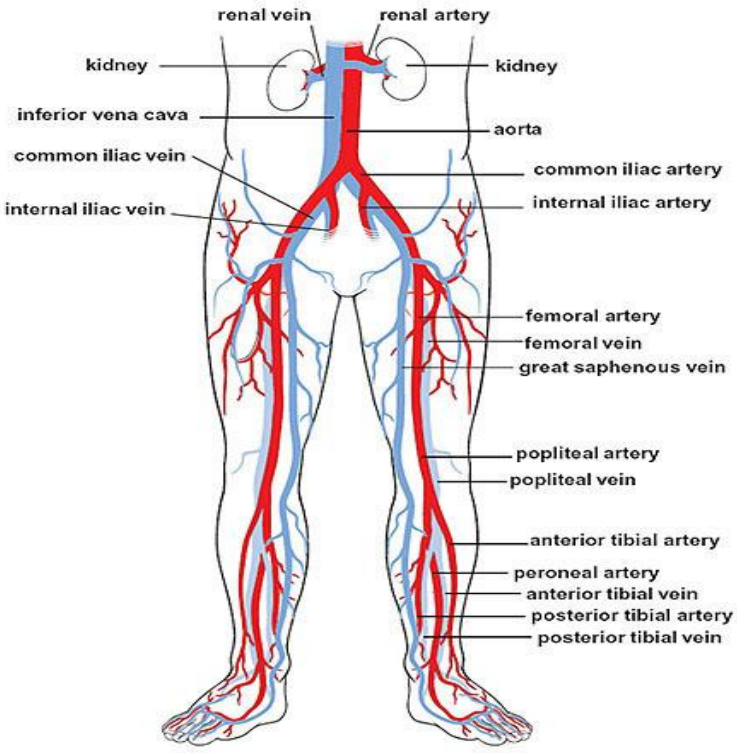
2.6.2.1. Superficial veins

Superficial veins are found in subcutaneous tissue, which is just below the skin, (Sumner, 2000). They can perforate the deep fascia and connect to the deep veins (Tibbs 1992). The plantar cutaneous arch of the foot is formed by superficial veins in the sole of the foot. These veins play a role in the venous pump system (Browse *et al.*, 1988; Strandring, 2005).

Superficial veins usually have thicker walls than deep veins. They are known as the long saphenous vein (LSV) and the short saphenous vein (SSV) (Porter and Moneta, 1995). The LSV (Figure 2.15) also known as the great saphenous vein, begins in a tiny plexus found in the dorsum and medial side of the foot. It passes in front of the ankle and runs subcutaneously up the inner leg and thigh to the groin, where it passes through an opening in the fascia lata and then terminates in the femoral vein (Gray, 2001; Monkhouse, 2001; Rautio, 2002).

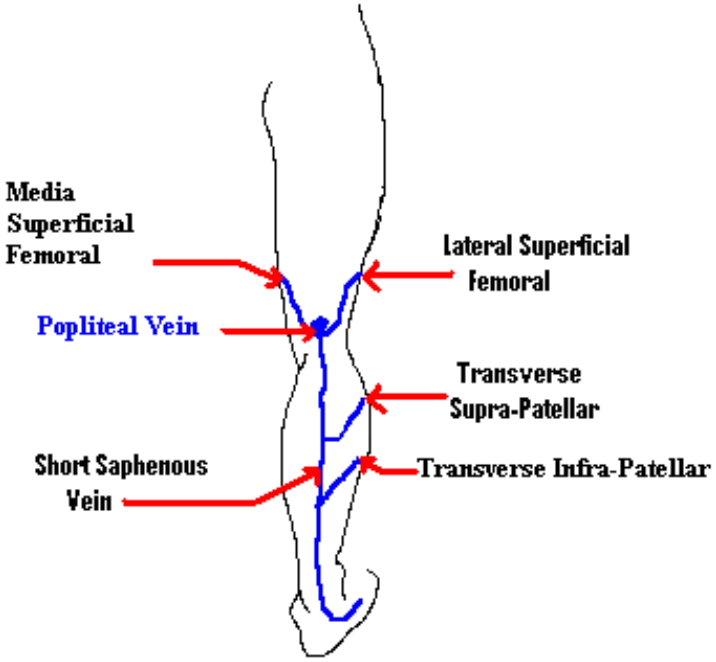
In the foot the LSV communicates with the internal plantar vein. In the leg it communicates with both the posterior tibial (PT) veins (by branches which perforate the tibial origin of the Soleus muscle) and the anterior tibial (AT) veins (with the articular veins at the knee). When passing through the thigh area the LSV communicates with femoral vein at one or more branches.

The SSV (Figure 2.16) commences in the dorsum and lateral side of the foot. It passes subcutaneously behind the ankle, along the tendo Achilles at such an angle that it travels towards the middle line of the posterior aspect of the leg. As the SSV ascends upwards it perforates the deep fascia at the lower end of the popliteal space, terminating in the popliteal vein. The SSV communicates with deep veins in the dorsum of the foot and behind the lateral malleolus.



Source: Cleveland clinic (2007).

Figure 2.15. Deep and Superficial anterior veins of the leg



Source: Netterimages.com.

Figure 2.16. Superficial posterior veins drain to the Popliteal Vein

2.6.2.2. The Deep System.

The deep veins of the lower extremities (Figure 2.17) begin in the deep plantar arch of the foot (Menzoian *et al.,* 1997). Each of the deep veins accompanies the arteries. Pairs of deep veins exist for both the tibial and peroneal arterteries and these deep veins are termed the *Venae Comites.* The main function of these veins is the collection and conduction of blood. Each of these venae comites has a diameter 35 per cent greater than the adjacent artery (Strandness and Sumner, 1975). Larger arteries such as the popliteal and femoral arteries usually have only one accompanying vein.

The lateral and medial plantar veins (which are the deep venous system of the sole of the foot) join together to form the posterior tibial veins (Figure 2.19) behind the ankle joint (Mozes and Glovicki, 2004; Strandring, 2005). They accompany the PT artery and are joined by the peroneal veins (Gray, 2001).

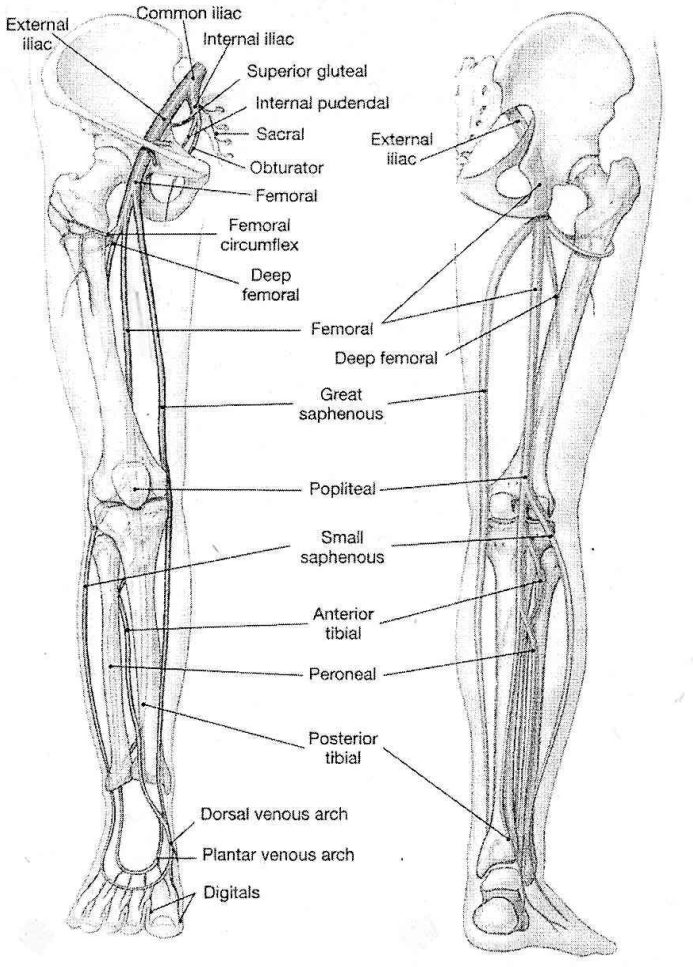
The AT veins are a direct continuation of the dorsalis pedis veins. They drain the blood from the dorsum of the foot and they perforate at the interosseous membrane at the upper part of the leg and together with the PT veins they become the Popliteal vein.

"The popliteal vein is formed by the junction of the venae comites of the AT and PT vessels; it ascends through the popliteal space to the tendinous aperture in the Adductur magnus, where it becomes the femoral vein." (Gray, 2001). From the popliteal veins, blood flows to the superficial and then common femoral veins (Porter and Moneta, 1995; White *et al.,* 2000).

The femoral vein accompanies the femoral artery in the thigh area. It terminates beneath the crural arch where the external iliac vein commences. The external iliac passes along the edge of the pelvis and unites with the internal iliac vein to become the common iliac vein (Gray, 2001).

The inferior vena cava is formed by the junction of the two common iliac veins on the right side of the intervertebral substance, between the fourth and fifth lumbar vertebrae. It travels upwards along the spine on the right side of the aorta artery until it perforates the tendinous centre of the Diaphragm. From there it enters the pericardium until it terminates in the lower posterior side of the right auricle (Gray, 2001).

If a deep vein becomes occluded venous return must flow by an alternative pathway; through another deep vein or overlying superficial veins. These channels of alternative flow are known as collateral veins. If this occurs these veins will become enlarged.



Source: Martini *et al.*, (1998).

Figure 2.17. Deep Veins of the Lower Limbs

2.6.2.3. Sinuses

Sinusoidal veins are present in both the foot and lower limb and are situated within the "skeletal muscles" (Sumner, 2000). These veins within the foot are defined as "…dilated segments of the venous arcades …" (Browse *et al.,* 1988, p. 32). Between one and four large veins pass through the deep layer of the plantar plexus, usually under the arch of the foot. These segments or chambers are surrounded by muscle, and have a large capacity and a thin wall so that the chamber can fill with little or no resistance when the muscle is relaxed (Figure 2.19). In the calf the *"...soleal sinuses are pouch-like areas that receive blood from the soleus muscles which lie posteriorly and distal to the gastrocnemius muscles and drain into the posterior tibial and peroneal veins."* (Cole, 2001b, p.2).

Inflow of blood to these chambers comes from other deep veins, superficial veins via perforating connecting veins and venules draining muscle capillaries (White *et al.,* 1996).

2.6.2.4. Physiology of lower limb venous return

The process of venous blood flow in the leg, against gravity, towards the heart is instigated by compression of the plantar plexus of the veins, which are situated between the deep and superficial intrinsic muscles of the foot (Menzoian *et al.,* 1997; Sumner, 2000). The veins of the plantar plexus are 1.9 times the size of the PT vein, which they empty into upon plantar flexion or stretching. This creates a high velocity of blood flow into the PT veins (White *et al.,* 1996). Contraction and subsequent relaxation of the calf muscles cause ejection of a volume of venous blood flow from the calf veins to the popliteal vein and subsequently to the femoral vein, the iliac vein and the IVC, before entering the heart, completing the process (Strandness and Sumner, 1975, O'Donovan *et al.,* 2005).

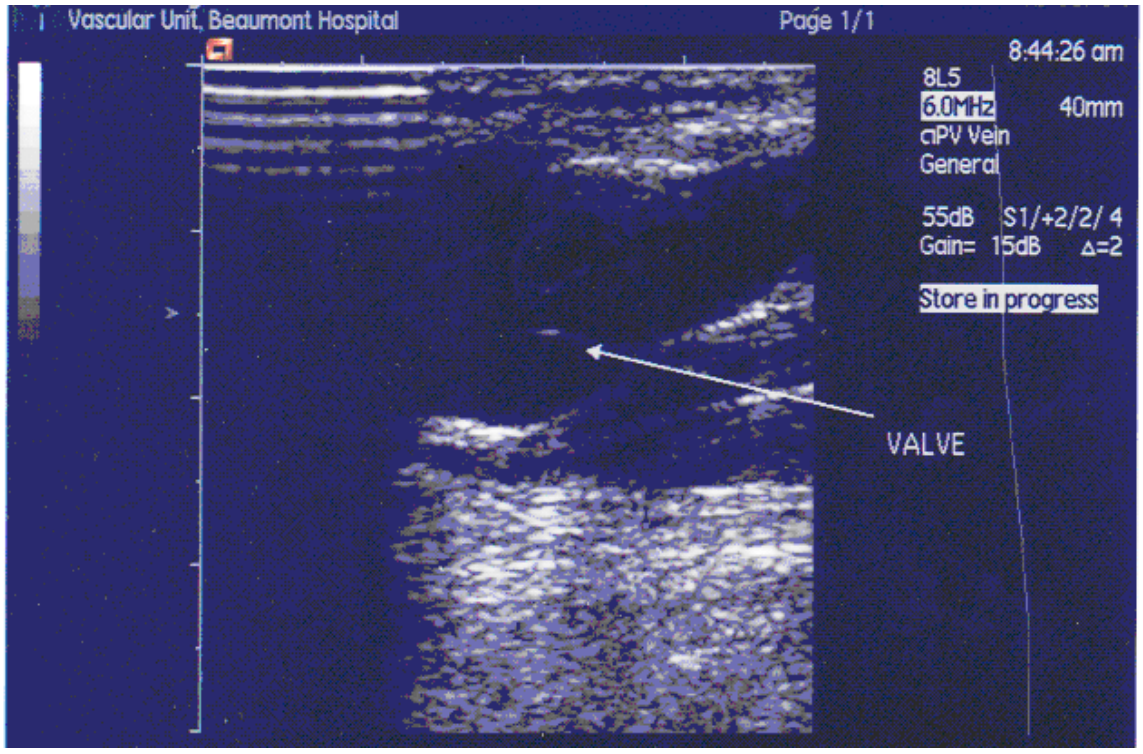
When a person is walking, the foot is in contact with the ground only 60 per cent of the time. At the mid segment of the foot is a transverse arch. This arch is high medially and low or virtually non-existent laterally so therefore the ball of the toes, the heel and the plantar surface of the foot, bear the majority of the weight of the body. Walking is achieved when the calf muscles contract to facilitate heel strike off. Muscle contraction is the main activator of venous pumps (Strandring, 2005). Stretching may promote pumping by causing intramuscular pressure (Stranden, 2000). During normal movement, the venae comites are the channel employed to empty the foot pump (Gardner and Fox, 1989). Prior to the foot bearing any weight, (i.e. being placed on the ground), the ankle is dorsiflexed, causing the bulk of the calf muscle to descend within the fascial sheath, resulting in the emptying of the distal calf pump (Gardner and Fox, 1993).

This is pertinent to the research programme, described in that the action occurs when the passenger places his/her foot on the uncompressed Tromped pedal. Weight bearing is achieved by initial pressure on the foot pedal, emptying the foot pump into the deep veins of the calf which are relaxed. This results in extension of the tarso-meta tarsal joints and flattening of the tarsal arch, which empties the foot pump (Stranden, 2000). Depression of the pedal against resistance activates the calf muscles, emptying the proximal muscle pump (Gardner and Fox, 1989). The foot pump will empty into the long and short saphenous veins if the deep veins of the calf are blocked, when the calf muscles may have tightly contracted, dependant on ankle positioning (Gardner and Fox, 1989).

The flexing of the plantar area of the foot empties the proximal calf pump into the popliteal (knee area) and femoral veins (Gardner and Fox, 1989; Sumner 2000). The muscle group of the thigh compress the femoral veins which ejects the blood into the inguinal area (Gardner and Fox, 2001).

2.6.2.4.1. Venous Valves

Venous valves *"are bicuspid with gossamer thin highly flexible cusps"* Tibbs, (1992, p. 13). Valves *"…are folds of the intima that contain collagen and elastin but no smooth muscle…"* and "*…prevent retrograde venous flow with changes in position and muscular contraction…"* (Strandness and Sumner, 1975, p.5). There are numerous valves in each of the venae comites. There are approximately seven in the peroneal, four in the popliteal vein and four or five in the femoral vein. There can be as many as six valves in the LSV and only two within the SSV (Gray, 2001). Perforating veins have valves which allow flow only one direction (Tibbs 1992). A valve can be seen in the ultrasound scan (Figure 2.18) which was obtained from the Non-Invasive Vascular Unit in Beaumont Hospital, Dublin.



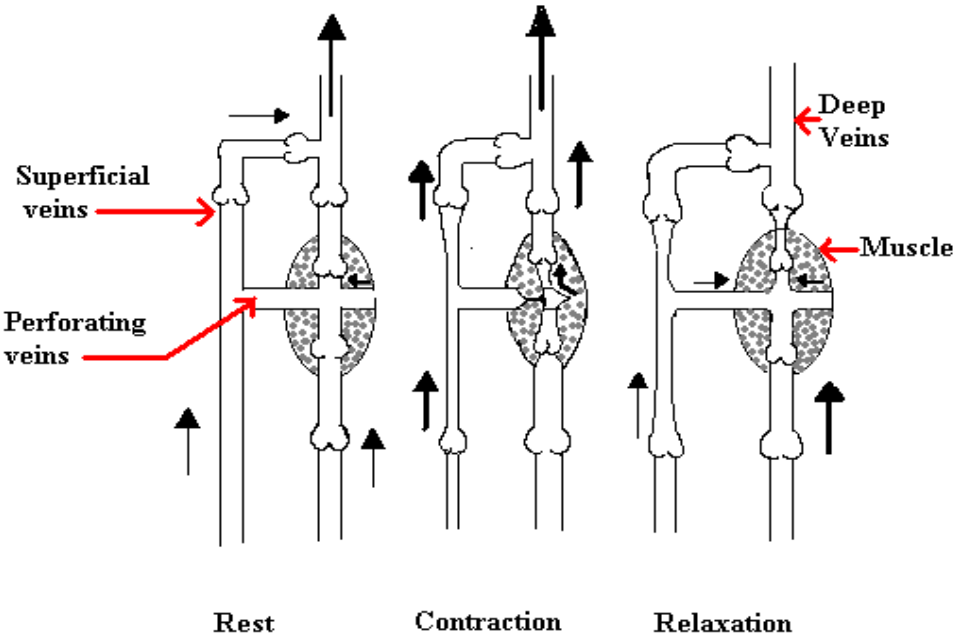
Source: Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 2.18. Ultrasound image of Venous Valves

2.6.3. Calf muscle pump function

In the normal venous circulation, the deep venous system carries 90 percent of the venous flow" (Cole, 2001b, p. 18).

The pumping chambers of the lower limb empty directly due to each muscle contraction (Tibbs 1992). When exercise has stopped, valves (Figure 2.20) above the compression site close, preventing reflux due to gravity, with the veins remaining partially collapsed until the vein segments are refilled by venous inflow from capillaries (Sumner, 2000). The soleal sinusoids empty venous flow into the PT vein. The gastrocnemius sinusoids usually empty venous flow into the popliteal vein (Hirsh & Hull, 1987; Tibbs, 1992).



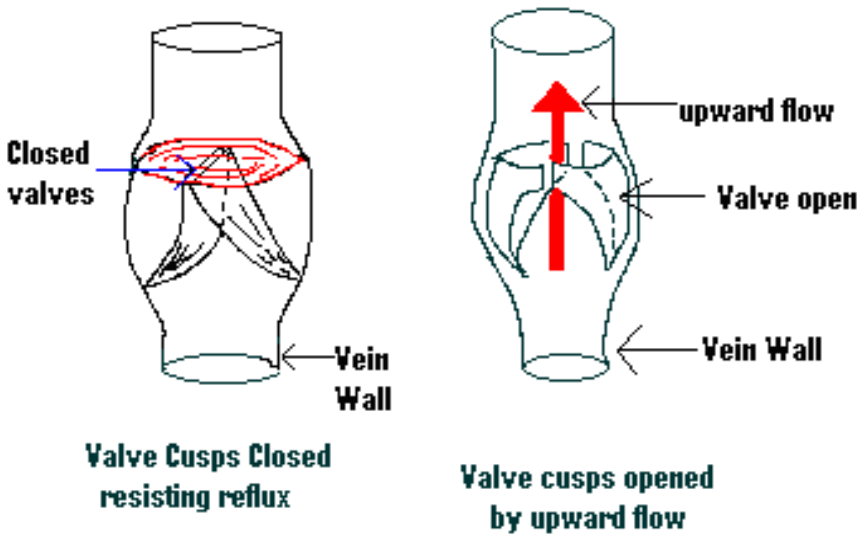
Source: Giordano, 2000.

Figure 2.19. Dynamics of venous blood flow in response to the calf muscle pump.

Blood pools in the Soleal and Gastrocnemius sinusoids before it is ejected by the calf muscle pump (Menzoian *et al.*, 1997). The leg muscles are in effect a power source

whereby during exercise, these sinusoids act as bellows of the muscle pump mechanism (Sumner, 2000). In a healthy limb, during the muscle contraction activity, all perforating veins are closed off from the deep veins by valves and fascial gates, allowing blood to flow in one direction. Once the muscle has relaxed, free flow can occur in either direction depending upon pressure gradients. Every time deep vein pressure drops as a result of one muscle contraction, blood from the superficial veins drains into the deep veins via a perforating vein (Tibbs 1992).

The venous valves in the deep and superficial veins prevent the reflux of blood against the normal direction of venous flow. If and when these valves collapse or fail, varicose veins may develop, as a result of blood pooling at the most dependent section of the vein and remaining there (Gardner and Fox, 1999; Fowkes *et al.*, 2001). In addition to these valves there are also peripheral venous valves which function to protect the capillaries and venules during exercise from large increases in pressure (Lee *et al.*, 1999). Venous valves can be imaged with ultrasound (Figure 2.20).



Source: Giordano, 2000

Figure 2.20. Valves in the veins.

Figure 2.20 demonstrates the operation of venous valves, preventing venous reflux (on the left of the diagram) and permitting venous return (on the right of the diagram). If the valves at the ankle become incompetent, contraction of the calf muscle sends venous blood through the perforators and not to the heart resulting in a reverse flow and a subsequent high pressure reflux (Clain, 1980). Distension of veins due to posture may result in impairment of venous valve function, resulting in reflux in one or more vein segments (Tibbs 1992; Lee *et al.,* 1999).

2.7. Venous Haemodynamics

There are four aspects of normal venous hemodynamics. Venous pressure and the role of gravity, venous volume and its relationship with compliance, pressure flow phenomena in collapsible tubes and venous valves and their contribution to the venous pump mechanism (Rautio, 2002).

Venous flow is intermittent, so therefore it changes from periods of high velocity flow to almost flow cessation (Strandness and Sumner, 1975). Venous flow is affected by gravity, venous pumping and arterial flow. The peripheral pumping mechanism (provided by the calf muscles) alone will cause full venous flow against gravity. This occurs when veins are compressed by the muscles. A vein's ability to collapse means veins empty completely on compression so they can refill prior to the next pumping action. "Veins are thin walled, elastic, collapsible tubes and not 'pipes'of fixed capacity" (Tibbs 1992, p.13). Valves in the veins act against gravity by preventing the blood flowing backwards when directing it towards the heart (Tibbs 1992).

CHAPTER 3

DEEP VEIN THROMBOSIS & FLIGHT RELATED DEEP VEIN THROMBOSIS.

3.0 Introduction

Normal venous function is the return of blood to the heart by means of the venous system (Strandness and Sumner, 1975; Sumner, 2000; Rautio, 2002).

Blood remains in a fluid, clot-free state in healthy vessels (Underwood, 2004). However, in the event of damage to a vessel wall a clot is normally produced. The medical term for a clot is a thrombus. "Clotting that occurs in an unbroken blood vessel is referred to as thrombosis" (Solomon *et al.,* 1990, p. 661). Venous thromboembolism (VTE) is a multicausal disease, in which inherited and acquired risk factors interact together to produce thrombi and/or emboli (Rosendaal, 1999).

In this chapter the pathology of deep vein thrombosis (DVT), pulmonary embolism (PE) and venous thromboembolism by inherited and/or acquired risk factors is outlined. The life long implications associated with DVT and the forms of prophylaxis currently employed to alleviate/prevent DVT and FRDVT are discussed, underlining the necessity for a universal solution to address the problem. Other modes of travel related DVT will also be considered. Implicating factors such as a passenger's designated seat on board aircraft, the use of compression stockings and other risk factors related to this syndrome will then be outlined. Airline cabin environmental factors such as the effects of cabin pressure, hypoxia and humidity on the development of FRDVT will also be highlighted.

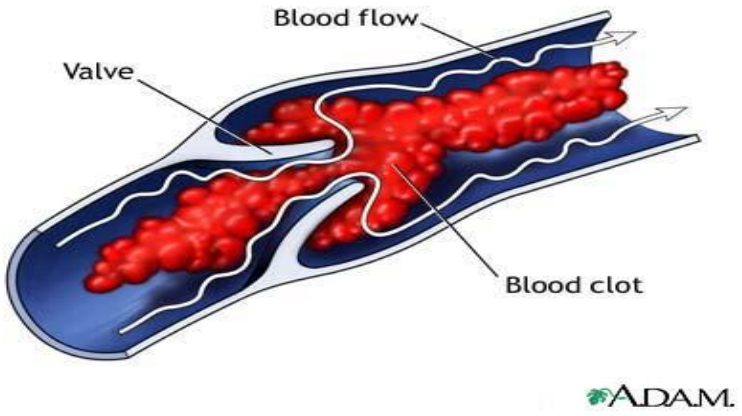
3.1. Thrombus Formation

The endothelium is a single layer of cells separating blood from the vessel wall. The endothelial cells are responsible for maintaining blood in a fluid state or initiating plasma coagulation and platelet activation which are necessary to thrombi development (Browse *et al.*, 1988; Gallagher and Sumpio, 1997; Radomski and Radomski, 2000). A blood clot is "a gel consisting of insoluble fibres and trapped blood cells and platelets" (Solomon *et al.*, 1990, p. 658). There are three stages in the blood clotting process.

When a vessel is damaged, a series of reactions occur which result in the formation of prothrombin activator. The vessel wall damage (endothelial injury) exposes the inner part of the wall which is termed the extracellular matrix (ECM). Prothrombin activator and calcium ions are responsible for the second stage where the prothrombin develops into thrombin (Woolf *et al.*, 2002). The exposed ECM activates platelets to change their shape and release the necessary substance to attract yet more platelets along with Tissue Factor (TF) which works with the platelets to activate the coagulation process (Mitchell, 2005). The final stage is when the thrombin converts fibrinogen into fibrin, which holds the blood cells, platelets and plasma within its threads, making the basis of the clot. When the platelets stick to the fibres they emit a substance called adenosine diphosphate (ADP), which attracts more platelets to the site of damage. Platelets emit a prostaglandin, which activates other platelets (Solomon *et al.*, 1990).

One of the first signs of possible development of a thrombus (Figure 3.1) is platelet aggregation, which may occur in valve cusp pockets, vein junctions or in venous saccules (Ramaswami and Nicolaides, 1994). These initial thrombi grow by layers of platelets which adhere to injured endothelial cells and subendothelium, along with red blood cells and fibrin gathering together in the direction of the blood flow (Ramaswami and Nicolaides, 1994; Kumar and Clark, 2002; Ulutin, 2002).

The main determinants thought to influence thrombi formation include blood flow, the vessel wall, coagulation factors, platelets and red blood cells (Kumar and Clark, 2002). This was first described in 1856 by Virchow and is known as Virchow's Triad (Galili and Bass, 2002).



Source: Medlineplus.

Figure 3.1. Venous Blood Clot.

It is summarised below:

i. Changes in blood flow;

Stasis and/or reduced blood flow, will encourage the development of thrombi. Clotting may occur when blood flow is sluggish. This condition is known as stasis (Solomon *et al.,* 1990). Stasis allows activated clotting factors to become concentrated in the veins and therefore interact with one another, with the end result of thrombus formation. Comerota (1994a, p.32) stated *"...it is logical that reduced flow might prolong the contact time of activated platelets and clotting factors with the vein wall thereby permitting thrombus formation,..."*;

ii. Changes in the vessel wall;

This may be caused by trauma or injury to the endothelial lining. Within two seconds of a vessel wall becoming damaged, the wall of the vessel contracts in what is termed a vascular spasm. This is to reduce blood flow, enabling the platelets to come into contact with the collagen fibres of the wall which are exposed, so platelets can adhere to them (Solomon *et al.*, 1990). The damaged tissues emit substances known as tissue thromboplastin (FIII), which in turn activates the stable factor (FVII) to activate plasma thromboplastin (FIX) and FX so the repair process may begin (Solomon *et al.,* 1990);

iii. Alterations in the blood constituents;

A hypercoagulable state is one in which "…*the normal balance between clotting and anticlotting mechanism becomes altered…*" and so predisposes an individual to thrombus formation (Cho, *et al.,* 2002). Hypercoagulability is concerned with changes in blood elements such as an increase in platelet count and adhesiveness. In addition to this, deficiencies in Antithrombin III, proteins C and S all aid in the development of a thrombus (Comerota, 2000).

The flow of blood through the circulation system ensures that the clotting factors cannot remain in the damaged area. This is to ensure that the clotting process does not continue and completely obstruct a vessel, preventing flow (Solomon *et al.,*, 1990: Mitchell, 2005). Thrombi undergo one of the following four processes once formed;

i. Propogation – the accumulation of more platelets and fibrin, which can lead to the vessel becoming occluded;
ii. Embolisation – where the thrombus dislodges and moves to another site;
iii. Dissolution – be removed by fibrinolysis;

iv. Organisation and recanalisation – thrombus induces inflammation and fibrosis and becomes recanalised. In other words blood flow occurs again as the thrombus becomes part of the vessel wall (Mitchell, 2005).

Fibrosis is the generation of fibrous tissue during healing of tissue or cells (Wilson and Waugh, 1998).

Recanalization and valve obstruction can result in the muscular pump mechanism malfunctioning which can result in an increased pressure in the deep calf veins (Hirsh and Hull, 1987). High pressure can result in blood flow being redirected from the deep system to the superficial venous system, during muscular contractions, resulting in the development of oedema (Hirsh and Hull, 1987). Venous thrombosis can occur in any vein of the body. However veins of the leg or the pelvis are the most common areas (Kumar and Clark, 2002).

3.1.1. Deep Vein Thrombosis.

If venous thrombosis occurs in a deep vein such as the popliteal or femoral vein it is termed a DVT (Weitz, 2000). A DVT may be classed as a proximal thrombosis which occurs in the popliteal and thigh veins or a distal thrombosis which occurs in the calf veins. Proximal DVT "…is a serious disorder with potentially life-threatening consequences…" as it is likely to progress into a pulmonary embolus (Riddle and Wells, 2004, pp.729-30).

The incidence of DVT is estimated as one in 1000 person years (Kelman *et al.*, 2003). Left sided DVT episodes are more prevalent than right limb episodes, as there is a tendency for the left common iliac vein to be compressed by the right common iliac artery, which it crosses and so causes damage (O'Sullivan *et al.*, 2000).

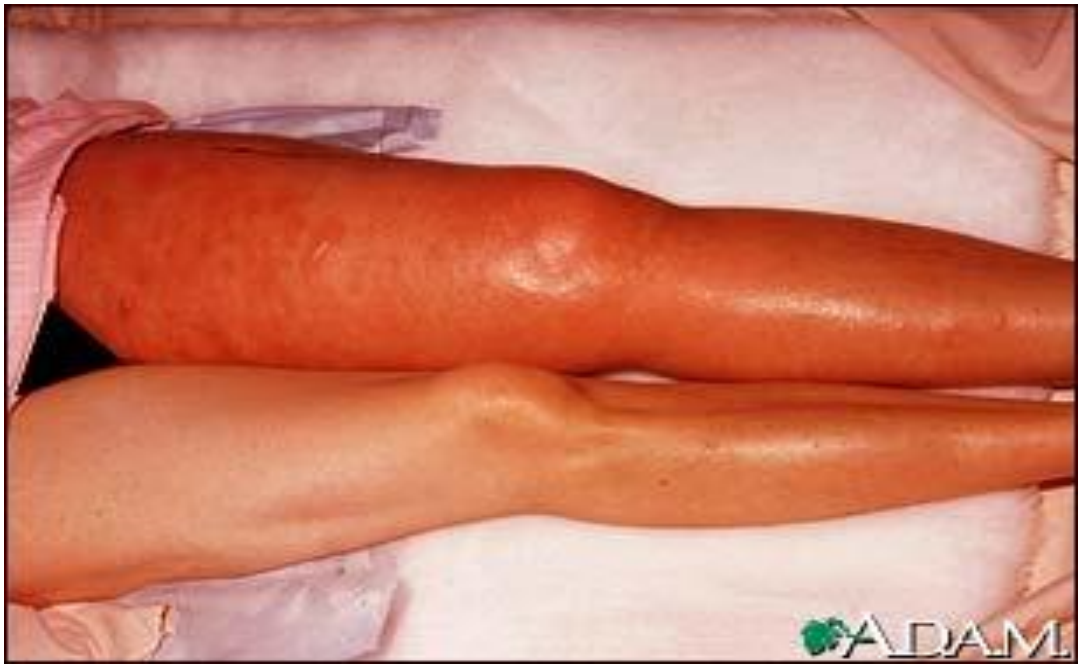
Varma *et al.*, (2004) report that mortality as a result of DVT at 20 percent. Anderson and Audet (1998) reported that DVT occurred in 250,000 patients with 50,000 deaths in the Worcester, Massachusetts, study. This study was conducted over 18 months in the mid 1980s by reviewing the hospital discharge records of all patients with venous thromboembolism (VTE), including both recurrent and first-time episodes.

3.2. Symptoms of DVT

"Venous Thrombosis in the lower extremity may cause little or no acute pain unless the associated inflammatory reaction is significant, in which case there may also be localized tenderness along the course of the involved vein" (White *et al.*, 2000, p. 6).

Small non-occlusive thrombi produce no recognisable physiologic defects (Sumner, 2000). Some of the common symptoms of thrombi include pain in the calf, swelling, redness, warmth of the affected limb and possibly oedema in the ankle (Stranden, 2000; Mitchell, 2005; Clarke *et al.*, 2006).

Swelling may occur if thrombus is extensive and causes complete obstruction (Ramaswami and Nicolaides, 1994). Swelling in the ankle and foot may suggest a thrombus is present in the deep veins of the calf. Swelling of the thigh suggests thrombus in the ileofemoral area, (Figure 3.2) whilst swelling of the groin, thigh and calf suggests the presence of iliac thrombosis extending to the inferior vena cava (Ramaswami and Nicolaides, 1994).



Source: Medlineplus.

Figure 3.2. DVT in the ileofemoral (groin) area

3.3 Superficial venous thrombosis

Thrombi may form in superficial veins such as LSV or the SSV. Superficial venous thrombosis (SVT), also known as superficial thrombophlebitis, is a less serious condition than DVT. Complications can occur where the thrombus may extend along the perforating vein to the deep veins however this only occurs rarely (Clain, 1980). Symptoms if any could be similar to those of a DVT (Mitchell, 2005).

3.4. Thrombophilia

Thrombophilia is defined as a tendency to have recurrent venous thromboembolism (Wood, 1996, p.1817). It is an uneven balance between procoagulants and anticoagulants present in the blood (Laffan, 1998). Individuals with a history or family history of DVT, PE, miscarriage, who develop DVT at an unusual site, may have a genetic thrombophilia (Bucciarelli *et al.*, 1999; Lowe and Rumley, 1999; Kumar and Clarke, 2002).

3.5. Lysis of thrombi

Natural lysis of the thrombi may occur due to what is termed fibrinolytic activity. Plasmin and activated Protein C, work together to break down fibrin and fibrinogen into fibrin degradation products (FDP) (Labelle and Kitchens, 2005; Kumar and Clark, 2002). Plasmin can break down Factor V and Factor VIII coagulation factors. Plasminogen activators come from plasma or blood cells or tissues, which convert the plasminogen into plasmin (Kumar and Clarke, 2002; Labelle and Kitchens 2005).

Several factors play a role in determining how slowly or quickly a thrombus can lyse (Blombery and McGrath, 2000):

i. The site where the thrombus developed;
ii. The size of the thrombus and if it is fully occluding the vein;
iii. The degree of fibrinolytic activity;
iv. If anticoagulation treatment is being administered and if so for how long.

The process of clotting is regulated by three natural anticoagulants. Antithrombin III is activated by binding to heparin-like molecules on the endothelial cells. Protein C and Protein S inactivate FVa and FVIIIa. TFPI is released from the endothelium to inactivate Fxa and FVIIa (Mitchell, 2005). Plasmin is activated by FXIIa, thrombin and lysosomal enzymes from damaged tissues. Its purpose is to dissolve fibrin and to reduce the size of clots when the healing process is occurring (Solomon *et al.,* 1990). If the thrombus is large, it may not fully lyse leading to a "reduction in the luminal diameter of the vein" and an increased risk of recurrent, future thrombi developing and/or valvular incompetence (Ramaswami and Nicolaides, 1994).

3.6. Post thrombotic syndrome

The long term outcomes of DVT include resolution, valve damage, the post thrombotic syndrome (PTS), and/or recurrent DVT.

"A history of DVT increases the risk of chronic venous insufficiency 25.7 fold, compared with those without a history of DVT." Blombery and McGrath (2000). This increased risk of chronic venous insufficiency (CVI) may result from the following three factors; a remaining thrombus obstructing venous flow, an increase in venous valve incompetence as a result of previous thrombus and dilation of veins or calf muscle pump dysfunction (Nicolaides and Summer, 1991; Blombery and McGrath, 2000).

A review of literature was conducted to determine the length of time before PTS presented with symptoms after an episode of DVT. It was concluded "… most cases become clinically apparent within the first 1 to 2 years of the acute DVT" (Kahn *et al.*, 2000, p. 426). Thirty percent of patients diagnosed with DVT could suffer from PTS (Hyers, 1999). Common symptoms of chronic venous disease (CVD) range from moderate limb swelling to pain, discolouration and possibly ulcers (Neglén, 2003; Padberg *et al.*, 2003). The cost in treatment of venous ulcers in the United States is greater than one billion dollars and between four and 600 million pounds sterling, per year in the United Kingdom (Nicolaides, 2000).

Both venous hypertension and valvular incompetence are precursors to PTS (Comerota, 2000; SIGN, 2002). Patients suffering from PTS may present with pain and swelling and some may even develop ulcers (Ramaswamai and Nicolaides, 1994; Meissner, 2002; SIGN, 2002).

CVI is defined as "*an abnormally functioning venous system caused by venous valvular incompetence, …which may affect the superficial venous system, the deep venous system or both."* (Porter and Moneta, 1995, p.639).

To begin with symptoms such as discomfort and swelling of the ankle may occur, with edema and pain increasing and the skin becoming inflamed. As the disease progresses, ulcers may develop. Ulceration may occur two to three years after a first episode of DVT (Tibbs, 1992).

3.6.1. Cost Effectiveness of Prophylaxis

As a duty of care and a preventative measure, patients undergoing surgery must wear TED stockings prior to, during and after surgery to prevent a thrombus forming. This is a hospital procedure and one which recognises the risk of thrombus formation as a result of immobility.

It is reasonable to argue that the use of prophylaxis should not be determined by how much it will cost, instead it should be provided to prevent an unnecessary death by PE (Hull et al., 1986).

3.7. Flight Related Deep Vein Thrombosis

When a thrombus develops during flight it is termed Flight Related Deep Vein Thrombosis (FRDVT). FRDVT was termed Economy Class Syndrome, (ECS) in 1988 by Cruickshank *et al*., (Belvís *et al.*, 2005; Gispert *et al.*, 2006). Subsequently, it has been demonstrated to occur in first class passengers (Mohler, 1997; Galili and Bass, 2002), aircraft pilots (Johnson and Evans, 2001; Shrivastava, 2003) and also following car and train travel (Ferrari *et al.*, 1999, Belvís *et al.*, 2005; Cannegieter *et al.*, 2006). Death as a result of FRDVT has been reported in passengers as young as 28 years of age (Jameson, 2001; McDonald, 2003) and in travellers who have remained seated for the duration of a twelve hour flight (Paganin *et al.*, 1996). During air travel, two of Virchow's Triad factors are present, venous stasis can occur due to immobility from

sitting in an aircraft seat and hypercoagulation due to the cabin environment (Comerota, 1994a).

3.7.1. Incidence

The reported incidence of FRDVT ranges between 0.24 percent and 10.34 percent (Belcaro *et al.,* 2001a; Belcaro *et al.,* 2001b; Scurr *et al.,* 2001; Belcaro *et al.,* 2002; Cesarone *et al.,* 2003a).

The Lonflit 2 Study determined the incidence of FRDVT was 0.24 percent in the stocking group on a flight of ten to 15 hours duration (Belcaro *et al.,* 2001b).

Twenty-two DVTs in 19 participants (three of these individuals presented with bilateral DVTs) and eight SVTs were diagnosed in the control group of 422 participants (Belcaro *et al.,* 2001a).

The Lonflit-flite study reports a FRDVT incidence of 5.4 percent (92 volunteers) in the control group (Cesarone *et al.,* 2003a). The Scholl Flight socks study determined the incidence of FRDVT and FRSVT (without stockings) as 2.12 percent and 1.06 percent respectively, on flights of seven to eight hours duration (Belcaro *et al.,* 2002). Belcaro *et al.,* (2003b) determined the incidence of FRDVT in a high risk control group (flight eleven to thirteen hours duration) as 5.8 percent.

Hughes *et al.,* (2006) reported an incidence of FRDVT of 4.68 percent in a study of 576 patients whom were admitted for VTE. Sixty of these patients had travelled by air, with 43.3 percent travelling for at least ten hours duration.

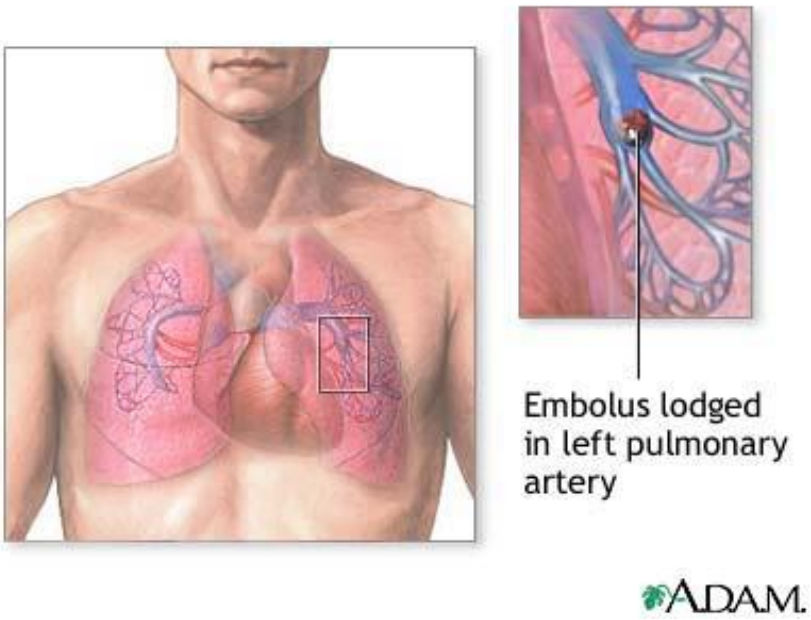
The Mediven stocking trial determined the incidence of FRDVT was 10.34 percent in those not wearing compression stockings on a flight of greater than eight hours duration (Scurr *et al.,* 2001).

FRDVT alone is not life threatening (although it may result in long-term lower limb disease), it is its potential to cause pulmonary emboli that can have serious consequences.

3.8. Pulmonary Embolism

When a venous thrombus becomes dislodged from its site of formation, it becomes an embolus. This embolus may then move through the venous system until it becomes lodged again (Solomon *et al.,* 1990; Goldhaber, 1998; O'Donovan *et al.,* 2005). Pulmonary embolism (PE) occurs when the embolus becomes trapped in the pulmonary arteries of the lung (Figure 3.3) (Solomon *et al.,* 1990; Damjanov, 2002). *"Acute PE impairs the efficient transfer of O_2 and CO_2 across the lungs"* (Goldhaber and Elliot, 2003). If an embolus is large enough to occlude the artery, it may cause death (Ramaswami and Nicolaides, 1994). This is known as pulmonary arterial obstruction. One of the affects of this is redistribution of blood flow. When the platelets release serotonin, pulmonary vascular resistance increases, creating alveolar dead space (Goldhaber, 1998). As the dead space increases resulting from the embolus, the breathed gas cannot enter the gas exchange units of the lung, thus impairing the necessary removal of CO_2 in the body by the lungs. The gas exchange units of the lung are known as the respiratory bronchioles, alveolar ducts and alveolar sacs. If the blockage is large enough, it may even prevent venous blood entering the lungs and so it remains in the venous system (Goldhaber and Elliot, 2003).

When people develop PE unexpectedly it may be due to an asymptomatic thrombus travelling into pulmonary vessels, which causes cardiogenic shock, followed by circulatory failure and death (SIGN, 2002). One associated hazard of PE is that as patients become older, the presence of a thrombus can mimic other illnesses such as acute coronary syndrome.



Source: Medlineplus

Figure 3.3. Pulmonary Embolus

So if a patient presents with two coexisting illnesses it can be difficult to accurately diagnose PE (Goldhaber, 2004). This may result in an underestimation of the incidence of PE related to travel. It is reported that PE's originate in the deep veins of the legs in 90 percent of cases (Hull *et al.*, 1986; Perrier, 2000 and Loud *et al.*, 2001).

The incidence of PE is 500-1000 per 1000000 person years (Kelman *et al.*, 2003). It has been estimated to occur in greater than 600,000 patients per year in the United States of America and resulted in death for 100,000 of these patients per year (Tapson, 2001).

3.8.1. Flight related pulmonary embolus (FRPE)

FRPE is the term used to describe a PE which has developed as a result of long haul flights. FRPE was first reported by Homans in 1954, two cases occurred directly due to long haul flights and another two cases of PE resulted from travel by car (Dalen, 2003).

Doctors in Kings College London have claimed that 30,000 people die each year in Britain from PE and they estimated that about 1000 of these are due to flying (Wright, 2003, p.1).

Incidence as low as 0.39 cases per million per year have been reported (Pérez-Rodríguez *et al.,* 2003). Symptoms presented at varying times; from during flight to post disembarkation in the airport and up to eight weeks post flight. FRPE in this study was attributed to flights of greater than six hours duration, with the majority travelling greater than eight hours duration (Pérez-Rodríguez *et al.,* 2003).

Lapostolle *et al.,* (2001) reported the incidence of FRPE as 4.8 cases per million. This incidence increasing with the total distance travelled, i.e. in passengers who travelled greater than 5000 km, the incidence of PE was 1.5 cases per million, while those who travelled greater than 10,000 km the incidence of PE increased to 4.8 cases per million. This study defined a flight as "the period between take off and landing (including stopovers"). Of the 135.29 million passengers from 145 countries that arrived at that airport, only 56 passengers were documented as having PE. Symptoms presented at varying times as in the Pérez-Rodríguez study. Eight passengers during flight, 16 passengers developed symptoms upon landing and the remaining 32 post travel. Sadly, one incidence resulted in death (Lapostolle *et al.,* 2001).

A ten year study conducted by Caillard and Clerel (2001) at the Aeroports de Paris emergency unit, which concluded in the year 2000, revealed that 109 patients presented with symptomatic PE. Eighty three women and 24 men with a mean age of 57.3 years were diagnosed. Thirty eight of the passengers had no risk factors and no previous history of DVT/PTE. Ninety five percent travelled for greater than six hours and 75 per cent greater than twelve hours. Only emergency cases have been documented.

The incidence of FRPE was reported as 6.94 percent by Hughes *et al.,* (2006). This study was a follow up study from the New Zealand Air Travellers Thrombosis (NZATT). It examined admissions in Wellington, Auckland and Green Lane hospitals for flight related VTE, in the period between 1997 and 2001. Recent air travel (at least ten hours duration) was recorded in 60 of the 576 cases which met the inclusion criteria. Twenty seven cases of FRDVT and 40 FRPE cases were identified, with both DVT and PE present in seven of these individuals. Again varying time and presentation were reported. Sixty five percent of the 60 individuals presented with symptoms to the hospital within one week (Hughes *et al.,* 2006).

Eklof (1996) and Ferrari *et al.,* (1999) have both stated that PE may develop in passengers several weeks post travel. This is very likely as FRDVT can be asymptomatic with symptoms not appearing for as long as four weeks after the flight (Gorshtein, Levy & Shoenfeld, 2002; Watson, 2005).

According to Murphy (2001) *"two thirds of travel-related VTE presents after patients leave the airport".* As a result many people may die directly from the consequence of FRDVT and yet this reason may never be attributed as their cause of death.

3.8.2. Symptoms of PE.

Symptoms of PE may include chest pain, dyspnoea or haemoptysis. (Hull *et al.,* 1986; Goldhaber, 1998). Dyspnoea (breathlessness) can be as a result of cardiac or respiratory causes (Kumar and Clarke, 2002). Haemoptysis (coughing up blood) is defined as "…the expectoration of gross blood or blood-streaked sputum" as stated by Flores and Sandur (2006, p.37). It is not always possible to identify the initial source of the embolus (Ögren, *et al.,* 2005). However a PE which originated in the proximal veins of the legs is usually larger than those that originated in calf veins (Hirsh and Hull, 1987).

3.9. Venous Thromboembolism

Venous thromboembolism (VTE) is the term used to describe DVT and/or PE (Cook *et al*, 2004; Klatsky & Baer, 2004; Grand'Maison, *et al*., 2005; Ögren *et al*, 2005). There is a significant difference between deep and superficial VTE. Deep VTE describes a thrombus which has formed in a deep vein that may embolise and travel to the lungs. Where as a superficial VTE describes a thrombus forming in a superficial vein which seldom embolise or extend to the deep system. Research on post mortem studies reported that 50 percent of cases of DVT and PE were asymptomatic (Kesteven, 2000).

3.9.1. Flight related venous thromboembolism (FRVTE)

FRVTE is the term used to describe both a FRDVT and FRPE.

The Lonflit-flite study determined the incidence of flight related DVT events was 5.43 percent in the control group (Cesarone *et al.*, 2003a). Kelman *et al.*, (2003), recorded hospital admissions for flight related VTE up to 100 days post flight. During the study period, 9.4 million passengers flew into Australia, corresponding with 16,205 hospital admissions for VTE. Of these, 5,508 were post international flights, with the incidence of VTE (0.05 percent) four times greater in the first two weeks (Kelman *et al.*, 2003). The report "Travellers Thrombosis Review of Deep Vein Thrombosis associated with Travel" (2001) published by The Aerospace Medical Association Air Transport Medicine Committee references the work of Sarvesvaran (1986) in which twelve of 104 deaths which occurred during or soon after flight were due to VTE (Bagshaw, 2001).

3.9.2 Incidence of VTE

The annual incidence of VTE in the northern European population was estimated at 1.6-1.8 per 1000 (Hansson *et al.*, 1997; Nordstrom *et al.*, 1999). In the United States there

are between "100,000 to 300,000 cases per year" of VTE (Bockenstedt, 2003, p. 1203). It affects approximately one in 1000 people each year (Margaglione *et al.*, 2000). These incidences are for all causes of DVT and PE.

In 2003, International airlines collectively carried 1.6 billion passengers (IATA, 2004). *"the occurrence of DVT and PE probably constitutes one of the main medical repercussions of air travel"* (Ferrari *et al.*, 1999, pp. 442-3). The actual incidence of FRDVT is unknown, however the annual incidence of VTE increased by 12 percent after one long haul flight (Kelman *et al.*, 2003). FRVTE is just one element of this disease spectrum.

In the Ferrari study thirty nine of 160 VTE patients had a history of recent travel. The incidence of combined travel related DVT was reported as 24.37 percent. Travel by car resulted in 71.79 percent of all travel related DVT, travel by air at 23 percent and travel by train accounted for approximately five percent (Ferrari *et al.*, 1999).

The difficulty of determining the true incidence of VTE is compounded by the length of time before symptoms developed after flight, reported from 96 hours after the beginning of a trip to up to 35 days later (Kesteven, 2000). This variation is also reported for the more serious consequence of PE established by the study conducted at the Ramón y Cajal Hospital. Two passengers presented with symptoms during flight and eleven post disembarkation, in the airport with one case failing to present until eight weeks post flight (Pérez-Rodríguez *et al.*, 2003).

3.10. Inherited risk factors associated with the development of DVT

Some inherited deficiencies make the individual more likely to develop DVT. This places the individual at a higher risk of FRDVT, particularly if the condition is undiagnosed.

Inherited risk factors include deficiency in natural inhibitors of coagulation or clotting (Samama *et al.,* 1994):

i. Factor V Leiden is the most common inherited risk factor predisposing individuals to venous thrombosis (Koppel *et al.,* 2001; Simioni *et al.,* 2002; Arsov *et al.,* 2006). Factor V Leiden is generally associated with venous thrombolic events rather than arterial events, (Nicolaes and Dahlbäck, 2002). It is more common in individuals suffering from DVT, than individuals who are diagnosed with PE. Meyer *et al.,* (2001, p.14) suggest the reason for this could be that the thrombi will not embolise in the presence of this mutation as "the thrombus is less susceptible to the fibrinolytic system". It may increase the risk of DVT development by 3.5-5 fold (Köppel *et al.,* 2001; BTS Guidelines, 2003). It was thought to only occur in white people (Rosendaal, 1999). However Klatsky and Baer, (2004), reported a low prevalence of the Factor V Leiden mutation among Asian groups. They believe that carriers of the mutation have a "*50- to 100-fold"* greater risk of a VTE episode occurring (Klatsky and Baer, 2004, p. 494). This mutation may be present in five percent of Caucasians in both Europe and North America (Hyers, 1999). Women taking oral contraceptives whom are carriers of Factor V Leiden have a greater potential to develop VTE (Aznar *et al.,* 2000).

ii. Activated Protein C (APC) resistance is a direct result of the Factor V Leiden mutation (de Visser *et al.,* 1999; Köppel, 2001.) Only discovered in 1993 by Dahlback and co-workers (Frederick *et al.,* 2001), it can be identified in approximately 50 percent of patients with thrombosis (Günay *et al.,* 2001). Nicolaes and Dahlbäck, (2002) and Anderson and Spencer,

(2003) take a less definite view by claiming that APC resistance is present in 20-60 percent of patients with VTE. It is common in approximately "…5% of the general population…" (Desmarais *et al.,* 1996, p.1374). Resistance to APC is a result of a reduced anticoagulant response of plasma to APC. It is associated with a three to seven fold increased risk of VTE (de Visser *et al.,* 1999). Those who have a poor anticoagulant response to APC have a seven fold increased risk of DVT developing (Kester *et al.,* 1993).

iii. Antithrombin (AT III) deficiency, not only inhibits thrombin but inactivates clotting factors such as IXa, Xa, XIa, XIIa and VIIa (Crowther and Kelton, 2003). There are two types of this deficiency. Type 1 is a reduced production of the antithrombin protein with Type 2 being a production of an abnormal protein. (Crowther and Kelton, 2003; Rosendaal, 1997). "Patients with AT III deficiency have thrombotic problems develop during the second or third decade of life, with 65% of affected individuals experiencing some form of thrombosis by age 30" (Bongiovanni, 2002, p.213).

iv. The role of Protein C (PC) is to ensure coagulation and fibrinolysis remains balanced. "PC is activated on endothelial cells by thrombin bound to thrombomodulin" (de Visser *et al.,* 1999, p.1271; Bongiovanni, 2002). Thrombotic events are usually of a venous nature and not arterial. Protein C deficiency and Protein S deficiency both increase the risk of VTE developing, (Bongiovanni, 2002; Cho *et al.,* 2002), however this type of deficiency is not highly prevalent (Tibbs 1992).

These inherited deficiencies can be triggered by the following acquired factors, shown in table 3.1.

Table 3.1. The incidence of factors which trigger the first episode of thrombus in patients with AT-III and Protein C deficiency

Triggering factors	AT-III deficiency %	Protein C deficiency %
Pregnancy	28	20
Surgery	13	15
Oral Contraceptives	4	7
Immobilisation	-	9
Others	-	3
Unknown	42	46

Source: Samama *et al.*, 1994.

There is a well documented relationship between AT-III, Protein C and Protein S deficiencies. Some of their common clinical features include; a first thrombus between 20 and 40 years of age, a thrombus developing in an unusual site, such as in the mesenteric veins in the abdomen, and a higher tendency for recurrence (Samama *et al.*, 1994; Grand'Maison *et al.*, 2005). Bucciarelli *et al.*, (1999) concluded that the risk of VTE occurring is greater in individuals who have AT–III deficiency than carriers of Protein C or S deficiency. Prothrombin 20210A gene mutation is a precursor of VTE (Aznar *et al.*, 2000; Bongiovanni, 2002). It is more prevalent in southern European inhibitants than elsewhere (Aznar *et al.*, 2000).

3.10.1. Inherited coagulation associated with flight.

Scurr *et al.*, determined an incidence of gene mutation Factor V Leiden and Prothrombin G20210A (PGM) were present in ten percent of European populations, based on a study into the incidence of FRDVT. Duplex ultrasound of the lower limbs and blood tests were

taken before and after flight to determine presence of Factor V Leiden and PGM and the absence of DVT. Twelve asymptomatic calf DVT in the control group (115) and four SVT in the stocking group (116) were diagnosed post flight (Scurr *et al.,* 2001).

Schreijer studied the impact of inherited conditions plus oral contraception to establish the relative risks. Seventy one healthy volunteers 15 males and 56 females (ranging from 29 to 39 years) were recruited. It was established that eleven had Factor V Leiden mutation, another 15 were taking the contraceptive pill, a third sub group of 15 volunteers with Factor V Leiden mutation were also taking oral contraceptives and the fourth sub group (30 volunteers) had no apparent VTE risk factors.

Three studies were conducted, (each eight hours duration); on a Boeing 757, the cinema and their normal daily routine. Cabin pressure was between 1800m and 2100m. Cigarettes, alcohol, drugs (other than the contraceptive pill) and the use of GECS, heparin or aspirin were forbidden. Everyone was encouraged to remain seated for as long as possible. These restrictions applied in all three parts of the study.

Median concentrations of thrombin-antithrombin (TAT) complex levels were identified before, during and after the three different studies. (TAT are markers of activated coagulation). TAT baseline levels were higher post flight than post cinema or the daily life study. Volunteers with the Factor V Leiden mutation taking the contraceptive pill had higher TAT values than the other subgroups of volunteers. Elevated D-dimers post flight were most prominent in the FVLM group who were taking the contraceptive pill.

Therefore "……a combination of a genetic predisposition (Factor V Leiden) and an environmental factor (oral contraceptives, hypobaric hypoxia) is probably the basis for venous thrombosis associated with air travel" in this subgroup (Schreijer *et al.,* 2006, p. 837).

3.11. Acquired risk factors associated with the development of DVT

Acquired risk factors include changes in coagulation factors and fibrinolytic functions (Samama *et al.,* 1994; Heit *et al.,* 2001). These changes may be a result of changing the environment that a person may be exposed to, such as hospitalisation or flying long haul or changing health status. The following outlines the main acquired risk factors:

i. Stasis of blood flow resulting from immobilisation is a well documented acquired risk factor (Comerta, 1994a, Tibbs, 1992, Kesteven, 2000). This may be caused by old age and the inability to walk (Porter *et al.,*, 1995), due to medical conditions or a result of the environment someone is placed in, such as flying long-haul. One interesting medical study, conducted by Hamer *et al.,* (1968), investigated the relationship between immobility and the partial pressure of oxygen (PO_2) within valve pockets of the veins. This study showed that when venous flow within valve pockets became stagnant, the PO_2 levels fell. The resulting fall in PO_2 levels results in damage to the cells of the vein walls, a factor which leads to the development of thrombi within valve sinuses (Strandness and van Breda, 1994). While in-flight there is a general reduction in PO_2 (Galili and Bass, 2002; AMA, 2003).

ii. All forms of cancer increase the risk of DVT development (Bastounis *et al.,* 1996; Hyers, 1999). Increased risk of DVT in cancer patients is reported between 2.5 to 4.1 fold (Samama *et al.,* 1994; Lee and Levine, 2003). This risk can further increase due to radiation and chemotherapy (Joung and Robinson, 2002; Liebman, 2005). The worrying factor with respect to cancer is that thromboembolism is also noted to be a long term cancer risk with a four fold increase in diagnosis over the general

population in the first year of patient's admission for VTE (Baron *et al.*, 1998). Hence passengers with undiagnosed cancer may be increasing their FRDVT risk by travelling.

iii. Times of pregnancy and puerperium are considered to be one of the greatest risk factors of VTE development (Tibbs, 1992, Porter and Moneta, 1995). Puerperium is a period of about 6 weeks following childbirth (Zotz *et al.,* 2005). "Pregnancy causes a hypercoagulable state and venous stasis in the lower limbs, which increases the risk of VTE" (Kingman and Economides, 2002). "…(PE) is still the leading *Direct* cause of maternal death in the United Kingdom." (Lewis and Drife, 2002). During pregnancy there is a four–to tenfold increased risk of VTE (SIGN, 2002; Brenner, 2005). One of the problems with pregnancy is that symptoms which mimick DVT and PE symptoms, namely swelling and pain of limbs, chest pain and dyspnoea, commonly occur in the pregnant woman and may or may not be related to a thrombus (Ginsberg *et al.*, 2001).

3.11.1. Surgery related issues

i. During surgery, the patient is in the supine position. The PT veins, gastrocnemius veins and soleal veins are all subject to increase in diameters. Pressure created from an individual lying on an operating table can "lead to vessel wall hypoxia" (Nandi *et al.,* 1998).

ii. Immobility occurs in the perioperative state, (the period immediately before or after an operation). Post-operative patients are further susceptible to clotting as "*venous sludging during anaesthesia is thought*

to induce a nidus of blood clot behind a venous valve" (Kesteven, 2000, p. S33).

iii. Venodilation of the lower limbs is a cause of a post operative DVT episode (Scurr, 1994). "Passive venodilation stretches the endothelium beyond the support of the tunica media" (Agu *et al.,* 1999, p.993). The resulting tear in the intima, means that contact of activated platelets and clotting factors with thrombogenic subendothelial collagen occurs (Krupski, 1997; Agu *et al.,* 1999).

iv. Hip replacement therapy may cause a "twisting" of major veins, which may predispose the patient to post operation DVT (Anderson and Audet, 1998). According to Bergqivst (2003/2004, p.360) elective hip surgery predisposes the patients to "…a prolonged coagulation activation and a decreased venous emptying for a few weeks…".

v. With orthopaedic patients, traction and plaster casts inhibit postoperative movement, which leads to the development of venous stasis and the risk of thrombus formation (Hirsh and Hull, 1987).

vi. Surgery heightens the risk factor within the period of 45-90 days post surgery (SIGN, 2002). Patients who have had orthopaedic surgery should avoid long haul travel post surgery (Nicholson *et al.,* 2003). Patients in the critical care units of hospitals have either a moderate or high risk of developing VTE (Geerts and Selby, 2003; Cook *et al.,* 2004). The study conducted by Heit, *et al.,* (2001) found that the incidence of VTE in hospitalised patients is 100 – fold greater than in community residents.

3.11.2 Female related issues

Oral contraceptive use and hormone replacement therapy have both been demonstrated to predispose women who are taking these medications to thrombus formation:

i. Oral Contraceptives (OC) contain oestrogen which interacts with antithrombin III, reducing its efficiency, thus increasing the risk of VTE (Tibbs, 1992). The risk of women developing spontaneous VTE when using second generation OC is reported as 15 per 100,000 a year (SIGN guidelines) and 30 per 100,000 per year when using third generation OC. Women who suffer from coagulation disorders, who smoke and who are obese while taking OC have an increased risk of developing thromboembolisms (Barton *et al.*, 2002).

ii. Hormone Replacement Therapy (HRT) is provided to postmenopausal women, who suffer from symptoms due to an estrogen deficiency. It can be administered orally, transdermally (through the skin) or locally (in the vagina), depending on necessity. Women treated with HRT are at an increased risk of VTE (Spiliotopoulou and Grouzi, 2003; Greer and Walker, 2004). The reason why HRT *'provokes an increased risk of VTE is unclear'* (Greer and Walker, 2004). Apparently the haemostatic system (which is responsible for preventing excessive bleeding) becomes altered by the menopause, leading to an increase in some of the coagulation factors. HRT produces a reduction in antithrombin, which will lead to an increased risk of thrombus formation. HRT produces a reduction in fibrinogen and Factor VII activation but enhances fibrinolysis (solubilisation of fibrin in blood clots) and increases the resistance to Protein C, (Spiliotopoulou and Grouzi, 2003; Greer and Walker, 2004,) all of which should result in a decrease of formation of

thrombin. It must be noted that studies investigating the effects of HRT on coagulation factors have differing conclusions.

3.11.3. Other health related issues

i. Obesity, according to some experts, is one of the most important risk factors of PE. A person is described as obese if his/her body mass index (BMI) is greater than 30 kilogram per meter squared (kg/m^2) (Lowe and Rumley, 1999). It is calculated by dividing the individual's weight (kgs) by their height in metres squared (m^2) (Marik and Varon, 1998; Padberg *et al.,* 2004). Obesity actually limits lung capacity by up to 30 per cent in patients with gross obesity, due to increased chest wall resistance and increased airway resistance (Marik and Varon, 1998). A BMI of greater than 30 kg/m^2 increases the risk of VTE by 10-fold, after long distance travel by car, train or bus (Cannegieter *et al.,* 2006). Critically ill obese patients, being treated in the intensive care unit (ICU) have a higher chance of developing VTE (Marik & Varon, 1998). Obesity rates have rapidly increased by "three-fold or more since 1980" (WHO, 2002, p.60).

ii. Stroke-patients with paralysis resulting from a stroke have a high risk of DVT developing in the paralysed limb as a result of venous stasis (Agu *et al.,* 1999; Nicolaides *et al.,* 2002; Mazzone *et al.,* 2004). VTE is a major cause of death in stroke patients (Scholten *et al.,* 2000).

iii. Prandoni, *et al.,* (2002), found that a residual thrombosis is a risk factor for recurrent VTE. As the years progress the risk of recurrent VTE decreases as does the mass of a residual thrombus. Another study conducted established that 58 of 313 outpatients presented with a recurrent episode, between six and

36 months after the first thrombotic event. Forty one of these 58 events developed in the presence of a residual thrombus (Prandoni, 2004).

3.11.4. Travel related issues

Long periods of immobility imposed by any mode of travel constitute a risk for DVT (Ferrari *et al.,* 1999). For the purpose of this dissertation, a long haul flight is considered to be a flight of four hours or longer. Ferrari and co-workers established that a flight of at least this duration posed a risk factor for FRDVT (Ferrari *et al.,* 1999). A World Health Organisation report into flight related DVT corroborates their findings and concludes that *"a flight of more than four hours increases the risk of deep vein thrombosis in the general population by between **three** and **five** times."* (Templeton, 2005). Venous stasis as a result of sitting, while travelling by land and air are causative factors.

One hundred patients, suffering from PE, in a Spanish Hospital were interviewed to determine risk factors for PE over two years. Mode and duration of travel was established prior to hospital admission. In this study a prolonged journey was defined as five hours duration or more. Each patient's medical history was examined and blood samples were taken to identify any coagulation abnormalities. Nine of the 100 patients had a travel related PE. Six travelled by land and the others by air, with a mean journey time of 8.8 hours. No patients had any coagulation abnormalities (Gispert *et al.,* 2006).

3.11.4.1. Seated Position

Sitting in one position for long periods of time has been implicated in FRDVT development due to resultant venous stasis. When humans are upright, approximately "70% of the circulating blood volume is below the heart" (Miller *et al.,* 2005, p. 925). Both the calf muscle pump (refer to section 2.6.3.) in conjunction with respiratory muscle

pump (section 2.3.1) facilitate the return of blood to the heart (Miller *et al.,* 2005). However the consequence of stasis (due to long periods of immobility) is that platelets come into contact with the endothelium, and the resultant activated clotting factors cannot be removed due to the lack of blood flow, thus creating an environment for thrombus formation (Kumar *et al.,* 2005). Wright and Osborne in 1952 demonstrated that sitting in one position reduces the venous velocity by two thirds**.** Passengers on board any form of transport who are required to sit for long periods of time will be at risk of DVT (Ferrari *et al.,* 1999).

The normal economy class seat pitch on most commercial aircraft is between 711.2 mm and 878.4 mm (Murphy, 2001). This restricts leg room for all except small individuals. Moreover, as most passengers use space below the seat for storage, leg room may be further reduced. Further reduction may occur if passengers recline their seats in order to sleep. As a result of the reduced space, normal leg movement is reduced and the muscle pump action of the lower limbs is curtailed resulting in inadequate return of blood from the legs. Swelling of the legs after sitting or standing can be as a result of an increased venous pressure, due to gravity, in the dependent parts of the body, when there is no increase of blood volume (Partsch *et al.,* 2004, p.737). Sitting with crossed legs can damage the endothelium of the veins in the legs which can act as a precursor to DVT (Aryal and Al-khaffaf, 2006). One study conducted by Hamer, concluded that PO_2 levels drop as a direct result of venous stagnation in valve pockets, due to immobility (Strandness and van Breda, 1994). This may act as the site for DVT formation.

3.11.4.2. Window or aisle seats

Passengers seated in the window and central seats have been documented to have an increased risk of FRDVT as all DVT events in three studies occurred in non-aisle seat subjects (Belcaro *et al.*, 2001a, b, 2002)**.**

3.11.4.3. First class or economy class

The reduction in leg movement due to restricted seat pitch is not present in first or business class seats, due to additional leg room provided. Normal business class seat pitch ranges between 787.4mm (compared to 711mm of economy class) to 863.6mm (Hodson, 2002; Seatguru, 2007). This led to the belief that the occurrence of FRDVT was an "economy class syndrome". Subsequently FRDVT and PE have been reported in both business and first class travel passengers (Hughes, *et al.*, 2003). However the cause reported by Mohler was a patient travelling first class with increased risk factors (six weeks post operation) (Mohler, 1997).

Also former presidents Nixon and Qualyle both developed flight related pulmonary embolus (FRPE) without documented additional risk factors (Mohler, 1997; Galili and Bass, 2002). This led Lapostolle *et al.,* (2001) to establish that there is no direct relation between the incidence of PE and class of travel.

3.11.4.5. Seatbelts

Governments have the power to make change by introducing legislation to provide an intervention such as mandatory seatbelt wearing. An intervention may be *"any health action - any promotive, preventive, curative or rehabilitative activity where the primary intent is to improve health"* (WHO, 2002, p.8.).

The European Aviation Safety Ageny (EASA) and the Federal Aviation Authority (FAA) have the power to enforce compulsory seat belts when the pilot deems it necessary. The purpose of this is to protect each passenger from a risk of harm, i.e. during turbulence (Nicholson, Cummins & Giangrande, 2003), or in the event of a crash landing. This is the enactment of aircraft legislation (EASA CS-25.785). Enforcing this requirement necessitates a reduction in passenger movement and hence provides the environmental factors which activate thrombus formation, such as Virchows' Triad (Section 3.1), which consists of venous stasis, vessel wall injury and hypercoagulability all of which seem to be present during air travel (Galili and Bass, 2002).

3.11.5. Risk factors associated with FRVTE.

Various studies have defined low, moderate and high risk factors associated with FRVTE (as shown in Table 3.2)

Table 3.2 Additional risk factors for FRVTE.

Low Risk Factors	**Moderate Risk Factors**	**High Risk Factors**
Age >40 Ω	Previous VTE Ω ά	Previous VTE Ω ά
Minor surgery	Stroke	Coagulation disorders
Bed rest (> than 3 days)	Knee surgery	Cancer
Obesity ά	Heart failure Ω	Joint replacement
Varicose veins ά	Antithrombin deficiency	Major surgery
Pregnancy	Protein C and Protein S deficiency	Major trauma
	Factor V Leiden Ψ	Hip fracture Ω
	HRT Ω	Oral contraceptive plus Factor V Leiden β

Sources: (Kesteven, 2000; ά - Belcaro, 2001a; Ψ - Scurr *et al.*, 2001; Ω - Gispert, Drobnic & Vidal, 2006; β - Schreijer *et al.*, 2006; Philbrick *et al.*, 2007)

3.11.5.1. Low versus High Risk

The LONFLIT Study consisted of a low risk group (355 participants) and a high risk group (389) to determine the incidence of FRDVT. Age ranged from 20-80 years (mean 46). Low risk subjects were classed as individuals with "no known clinical disease" (Belcaro *et al.,* 2001a, p.370) who had not taken any form of medication in the two weeks prior to the study taking place. High risk group consisted of those with a previous DVT, varicose veins, known coagulation disorder, obesity or those limited in mobility. The average flight duration was 12.4 hours long. An ultrasound scan of the femoral and popliteal veins was conducted within 24 hours of the flight concluding, to document the presence or absence of DVT. All thrombi were detected in the high risk group (13 DVTs and six SVTs) (Belcaro *et al.,* 2001a).

3.11.5.2. Coagulation factors

Flights of eight hours duration were found to cause an increase in two coagulants, Factor VII and Factor VIII, while decreasing activated partial thromboplastin time (aPTT) (Schobersberger *et al.,* 2003). The study concluded that "an activated coagulation plus a suppressed fibrinolysis could favour venous thromboembolism" (Schobersberger *et al.,* 2003, p. 24).

Bloods were taken 48 hours prior to the first flight of one hour duration, from Innsbruck travelling to Vienna. All 20 participants then travelled by air for eight hours 20 minutes to Washington. Everyone was seated in the last three rows of economy class during this flight. A second test was conducted after at least five hours in-flight. All participants stayed for two nights in Washington before taking a return flight to Vienna, upon which a third test was conducted after five hours flight. Upon landing in Vienna a fourth test was

conducted in the airport. Two more tests were conducted in Innsbruck, the first the day of return and the last three days after arrival (Schobersberger *et al.,* 2003).

One hundred patients over a two year period, suffering from PE, in a Spanish Hospital were interviewed to determine which risk factors were associated with the onset of each patients PE. Questions regarding mode and duration of travel were asked. A prolonged journey was defined as five hours duration or more. Each patient's medical history was examined and bloods were taken to identify any coagulation factors (Gispert *et al.,* 2006). Nine of the patients had taken a prolonged journey, six by coach/car and three had flown. All nine patient's d-dimers levels were greater than 552ng/ml, which was considered within the normal range.

3.12. Diagnosis of DVT

Both non-invasive and invasive forms of diagnosis are discussed in this section.

3.12.1. Non-Invasive Diagnosis to establish the presence of thrombi

3.12.1.1. D-dimer assays

The presence of D-dimers is utilised to establish the presence of thrombi. Following fibrinolysis of thrombi, plasma D-dimer fragments are present (Bockenstedt, 2003; Schobersberger *et al.,* 2003). They are generated from fibrin during degradation and are markers of "…thrombus formation and its subsequent resolution." (Hughes *et al.,* 2005, p.2445). Blood assays are the method used to determine D-dimer levels.

3.12.1.2. Thrombin-antithrombin III assays

High levels of thrombin-antithrombin III complex (TAT) present in plasma can also be an indicator of the presence of thrombi (Hommes *et al.,* 1994). This assessment is also conducted by taking bloods from the patient.

3.12.1.3. Compression Ultrasonography

A transducer is positioned in contact with the skin, above the vein or veins to be tested, by the investigator. "…..failure to compress the lumen of the vein fully" with the transducer is evidence of the presence of a thrombus in the deep veins (Cogo *et al.,* 1998 p.18). This is the first step in U/S diagnosis of a proximal DVT (Riddle and Wells, 2004). Compression ultrasonography of the femoral vein, popliteal vein and calf trifurcation is highly sensitive and successful at diagnosing thrombosis. It is less sensitive in the calf area of the lower limb (Wood, 1996, Cogo *et al.,* 1998) but the sensitivity has increased with newer ultrasound systems.

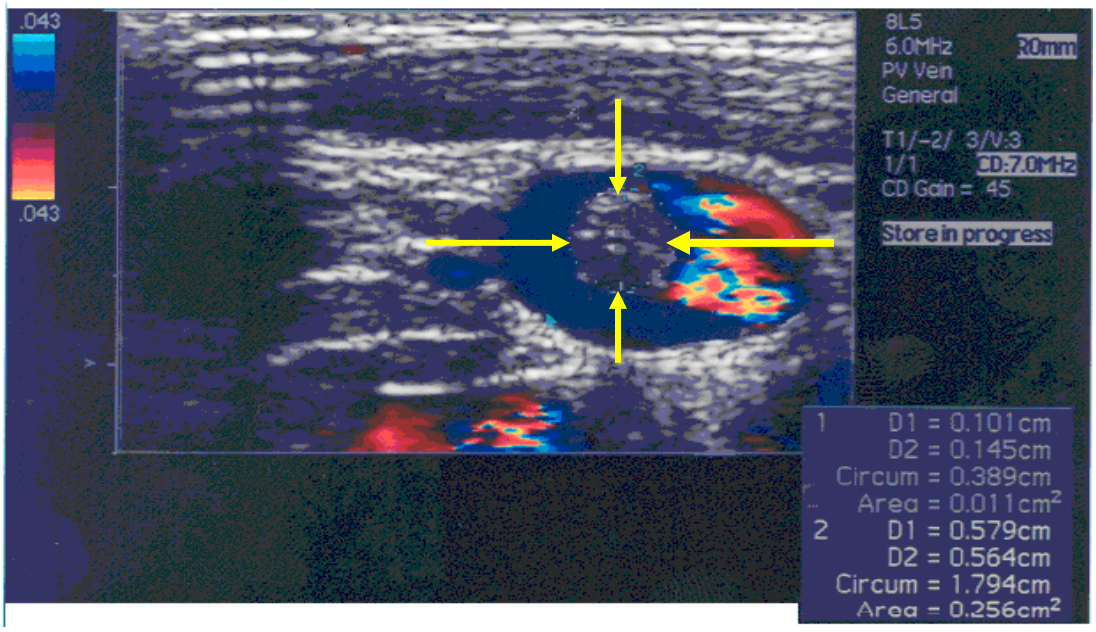
The absence of thrombi when using an ultrasound machine (Gardner and Fox, 1989) is noted due to the following criteria:

i. Spontaneity; the resting flow in a vein, a spontaneous signal is available from the major veins but may be absent from the superficial veins (Gardner and Fox, 1989). Absence of this signal in the proximal veins signals the possible presence of obstruction in the deep veins (Nicolaides and Kalodiki, 1994; Cole, 2001b).

ii. Phasicity refers to the variation of flow with respiration. In the supine position there is normally an increase in flow on expiration and a decrease of flow on inspiration (Gardner and Fox, 1989). Loss of phasicity may indicate obstruction in the deep veins (Nicolaides and Kalodiki, 1994; Cole, 2001b).

iii. Augmentation; the increase in the velocity of venous flow after compression of the foot or calf. If a venous obstruction exists, augmentation is not detected between the area of compression and the point of detection (Gardner and Fox, 1989; Cole, 2001b).

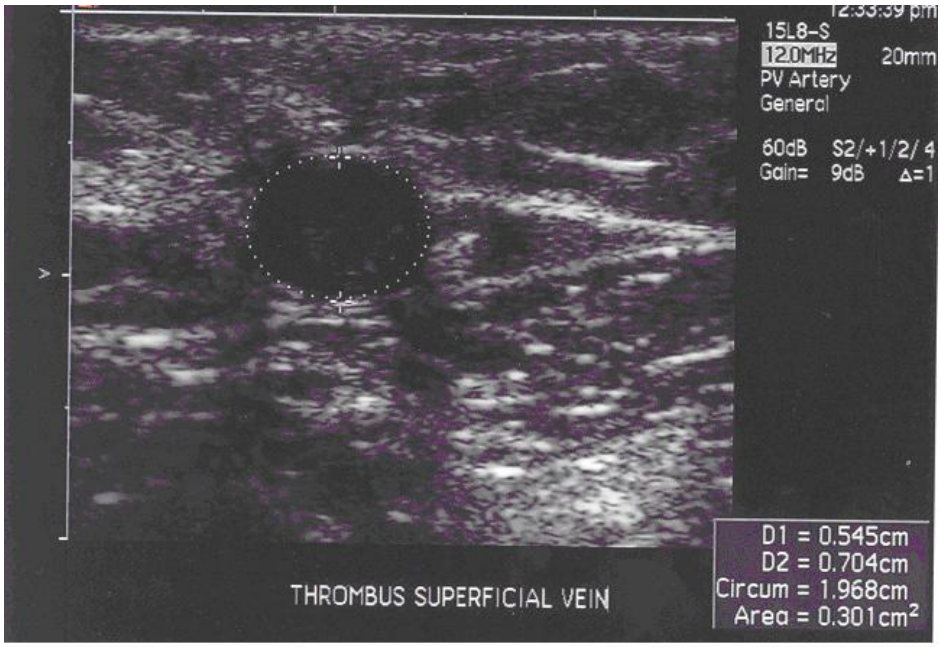
Figure 3.4 is an ultrasound scan of a vein which contains non occlusive thrombus. The vein is the black circle surrounding the thrombus in centre (highlighted by the yellow arrows).



Source: The Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 3.4. Cross-Sectional image of a vein (dark circle) containing non-occlusive thrombus (yellow arrows).

Figure 3.5 is an ultrasound scan of a thrombus within a superficial vein (Note: no accompanying artery).



Source: the Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 3.5 Cross-Sectional image of a thrombus occluding a superficial vein (surrounded by a dotted line).

3.12.1.4. Thermography

Liquid crystal thermography (LCT) is another non-invasive method used to diagnose DVT. The liquid crystal thermal detector is positioned in contact with the skin above the vein or veins to be tested. Liquid crystals are deposited onto a flexible latex membrane which is supported by a flexible detector which can conform to the shape of the limb being assessed. These liquid crystals change colour to represent differences in temperature on the limb being assessed (Harding, 1990). The detectors can measure temperatures in the range of 20 to 38º C. DVTs cause an increase in temperature in the affected limb, as the blood in that area is forced to seek another pathway. The patient is positioned in the supine position in a calibrated temperature controlled room of 20º C with the limb exposed for ten minutes prior to assessment. One disadvantage associated with LCT is that causes other than DVT may also increase temperature.

3.12.2. Invasive diagnosis of DVT

3.12.2.1. Invasive ascending venography

Invasive ascending venography is considered the "gold standard" diagnostic test for DVT. It involves placing a needle in a vein in the foot and injecting a contrast medium which can be imaged on an x-ray film. Thrombi show as filling defects (Hirsh and Hull, 1987). It has many disadvantages associated with it, in terms of expense and high failure rates in swollen legs (Keeling *et al.*, 2004; Pookarnjanamorakot *et al.*, 2004). This procedure is invasive and can be uncomfortable for the patient (Hirsh and Hull, 1987). There is a radiation dose and the risk of an allergic reaction and the possibility of renal toxicity exists (Comerota, 1994b, p. 63).

3.12.3. Diagnosis of pulmonary embolus

The following methods are the main diagnostic tools used, (Dixon, 2001):

i. Ventilation-perfusion (V/Q) scintigraphy, which is known as the lung scan is the technique largely used to diagnose the presence of a PE (Wood, 1996 Goldhaber, 1998). This procedure involves a patient inhaling a technetium-99m labelled aerosol or a radioactive gas to demonstrate the distribution of pulmonary ventilation (Goldhaber, 1998). An intravenous injection of technetium-99m labelled micro particles of macroaggrated human serum albumin is made, so the distribution of blood flow in the lung can be displayed (perfusion). Mismatch between ventilation and perfusion occurs in the presence of PE. The size is proportionate to the size of the embolus.

ii. Spiral computed tomography (CT) angiography, is achieved by injecting an iodinated contrast medium, which identifies the presence of emboli by the

presence of filling defects (Goldhaber, 1998; Dixon, 2001). Multiple x-ray images are taken and with the aid of a computer an image of the lungs is reconstructed.

iii. Helical CT Pulmonary angiography is considered the "gold standard" in the diagnosis for PE (Dixon, 2001; Lingamanaicker *et al.,* 2001).

iv. Magnetic resonance imaging is a costly procedure, however one advantage is that radiation is not experienced by the patient. This procedure can be conducted non-invasively and invasively with a contrast medium (Schmitz *et al.,* 2006). It provides a detailed image of the lungs and vasculature structures, thus allowing imaging of the pulmonary emboli.

3.13. Treatment of DVT

The aim of DVT treatment is to prevent the thrombus from enlarging or embolizing (Miller-Keane, 1997).

3.13.1. Anticoagulant therapy.

This method can be effective when treating a DVT and reducing the risk of PE (Turpie, 1994; Sharafuddin *et al.*, 2003) and is used to prevent primary and secondary DVT events. This section outlines pharmacological methods used to prevent and treat DVT in clinical settings:

i. Dextran is a glucose polymer which is available as two fractions of different molecular weights: Dextran-40 and Dextran-70. They exert antithrombotic effects by a number of different ways. Dextran is a plasma volume expanding agent which reduces blood viscosity, increases blood flow and therefore reduces venous stasis. Dextran is used in surgical patients over a four to six hour period

and then administered for two to five days after surgery. Dextran is as effective as low dose heparin for the prevention of PE (Bergqvist, 2004).

ii. Thrombin blockers work by inhibiting thrombin (Weitz, 2000). Desirudin is successful in the prevention of asymptomatic deep vein thrombosis after knee or total hip replacement surgery. Lepirudin is used to treat patients with VTE, with heparin associated thrombocytopenia (SIGN, 2002).

iii. Heparin can also be used in DVT prophylaxis. Heparin is administered subcutaneously and begins to work immediately. Heparin is a naturally occurring anticoagulant, preventing thrombi and further extension of already existing thrombi in the vessels. It allows the natural lysis process to work normally as it works in conjunction with the plasma cofactor antithrombin III. This binds to heparin and together they inhibit thrombin and factor Xa (Kakkar and Cohen, 1994). A review of more than 70 randomised trials, involving more than 16,000 patients, showed that the perioperative use of low-dose heparin prophylaxis prevented approximately 50 per cent of all PE, and 66 per cent of DVT (Haas & Haas, 1994, p.149).

iv. Coumarins are a Vitamin K antagonist used for long-term treatment of VTE. Warfarin is a coumarin which is used to decrease the plasma concentrations of FVIII and Protein C (Wood, 1996). Warfarin is administered orally. It takes longer to work then heparin however it is the oral anticoagulant of choice with patients undergoing orthopaedic surgery (Goldhaber and Fanikos, 2004). A study comparing the effectiveness of long term placebo versus low-intensity warfarin therapy for prevention of recurrent VTE was conducted over 4.3 years. Of the 253 patients receiving placebo, 37 developed a recurrent VTE. Fourteen of 255

patients receiving low-intensity warfarin therapy developed a recurrent VTE (Ridker *et al.,* 2003).

Recommended treatment durations are:

i. six to twelve weeks for symptomatic calf vein thrombosis;

ii. three months in patients presenting with a proximal DVT or acute PE;

iii. six months in patients presenting with idiopathic proximal vein thrombosis or recurrent VTE (Hirsh *et al.,* 2001a).

3.14. Prophylaxis.

There are two general means of prophylaxis; pharmacological agents and mechanical methods, which will be discussed in this section. The former methods of prophylaxis are used to reduce the coagulation process (Sochart and Hardinge, 1999) whereas the aim of mechanical methods is to reduce venous stasis (Sochart and Hardinge, 1999, O'Donovan *et al.,* 2005). Mechanical methods unlike pharmacological prophylaxis are attractive as they do not increase the risk of bleeding (Nicolaides *et al.,* 2002; Morris and Woodcock, 2004).

"...routine prophylaxis reduces morbidity, mortality and costs in hospitalised patients at risk of DVT and PE" (SIGN guidelines, 2003, p.1). If prophylaxis can reduce the occurrence of DVT and PE in hospitalised patients, it is reasonable to argue that it should be used for passengers on board aircraft and other forms of transport who are also at risk.

3.14.1. Medicines

Aspirin is an antiplatelet drug which is administered orally. It works by inhibiting the normal role of platelets in initiating the formation of thrombi (Turpie, 1994). Aspirin is attractive as it is easily obtained, but may interfere with other medication and can cause

gastrointestinal haemorrhage (Derry and Loke, 2000) Aspirin has been demonstrated to reduce the incidence of PE and DVT by as much as 33 percent in patients post hip fracture (PEP Trial Collaboration Group, 2000).

However aspirin has not been shown to be effective at preventing FRDVT (Cesarone, 2002; Hughes *et al.*, 2003). "The Impact of Flying on passenger health: a guideline for healthcare professionals", was conducted by the British Medical Association and Board of Science and Education (for the benefit of doctors and healthcare professionals). This report states that patients should be warned against the use of aspirin *"just for the prevention of travel-related DVT"* (BMA, 2004, p. 12).

3.14.2.. "Alternative Medicines"

The following products are available for purchase without prescription and can be taken to reduce the risk of travel related DVT:

i. Pycnogenol is a natural substance taken from French maritime pine bark. It is taken orally in tablet form. Pycnogenol® causes the blood vessels to relax, which aids the flow of blood. It prevents platelets from clotting unnecessarily (BMA, 2004).

ii. Flite Tabs consists of 150mg of pinokinase, (made from fermented soya) which consists of Pycnogenol® (made from the extract of marine pine bark) and Nattokinase. The Kinotase has an anticoagulant effect on the blood, while pycnogenol ensures an anti-inflammatory effect on the leg blood vessels (Johnston, 21/10/03).

iii. Vascular Guard is available in capsule form. It contains "natural vitamin E, lycopene and antioxidant extracts of pine bark and grapeseed to enhance blood-vessel function and bilberry to maintain blood flow to the extremities" (Harper-

Deacon, 2006, p.49). The recommended dose is two capsules per day, a few weeks before travelling and then for one week after the return journey (Harper-Deacon, 2006).

iv. Zinopin capsules contain French pine bark and ginger root which work together to boost circulation. These capsules, developed by Dr. John Scurr, relax blood vessels and improve circulation, thereby reducing stasis and possibly DVT (Scurr, 2005).

No controlled studies were conducted to determine the incidence of possible side effects from these products. The only study to determine the effectiveness of Flite tabs was the Lonflit-Flite Study. It was conducted to determine the incidence of FRDVT in high risk subjects. Participants in the Flite tab group (which contains 150 mg of pinokinase) were given two capsules two hours prior to flying, with 250 ml of water and another two capsules six hours later, again with 250 ml of water. Ultrasound scanning of major and superficial veins, D-dimer and fibrinogen tests were performed before and after flight Participants in the study group (94) displayed no signs of VTE, while five of the 92 participants in the control group presented with a DVT and another two presented with a SVT (Cesarone *et al.*, 2003a). Cesarone and colleagues determined that one dose of Enoxaparine (a form of LMWH) taken two to four hours before flight prevented FRDVT, however one SVT did occur. This study established that aspirin was not as effective as LMWH at preventing FRDVT or FRSVT (Cesarone *et al.,* 2002). Three hundred high risk individuals for DVT were randomised into three groups; a control group, an aspirin group and a LMWH group. The control group were given no prophylaxis. Everyone in the aspirin group took 400 mgs of aspirin orally for three days, beginning twelve hours prior to flight. With one dose of enoxaparine injected two to four hours before flight to

all those randomised into the LMWH group. This dose of enoxaparine was weight adjusted, for example 1000 IU per ten kg of body weight. Side effects to aspirin did occur, however they disappeared when the treatment was stopped (Cesarone, 2002).

3.14.3. Mechanical Methods

Mechanical methods used to prevent DVT are based on preventing venous stasis (Auguste *et al.*, 2004).

3.14.3.1. Graduated Elastic Compression Stockings

"Compression stockings improve the drainage of superficial venous blood, thereby reducing the risk of over-distension" (Thaler *et al.*, 2001). A graduated elastic compression stocking (GECS) exerts varying degrees of constant compression at different segments of the limb. The highest compression is at the ankle area, decreasing all the way up towards the knee or the proximal area of the thigh, depending on whether the stockings are knee or thigh length (Agu *et al.*, 1999). Knee length stockings are more commonly prescribed than thigh length as they are less expensive and more comfortable (Agu *et al.*, 1999).

External compression reduces the cross sectional area of the lower limb, along with the diameter of the veins. The resulting effect is to increase the velocity of blood flow (Agu *et al.*, 1999; Partsch, 1999; Morris and Woodcock, 2004) as the arterial inflow to the veins remains constant (Partsch, 1999). An external pressure of 15mmHg results in a 20 percent reduction in the veins cross sectional area with significantly increased blood flow through both the deep and superficial venous systems (Agu *et al.*, 1999). Thus GECS

reduce venous stasis which is one of the three factors described by Virchow (Agu *et al.*, 1999).

The hosiery is designed so that it is elastic both lengthwise and width-wise. In graduated compression stockings there are three different levels of compression along the stocking; at the ankle, calf and knee. These compression values vary according to the manufacturer and the country of origin. The British Standards Institution set out their standards in 1985, whereas the Germans (or European Standards) followed the German Hohenstein Compression Standard (refer to Table 3.3). Knee or thigh length GECS may be prescribed to patients depending on the diagnosis (Hsieh and Lee, 2005). These stockings are available in various colours so that they are almost indistinctive from normal socks. Flight socks sold without prescription are usually Class I.

Table 3.3. International Graduated Elastic Compression Stocking Values.

	Class I (mmHg)	Class II (mmHg)	Class III (mmHg)
British	14-17	18-24	25-35
German	20-30	25.2-32.3	36-46

Source: Harper *et al.*, 1995; Thaler *et al.*, 2001.

GECS are medically prescribed. Patients with peripheral vascular disease are advised against wearing GECS. This is established by a simple non-invasive examination entitled an ankle brachial index (ABI) (Agu *et al.*, 1999). The assessment is conducted with the patient in the supine position. Inflatable pressure cuffs are placed on the lower extremities and the upper arm. These cuffs are inflated until they occlude the arteries; as the cuff deflates, systolic pressure is determined when a pulse sound reappears. The ABI for each limb is then determined by dividing the higher systolic pressures (PT or AT artery) by the highest brachial artery systolic pressure (either right or left arm) (Schmitz

et al., 2006). If a value of less than 0.7 is recorded, (≥ 0.9 normal value) PAD is diagnosed. PAD patients are not permitted to wear GECS as they risk impairment of subcutaneous tissue oxygenation (Agu *et al.*, 1999).

Table 3.4., describes some of the most commonly used GECS.

Table 3.4. Brands of graduated elastic compression stockings available.

Brand name	Type and Grade	Compression value at the ankle
Mediven Travel	UK Grade II	18.4 – 21.1 mmHg
Scholl Flight Socks	UK Grade I	14 – 17 mmHg
Sigvaris Traveno Stockings	Switzerland, Grade I	14 – 17 mmHg

Source: Hsieh & Lee (2005).

A number of studies have been conducted to determine the effectiveness of GECS of various grades preventing FRDVT and FRPE.

GECS of compression value 25mmHg at the ankle (brand unknown) significantly reduced the incidence of FRDVT and prevented FRSVT (on flights of ten to 15 hours). One DVT was diagnosed in the stocking group (411 participants), demonstrating an incidence of FRDVT in the stocking group of 0.24 percent in comparison to 5.2 percent in the control group (Belcaro *et al.*, 2001a).

Mediven stockings, United Kingdom, Grade II, efficiently prevented FRDVT (Scurr *et al.*, 2001). Two hundred and thirty-one volunteers completed the study, 115 were randomly assigned to the stocking group, 116 to the control group (no stockings). Twelve asymptomatic calf DVT were diagnosed by ultrasound and D-dimer assays in the control group and four superficial thrombi were detected in varicose veins, in the stocking group. This study concluded that "Approximately one in ten passengers not

wearing elastic compression stockings developed symptomless DVT after airline travel" (Scurr, *et al.*, 2001, p. 1487).

Sigvaris Traveno (14-17mmHg) stockings (on flights of similar durations) while reducing oedema also prevented DVT (Cesarone *et al.*, 2003b).

Scholl Flight socks, 14-17mmHg, (lower compression grade than either the Mediven or those used by Belcaro, (2001a) also prevented FRDVT and FRSVT on flights of seven to eight hours and eleven to twelve hours duration (Belcaro *et al.*, 2002). The incidence of FRDVT and FRSVT (without stockings) was 2.12 percent and 1.06 percent respectively, on flights of seven to eight hours duration (Belcaro *et al.*, 2002). Part 1 of the study consisted of a flight (seven or eight hours) from London to New York. One hundred and three participants were randomly assigned into the stocking group and 108 into the control group. Part 2 of the study consisted of a flight from London to Phoenix which lasted approximately eleven to twelve hours. Eighty-three were assigned to stockings and 82 to the control group (Belcaro *et al.*, 2002). Unfortunately Scholl stockings worn by a high risk group were not effective at preventing DVT development on flights of eleven to thirteen hours duration. The incidence of FRDVT in a high risk control group was 5.8 percent. Scholl stockings reduced this incidence to 0.97 percent (Belcaro *et al.*, 2003b). This is presumably due to the increased risk associated with these patients and the lower compression grade of Scholl GECS. This underlies the usefulness of GECS, but highlights the need for relevant prescribing.

3.14.3.2. The skywalker™

The skywalker is manufactured from light-weight plastic. It consists of two foot-pedals (Figure 3.6)

When unfolded it is approximately ten and half inches wide and six inches long with a height of over three and half inches. The pedals are placed on a curved pivot (Figure 3.7). The user places one foot on each pedal before consecutively pressing one pedal at a time.

This device has been **"**Clinically proven to increase blood circulation, prevent swollen ankles and relieves the numb and tired feeling in your legs" as stated on the Aviation Health website: http://www.aviation-health.com/shop/product_info.php?products_id=55. However no documented evidence could be found to support this claim.

Source:Skywalker.

Figure 3.6. The Skywalker

Source: Skywalker

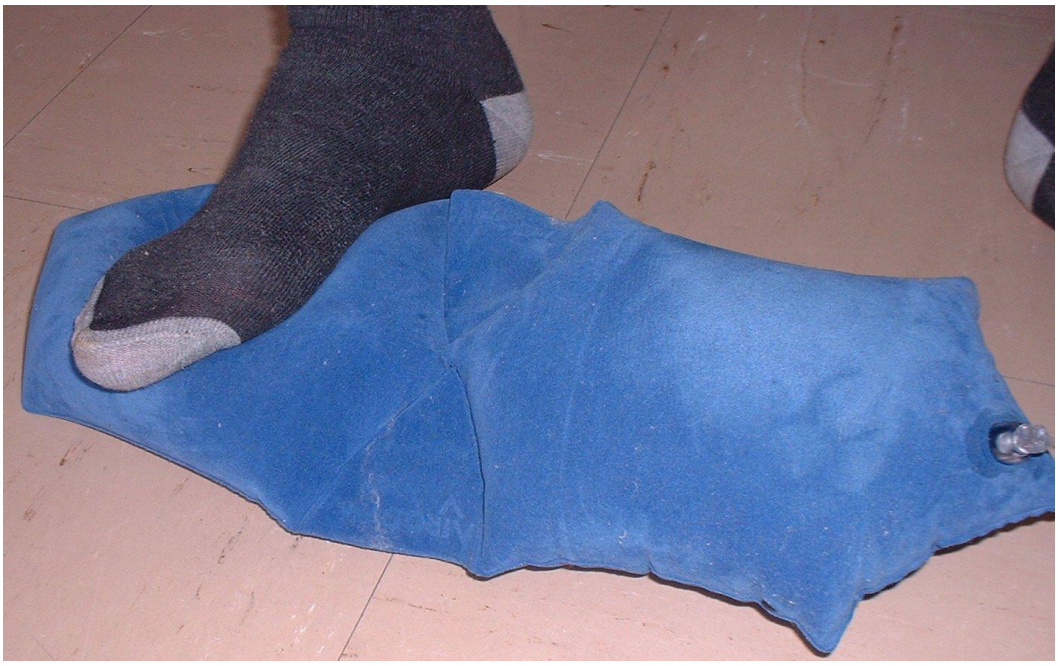
Figure 3.7. The Skywalker (curved pivot)

3.14.3.3. The Airogym

The Airogym was designed for aircraft passengers by senior pilot Paul Richards, following an emergency landing required by a passenger suffering with flight related PE (http://www.airogym.com/whatisit.php).

It consists of an air chamber connected between two cushions (Figure 3.8) made from a composite material. It is light in weight and can be carried in a handbag or suitcase. As the right foot presses down on the cushion, the air is transferred to the left foot cushion. The airogym acts by compressing veins in the foot which should initiate venous return.

It was established that the Airogym is effective in activating the calf muscle pump, increasing the peak flow velocity of blood in the femoral vein by three fold, during use (www.airogym.com/trials.php). The airogym however can slide on smooth surfaces during use (Collins, 2002/3).



Source: Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 3.8. Image of the Airogym, with right foot on cushion resulting in transfer of air to the left side of the airogym.

3.14.3.4 The Veingaurd Exercise Cushion

The Veingaurd cushion was designed in Great Britain by Hughes DVT Cushions Ltd (Medical Approval, 2007).

The Veingaurd Compact Anti-DVT Exercise Cushion (Figure 3.9) is designed to promote leg exercise. It slips into its own pouch, which could fit in a handbag and can be inflated if needed (HELP AT HOME, 2002).

This device is made from a flame retardant P.V.C. Both an inflation valve and a pressure relief valve are fitted into the design, specifically for use on board aircraft ("Veingaurd Anti-DVT Cushion", 2007).

A pilot study established that this device when used can increase the venous return approximately ten fold (Medical Approval, 2007).

Source: Veingaurd™

Figure 3.9. The Veinguard Exercise Cushion.

3.14.3.5 The LymGym™

This device was developed following a conference in 1999, which highlighted the problem of travel related thrombosis. Doctors Osman and Hodgkinson, of Ipswich Hospital, in the United Kingdom were involved in its design (Osman *et al.*, 2006).

It is an inflatable foot cushion (Figure 3.10). Compression of one side of the Lym Gym at a time enhances venous return in the seated position, similar to both the airogym and the veingaurd exercise cushion.

It was established by Doppler ultrasound that the Lym Gym™ increased peak blood flow velocity by eight fold, when used, compared to the peak flow velocity of all participants remaining passive in the seated position (Caruana *et al.*, 2003).

Source: Lymgym™

Figure 3.10. The Lym Gym.

3.14.3.6. The Novamedix Foot Pump

Gordon Cook invented the foot pump, with Novamedix Ltd the assignee (www.google.com/patents).

External Compression Foot pumps, (IPC device) applied to the foot and ankles are used to increase the venous flow in the lower limbs and reduce VTE (Fleming *et al.,* 2000; Dai *et al.,* 2002). Intermittent Pneumatic Compression Devices (IPCs) also stimulate fibrinolysis by compressing the calf and/or thigh muscles of the leg, at regular intervals (SIGN, 2002). Upon compression, the veins collapse (Dai *et al.,* 2002). Generally inflation pressures range at 35-40mmHg at ten cycles per minute. IPCs were developed for use before or during surgery and then replaced with compression stockings post surgery (Hull *et al.,* 1986; Goldhaber, 1998). The blood is squeezed from the veins which lie under the cuff, so that it flows against gravity into the proximal veins. Deflation of the cuff ensures the deep veins have time to refill, prior to re-inflation of the

cuff (Morris and Woodcock, 2004). The Novamedix A-V Impulse System thus mimics the natural physiological processes ensuing blood circulation in the legs. The Foot Pump is one such system designed for hospital patients. A foot pad (Figure 3.11) is placed on the limb, which consists of an inflation pad, within a fabric covering. The pad is inflated by an air compressor, (Figure 3.12) which causes emptying of the plantar venous plexus.

Source: AV – Impulse System

Figure 3.11. Novamedix Inflation pad foot cover

This device produces an impulse every 20 seconds and has been shown to create a significant increase in velocities in both the popliteal vein and common femoral vein (Killewich *et al.*, 1995). IPC devices "…*have been proven clinically effective for DVT prophylaxis."* (Killewich *et al.*, 1995, p. 604).

This system would be unusable for use on board an aircraft due to the air compressor which inflates the foot pads.

Source: AV – Impulse System

Figure 3.12. Novamedix A-V Impulse System.

A study carried out by Killewich *et al.,* (1995), recorded the results obtained from 30 limbs (15 volunteers) which had foot pumping performed using the A-V Impulse Pump. Foot pumping took place for five to ten minutes. Then the venous velocities were measured with a HDI-UM nine Ultra-sound machine at two points. The popliteal veins behind the knee joint and the Common femoral vein, two centimetre cephalad to the saphenofemoral junction with the patient in the supine position and then later after more foot pumping measurements were recorded in the reverse Trendelenburg position. (Killewich *et al.,* 1995).

While all the devices available show an increase in venous return none of them match the normal venous function when walking.

3.15. Prophylaxis used in the aircraft cabin

3.15.1. Walking

Activation of the plantar venous plexus in conjunction with contraction of the calf muscle pump, during walking, permits venous return to the heart in a healthy individual (Sochart and Hardinge, 1999).

3.15.2. Impact of inflight exercises

Many inflight magazines and audio channels promote inflight exercises. The effect of exercise as a prevention for FRDVT was investigated in the LONFLIT 2 Study. Travellers were advised to move (three minutes every hour), stretch their limbs for two minutes every hour and to avoid restricting their leg room. This was unsuccessful in preventing thrombi formation demonstrated by an incidence of 4.5 percent DVT in the control group (Belcaro *et al.,* 2001a). Another study showed volunteers an exercise video explaining about DVT and its prevention. The exercise consisted of standing and moving legs for 5-10 minutes every hour and drinking water regularly. However five (limbs) DVT and two (limbs) SVT were detected by ultrasound in the control group (Cesarone *et al.*, 2003a).

3.16. Cabin Environment

Dr. Suzanne Cannegiester, a co-author of the study conducted by Schriejer *et al.,* (2006) stated "There is something extra in a plane that would increase the risk more that just sitting still" in a car, or other form of transport for up to eight hours (Reuters, 2006). Thirty one of the 60 cases of DVT/PE had no other obvious risk factors other than long haul travel itself (Hughes *et al.*, 2006).

It is essential that both passengers and the crew of any aircraft are exposed to an adequate cabin environment during flight. The Environmental Control System (ECS) is responsible for maintaining comfortable atmospheric conditions at all times inside the cabin area. The primary role of the ECS is to ensure a prerequired environment for aircraft instruments and equipment and personnel (the pilots, their crew and the passengers). The ECS achieves and maintains this required environment through the provision of cabin pressurisation, engine bleed air and environmental control.

3.16.1. Cabin pressurisation

Pressurisation "…is accomplished by flowing more air into the cabin than is needed and allowing the excess air to leak out." ('Jeppesen…", 2002, pp.14-22). The excess air leaks out by both controlled and uncontrolled means. Controlled leakage is via an outflow valve and a safety valve. Uncontrolled leakage occurs through openings and by air escaping from door and window seals etc ('Jeppesen…", 2002).

3.16.2. Engine bleed air

There are two types of engine bleed air systems, namely the open loop and closed loop systems. The open loop system continuously bleeds large amounts of air from the aircraft engines. Two air conditioning packs cool the air which is then distributed through a number of valves and fans to cool aircraft equipment and the occupants before releasing it overboard. The closed loop system differs in that equipment and the aircraft interior are cooled, the air is recycled and the process begins again (Moir and Seabridge, 2003).

3.16.3. Environmental control

The innermost shell of the earth's atmosphere is known as the troposphere. This shell begins at ground level and extends to an altitude of 9144m at the north and south poles, but extends further at the equator to a height of 18,288m. For every 305m upward increase in altitude there is a proportionate decrease in temperature of 1.98 degree Celsius (°C). The troposphere has a constant gas composition of 21 percent oxygen, 78 percent nitrogen and a remaining one percent which is made up of other gases. Zero point zero three percent of which is carbon dioxide ("BTS ..", 2002).

An aircraft flies within the troposphere. In order for it to withstand the atmospheric pressure experienced at such altitudes, the internal aircraft cabin must simulate an altitude equivalent to 2438m (8000ft). This creates a differential pressure of approximately of 0.5atm or 50kPa (Moir and Seabridge, 2003). Aircraft in flight at altitudes such as 12,200m are not pressurised to replicate atmospheric conditions at sea level, (Hinninghofen and Enck, 2006), as the resultant differential pressure would result in the aircraft collapsing inwards.

Cabin temperature controllers are responsible for ensuring the control of the temperature of the cabin and cock pit, at 17 - 18°C on average. Cabin pressurisation is maintained at safe values by cabin pressure valves. These are installed in the cabin walls to control the pressure depending on the aircrafts altitude. So once the cooled air passes through the air conditioning packs, it then moves through the control outflow valves, which control the pressure of the cabin. These outflow valves ensure that the interior cabin simulated altitude of 2,438m is never exceeded (Moir and Seabridge, 2003; BMA 2004). The resultant reduced barometric pressure in the aircraft cabin is another unnatural condition experienced by passengers.

At sea level ambient pressure is approximately 760 mmHg or 101kPa. The partial pressure of oxygen (inspired oxygen) PO_2 is 149 mmHg (19.6 kPa) and the arterial pressure of oxygen (PaO_2) experienced is 94mmHg to 98 mmHg (Refer to table 3.5.) (Peacock, 1998; Jeppesen…", 2002, Cummin and Nicholson, 2002).

During flight the ambient pressure at 12200m is approximately 140mmHg or 18.7kPa, which is insufficient to allow normal breathing in passengers. The interior cabin pressure experienced by passengers will be the equivalent to an altitude of approximately 1524 – 2438m above sea level (Cummin and Nicholson, 2002; Hodkinson *et al.,* 2003). An altitude of 1524m, is the equivalent of breathing 17.1 percent oxygen at sea level, or at 2438m the equivalent of 15.1 percent oxygen at sea level (BTS.., 2002). These corresponding ambient pressures range from approximately 632 mmHg or 84.3 kPa at 1524m to approximately 565mmHg or 75.3 kPa at 2438m. Thus the ambient cabin pressures result in a reduction of the PO_2, available to passengers, even though the concentration of oxygen (at 21 per cent) remains as normal (Cummin and Nicholson, 2002).

Table 3.5. Pressure versus altitude values.

	Ambient Pressure	Partial pressure of oxygen (PO_2)	Arterial Pressure of Oxygen (P_aO_2)
Sea Level	760 mmHg	149 mmHg	94mmHg
2,250m	565 mmHg	109 mmHg	55mmHg.
12,200m	140 mmHg		

Source: (Cummin and Nicholson, 2002; Jeppesen…", 2002; AMA, 2003)

3.16.4. Hypoxia

Inhaling air at high altitudes, with reduced atmospheric pressure, results in a reduction of alveolar oxygen and a reduced oxygen supply to the body and the brain. This is known as hypoxia. Pressurising the aircraft cabin during flight reduces this problem however it does not completely alleviate it (Moir and Seabridge, 1992).

A Report prepared by the Institute for Environment and Health (IEH) for the Department of the Environment, Transport and Regions in January 2001 states "***Although the percentage of oxygen in cabin air remains unchanged (21%) at all flight altitudes, the partial pressure of oxygen and its availability to the body decrease with increasing altitude"*** (IEH, 2001, p13).

Lennon (2004) wrote in an Irish Independent article that there can be as much as a 25 per cent reduction in oxygen available to passengers which results in an increase of coagulation factors by increasing the number of red blood cells produced by the body over days. If a passenger took two connecting flights this could result in an increase of red blood cell count. The reduction in the barometric pressure experienced in the aircraft cabin is responsible for dehydration and low arterial pressure of oxygen (Kelman *et al.*, 2003). This has been established by Schreijer *et al.,* (2006) as one of the underlying factors contributing to the pathology of FRDVT.

The Aerospace Medical Association's (AMA) Medical Guidelines for Airline Travel, 2nd ed., (2003) states that the PO_2 experienced at a cabin altitude of 2438m is 108 mmHg, with the P_aO_2 experienced being 55mmHg. This means therefore that there is a subsequent reduction of PO_2 by approximately 41 mmHg and a PaO_2 of approximately 39 mmHg. Refer to Tables 3.5 and 3.6.

Table 3.6. Levels of arterial pressure of oxygen within the body.

Arterial Pressure of Oxygen P_aO_2	Sea Level	Altitude of 2438m when flying
Inspired air	150mmHg	110mmHg
Arterial blood	100 mmHg	64mmHg
Capillary blood	60 mmHg	46mmHg
Venous blood	37mmHg	32mmHg

Source: Kingman and Economides, (2002)

What this means is that passengers experience approximately 90 per cent blood oxygen saturation. In a sense passengers with normal healthy lungs are experiencing hypoxia due to the reduction in oxygen available to the blood (Galili and Bass, 2002; AMA, 2003). The majority of passengers can carry on as normal with the exception of passengers suffering with anaemia, pulmonary and coronary diseases.

As inhaled atmospheric air is transported towards the lungs, the levels of PO_2 reduce at each stage (Table 3.5), which is otherwise known as the Oxygen Cascade (Goldhaber and Elliot, 2003; Colbert, 2004). A reduction in PO_2 levels can cause an increase *"in platelet adhesiveness"* increasing the tendency of thrombus formation (Colbert, 2004). An individual's rate of oxygen consumption at rest is 220-260ml/min (Roy, 2002). At high altitudes, the density of the air is less than at sea level. The consequential affect of this is that greater volumes of air are required to supply the adequate volumes of oxygen to the body (Schoene, 2001).

An experiment was conducted with 15 participants, placed in a hypobaric chamber with internal ambient pressure of 75.8kPa to replicate a typical aircraft cabin pressure during flight. They determined that the oxygen saturation of haemoglobin (SaO_2) was indeed 90 percent after individuals were exposed to this ambient pressure level for 30 minutes. Simons and Krol (1996, p. 416) stated "There is considerable interindividual variation in the responses to a lowered partial O_2 pressure". In other words, some people seated in cramped conditions may suffer with hypoxia and/or drowsiness together with reduced respiratory activity.

The Boeing 747-400 and B777 create a cabin altitude, equivalent to an atmospheric altitude of between 1,524m and 1829m at an altitude of 10,688m, in flight. The arterial oxygen saturation experienced by passengers at that cabin altitude is approximately 70mmHg in a healthy individual (Bagshaw, 1996) and not 55mmHg as stated by Galili

and Bass (2002) and Aerospace Medical Association, (2003). Bagshaw is an airline employee and so is open to a suggestion of bias.

Relative humidity at sea level is approximately between 30 and 40 percent. An aircraft cabin (which mimics an altitude of 2438m) will have relative humidity levels between eight and ten percent (Simons and Krol, 1996; Possick and Barry, 2004). "The low cabin humidity of 8-12% increases fluid loss, which leads to dehydration" (Galili and Bass, 2002, p.1020). At a cabin altitude of 2438m the cabin ambient pressure experienced is 75.8kPa and this value is the maximum acceptable cabin altitude provided by airlines cruising at altitudes of up to 13,106m according to Simons and Krol (1996). Also reduced oxygen levels during flight along with dehydration may predispose an individual to FRPE (Gispert *et al.,* 2006).

3.16.5. Dehydration

Dehydration can increase blood viscosity (Samama *et al.,* 1994). It can also lead to the development of headaches, tiredness and fatigue (Hunt and Space, unknown).

3.16.5.1. Aircraft Cabin

The reduction in the barometric pressure experienced in the aircraft cabin is responsible for dehydration (Kelman *et al.,* 2003). The change experienced in the aircraft cabin results in a dry atmosphere.

Distension of the gastrointestine as a result of lower ambient cabin pressure can result in reduced respiratory activity through restriction of diaphragm movement (Simons and Krol, 1996). The increased abdominal pressure can also reduce the efficient return of blood to the heart from the lower limbs, due to pressure on the IVC (main vein returning blood from the legs to the heart, via the abdomen) (Miller *et al.,* 2005).

3.16.5.2. Alcohol and diuretics

This in conjunction with a low fluid intake (such as water) and drinking alcohol and/or coffee increases the risk of haemoconcentration (Carruthers *et al.,* 1976; Eklof *et al.,* 1996). Haemoconcentration increases the risk of clot formation.

3.16.5.3. Humidity

A reduction in humidity may affect clotting factors (Lennon, 2004).

3.16.5.4. Intake of Fluids

Dehydration should be avoided by the consumption of water and a low intake of alcohol (Goldhaber and Fanikos, 2004). Participants of the LONFLIT 2 Study were advised to drink at least one glass of water every two hours to avoid salty food and to wear comfortable clothes. However these attempts to prevent thrombi formation were unsuccessful). One DVT in the stocking group was diagnosed with 22 DVTs and eight SVTs diagnosed in the control group (Belcaro *et al.,* 2001b).

Excessive alcohol may result in passengers sleeping through the flight thus limiting their mobility and hence inactivation of the calf muscle pump, which is responsible for returning blood towards the heart.

3.17. Oedema

Oedema results from increased fluid in the interstitial tissue spaces (Gardner and Fox, 1993; Kumar *et al.,* 2005). Impaired venous return and venous obstruction in the lower extremities due to prolonged immobility can result in oedema (Kumar *et al.,* 2005). Prolonged sitting during long haul flights constitutes a risk factor for oedema. Swelling

at the ankle and in the calf region of passengers is not an uncommon occurrence during flight (Belcaro *et al.*, 2002; Cesarone *et al.*, 2003a, b).

Scholl stockings were effective in reducing the severity of oedema and preventing DVT (Belcaro *et al.*, 2002). The efficiency of Scholl Flight socks (14-17 mmHg) was investigated on flights of seven to eight hours duration and eleven to twelve hours duration. Eighty percent of the control group (179) presented with signs of oedema and an increase in ankle circumference and volume, on flights of seven to eight hours duration. One hundred and forty two of the stockings group completed the study. Volunteers in the control group had a higher incidence of oedema (Belcaro *et al.*, 2002).

Sigvaris Traveno (14 -17mmHg) elastic stockings have been demonstrated to be effective at preventing oedema on flights of seven or eight hour's duration but not on flights of eleven to twelve hours. The incidence of oedema in the control group was 89 percent on flights of seven to eight hours (Cesarone *et al.*, 2003a).

Part II of the study was conducted on flights of eleven to twelve hours duration. The control group did present with oedema, with an odds ratio of 8.9 compared to 2.56 for the stocking group. Eighty-three percent of the control group did present with an increased ankle circumference and ankle volume, while the stocking group did not (Cesarone *et al.*, 2003b).

3.18. Discussion

This chapter outlined the failure associated with the development, incidence, treatment and prophylaxis of DVT and PE. Not only can FRDVT result in chronic sequelae it can also be life threatening. In the context of FRDVT prophylaxis, mechanical methods would seem most attractive, however no ideal device has as yet been described.

Air volume systems, Lym Gym, Airogym and Veinguard all aim to increase flow in the seated position by movement of air in a partially inflated system. Changes in air pressure occur at different altitudes, resulting in inconsistent work achieved by movements. This increases the difficulty in quantifying the amount of work required to effectively achieve the CMPF, thus reducing venous stasis adequately.

Thus a mechanical device independent of cabin pressure seems more appropriate. The Skywalker's pedals are not securely attached to the base. The semi-circular pivot is detachable which means the design does not conform to aviation standards.

A device such as the Novamedix A V impulse system, in its present form is unsuitable for use during flight due to the air compressor.

Hence there is a need for a more suitable inflight device along mechanical lines that will adequately activate the calf muscle pump function and result in sufficient venous return.

Long haul "…air travel is an important risk factor for VTE requiring hospital admission and represents a significant public health problem in New Zealand" (Hughes *et al.*, 2006, p. 78).

The age matched control group, of 160 patients, used in the study conducted by Ferrari *et al.*, (1999) cannot be viewed as a desired control group due to the fact they were all medically ill and admitted to hospital for medical treatment. Also the study group had a greater proportion of obese patients than the control group.

The true incidence of FRDVT and FRPE is unknown. The study by Lapastolle *et al.*, may have underestimated the incidence of PE during air travel as non severe and those cases presenting outside the airport plus passengers who died in-flight or were found to be dead on arrival were not included in this study (Lapostolle *et al.,* 2001). The true incidence of FRPE may also have been underestimated in the study conducted by Pérez-Rodríguez *et al.*, (2003). Those who died in-flight and at the airport were not

documented. Also passengers who did not complete prior connecting flights (Asian passengers who had prior connections from London/Paris) possibly due to FRPE episodes were not included in this study. The possibility that some passengers had asymptomatic FRPE and so were not treated or referred to Ramón y Cajal must also be considered. According to Kumar *et al.,* (2005), 60 to 80 percent of PE were asymptomatic due to their size.

It has been established that compression stockings do not prevent FRSVT (Scurr *et al.,* 2001; Hughes *et al.,* 2003). Results presented by Scurr *et al.,* (2001) were criticised by Hirsh and O'Donnell (2001b, p.1462) for two reasons. The first being that *"no assurance was given that there had been no communication between volunteers and technicians. This shortcoming could have been avoided by having a 3rd party present during ultrasonography. Furthermore, the diagnosis of calf-vein thrombosis was not confirmed by venography, and since D-dimer results were negative, the thrombi were either very small or were false-positive findings".* They go on to say how unlikely it was that not one passenger who wore stockings developed a FRDVT. The NZATT study has been criticised for its lack of use of controls. Authors of the study did state that the "absolute proportion" of FRVTE due to lack of controls could not be determined (Hughes *et al.,* 2003).

It appears that fewer deep thrombi occur in first class compared to economy class. In the studies discussed, the last three rows of economy class seats were implicated in increased coagulation of all passengers. Passengers seated in the window and central seats of economy class are at greater risk of developing FRDVT as all DVT events occurred in subjects seated in window or central seats in both the LONFLIT and LONFLIT 2 studies (Belcaro *et al.,* 2001a, b)**.**

Both economy and first class travel on long haul flights has been associated with FRDVT and FRPE (Mohler, 1997; Lapostolle *et al.,* 2001, Hughes *et al.,* 2003). Two of the nine volunteers who developed a VTE in the NZATT study travelled business class. Their mean age was 59.5 years, which in itself is a risk factor for VTE (Klauser *et al.,* 2004, p.896).

Both Dudley Miller (2004) and Lapostolle *et al.,* (2004) state the necessity for control groups in studies into FRDVT, as without them inconclusive results are determined (Klauser *et al.,* 2004, p.896).

Factor V Leiden and prothrombin gene mutation are common inherited risk factors for FRDVT (Scurr *et al.,* 2001). It was determined by Schreijer and co-authors that TAT, D-dimer and prothrombin Fragment 1+2 levels were all higher post the three exposures in the FVLM and in the oral contraceptive group of volunteers. There was no difference between F1 + 2 levels in either of the subgroups of volunteers after any of the three studies (Schreijer *et al.,* 2006). However TAT and d-dimer levels remained normal after eight hour flights in the study conducted by Schobersberger *et al.,* (2003).

The occurrence of oedema in the lower extremities during long haul flight may be a predisposing factor of FRDVT as the authors of one study hypothesised that it "could" cause compression of the veins (Belcaro *et al.,* 2002). However in both control and the stocking groups, the presence of oedema was not sufficient to trigger thrombus formation in the LONFLIT4 Concorde Sigvaris Traveno Stocking study (Cesarone *et al.,* 2003b).

Many experts in FRDVT have disagreed with the findings of the study conducted by Kraaijenhagen *et al.,* (2000), which invalidates the relationship between long haul flights and the development of DVT and PE (Ferrari and Morgan, 2001; Burnand *et al.,* 2001).

Two different studies (The BEST Study, 2003 and The Lonflit-Flite Randomized Control Trial, 2003), researching into D-dimers, published in the same year, have published

contradictory findings. This phenomenon must strengthen the requirement for a database which will display actual events and any genetic associations contributing to DVT and PE. However D-dimers were elevated post flight, decreased post cinema and remained unchanged after daily activity in the study conducted by Schreijer *et al.,* (2006).

Authors of the Lonflit-flite study concluded that D-dimer and Fibrogen testing were not effective for early detection or prediction of thrombi (Cesarone *et al.,* 2003a). Whereas Hughes *et al.,* (2005, p.2448) stated that increased plasma D-dimer levels "…are associated with recognised risk factors for VTE such as age, female gender, hormone use, obesity, co-morbidity and thrombophilia states…". Three of the seven females who presented with a thrombotic event were taking oral contraception (Cesarone, 2002).

The authors of the LONFLIT and LONFLIT2 study concluded it was probable that the majority of their study participants who were diagnosed with a thrombus, (as a result of taking part in the studies) would not have sought medical care as they considered some form of swelling "as normal" post long haul flight (Belcaro *et al.,* 2001ab). Even short haul flights of two to four hours duration have been implicated in the development of oedema (Belcaro *et al.,* 2002). Scholl socks were effective at reducing the presence of edema (Belcaro *et al.,* 2002). Sigvaris Traveno stockings significantly reduced the occurrence of oedema on seven hour flights. In comparison, on flights of eleven hours a limited amount of edema, even with stockings was present (Cesarone *et al.,* 2003b).

Episodes of DVT and SVT were asymptomatic in a number of studies (Scurr *et al.,* 2001; Belcaro *et al.,* 2002). However in the study conducted which compared aspirin to LMWH, 60 percent of all thrombotic events were asymptomatic (Cesarone, 2002).

It is understandable that sufferers of FRVTE would present themselves to Kings College Hospital as there are four airports, Heathrow, Gatwick, Standstead and London City in

the surrounding area. Yet as sufferers of FRDVT or PE may be asymptomatic, it is certain that this figure of 1000 flight related deaths per year is greatly underestimated

Jet lag may be a contributing factor to the occurrence of FRDVT. Some passengers suffering from jet lag upon their arrival at their destination may try to sleep to overcome the effects and thus become immobile once again. These two periods of immobility may encourage a thrombus to grow in size. Passengers who take sleeping tablets to induce sleep on a long haul flight should be persuaded that this could be a dangerous course of action, as sleeping limits movement of the muscles, enhancing the possibility of thrombus development due to venous stasis. Passengers should also be encouraged to avoid alcohol to aid sleep as this not only reduces movement but may also results in dehydration. Finally, conditions experienced during flight in addition to possibly cramped seating conditions in cars or buses while travelling from the airport to the final destination, all may contribute to DVT.

Few accidents occur during flight (ACARE, 2002). The measure of wearing a seatbelt is to prevent harm during flight. If passengers are instructed to wear a seat belt for their personal safety then why is some form of prophylaxis such as the Tromped or the Airogym Cushion to aid in the prevention of harm by FRDVT also not provided by airlines? If engineering solutions to problems such as FRDVT are not introduced how can these solutions lead to the health improvements, which they were designed to achieve?

CHAPTER 4

METHODOLOGY

4.0 Introduction

This chapter explains the research methodology, methods and design employed. The research involved comprehensive reading of medical literature concerning the human body and the pathology of venous thrombosis and methods of prevention (chapters one to three). Literature relating to the normal operation of an aircraft and both the requirements and regulations of aircraft manufacture and safe operation was also referred to (chapters three and five).

A form of prophylaxis for FRDVT was designed and developed (named the Tromped), with the final aim of incorporating this device into commercial aircraft (chapter five). These devices were haemodynamically assessed for their viability with the help of recruited volunteers. Approval by both the Beaumont Hospital medical ethics committee and the DIT ethics committee was sought and given to conduct the final two haemodynamic assessments (chapters seven and eight respectively). Beaumont Hospital ethics committee required clarification to determine if the Tromped prototype was indeed a medical device (section 5.11).

4.1 Methodology

The methods used allowed for a wide-ranging study of the issues which are of concern to the flying public, airlines, aircraft manufacturers and the international medical society. A method of research, recording, design, testing and analysis of results was used.

4.2. Troubleshooting with Springs

Four demonstrator devices were developed using commercially available springs. These springs were made from spring steel and each had a different resistive value. These springs were blindly selected and one was placed into each demonstrator device. Following the first medical assessment, it was determined by Air Plethysmography that D2 and D3, produced a sufficient mean ejection volume fraction (EVF) (Collins, 2002/2003). These springs were tested in Lufthansa Technik Aermotive Ireland, using a Chatillion Digital Force Gauge, LTC-100 (DFGS). Each spring was placed separately on the stainless steel lower compression plate where its height and the force required to compress the spring were recorded (Figure 4.1).

The force required to fully compress the spring in D2 was 99.21 newtons (N). This jig produced a mean EVF of 65.99 percent and a mean residual volume fraction (RVF) less than the required 35 per cent at 21.54 per cent. The force required to fully compress the spring in D3 was 80.97 N, which produced a mean EVF of 62.17 percent. The mean residual value fraction was less than the 35 per cent required at 33.71 per cent.

When conducting the medical study all ten volunteers reported that the spring parameters of D3 were preferable to those of D2, in terms of ease of use. Even though less effort was required to compress the device pedal, they still achieved the required venous return in the seated position. Hence the spring parameters of D3 were used in the subsequent assessments conducted.

As a force of 99.21N was required to fully compress the spring of D2, a range of 80.97N to 86.75N force was considered for further testing so the spring will not be fully compressed. The height of the desired spring, diameter of the coils and the required compression value needed were known. Specifications such as spring deflection height, the number of spring coils, spring wire gauge and the type of environment the finished

spring would be subjected to were required. Calculations were performed to determine the design specifications for the desired spring used in D3 (Section 4.2.1).

Source: Lufthansa Technkik Airmotive Ireland.

Figure 4.1. LTC 100 Chatillion Digital Force Gauge.

The compression values determined by the DFGS represented the force required to compress the front edge of the pedal to meet the front edge of the base. It did not represent the exact downward force required to compress the spring which was situated a few centimetres away from the edge of the pedal. To determine the exact compression value of the spring, it was removed from the Tromped, and a simple harmonic test was conducted. Using weights, a spring deflection height of 38.4mm was achieved by applying a force of 82.04N. This was 0.98N greater than the compression value initially obtained. The same spring was then tested in Lufthansa Technik Aermotive Ireland to determine the required load to produce a deflection height of 38.1mm (as produced when

the pedal is compressed to meet the Tromped base). The same DFGS (that tested D2 and 3) was used to determine the force required to fully compress the spring in its free state. A load of 111.669N fully compressed the spring to a height of 25.4mm. The force required to deflect the spring to a height of 38.1mm was determined as 84.98 N, as seen in Graph 1 (Appendix C). A difference of 2.93N was recorded between the two methods used to test spring deflection and force. The DFGS is constantly used to test springs used in aircraft engines. As this method was used to test the compression values of D2 and 3 the values obtained by the DFGS were accepted as the true values.

The recorded errors of the Chatillion Force gauge are +/-0.89N. The accuracy of the DFGS series is +/-0.15% of full scale +/-1 least significant count (LSC) (AMATEK, 2001).

4.2.1. Compression Spring Calculations for prototype Option II

The spring used in D3, is an oil Tempered spring, with a modulus of Rigidity, G, of 78×10^3 N/mm^2. The diameter of the spring material, inside diameter of the coil and the outside diameter of the coil were all measured.

The diameter of the spring wire material was recorded as 2.3368 mm by a 150mm Digital Calipers. Its accuracy is +/-0.02 mm (<100mm).

D_1 or inside diameter of the coil was 25.4 mm.

D_2 or outside diameter of the coil was 30.07 mm.

N = 10 (coils in the spring).

Length of the spring was 101.6 mm

The force on the spring W, to fully compress the spring was 111.7 N.

The load required to deflect the spring to a height of 38.1mm was 84.975 N ≈ 85 N.

If: W = applied load d = diameter of the spring wire

G = Modulus of Rigidity N = number of coils in the spring

D = diameter of the spring coils, x = deflection

The spring force is calculated using equation 6.1, (SAE 1996, p.189). W was substituted for P (load or force) and *x* (to represent for deflection) was substituted for F, so that F would not be misconstrued as the force or load. The Load (W), "is the force required to compress the spring to a specified loaded length" (SAE, 1996).

Spring Force: $W = \frac{Gxd^4}{8ND^3}$ **Eqn 4.1.**

(SAE, 1996, p.189)

D is calculated by finding the mean of D_1 and D_2 as follows:

$$D = \frac{(D_1 + D_2)}{2}$$ **Eqn 4.2.**

So $D = \frac{(25.4 + 30.07)}{2}$

D = 27.73 mm.

The following calculation was performed to confirm the correct Modulus of Rigidity of the spring. The deflection height, x, of compression Spring 3, is determined using Eqn. 5.1., transposed:

$$x = \frac{8WND^3}{Gd^4}$$ **Eqn 4.3.**

$$x = \frac{8(85)(10)(27.73)^3}{(78\times10^3)(2.3368)^4}$$

Therefore $x = \frac{1.449\times10^8}{2.32\times10^6}$, x= 62.45 mm.

Determined from the previous equation, a force of 84.97 N would deflect the spring by a height of 62.45mm. However the Chatillion digital force gauge showed that a force of 84.97 N deflected the spring by a height of 63.39 mm. A difference of one mm clearance was not significant, thus it was accepted that the modulus of rigidity quoted for the spring material was approximately correct.

4.3. Medical Ethics

The Non-Invasive research conducted for the purpose of this work followed the criteria set out by the Declaration of Helsinki (1964). The assessments conducted can be classified as non-therapeutic research however the Tromped and Mediven® Travel Compression Stocking Assessment was considered as a Clinical Trial by the Beaumont Hospital Ethics Committee, as the Tromped was classed as a medical device by a representative of the Irish Medicine Board (IMB). Each subject acted as their own control, in all three haemodynamic assessments conducted.

The research conducted was non-invasive, which involved direct interaction with all participants and so is classed as intrusive research (Kirk, 1995). It consisted of an air chamber being placed around each participant's right calf, from knee to ankle, (refer to section 4.5.), to allow quantification of the calf muscle pump action during various manoeuvres.

Prior to conducting any of the three assessments, information leaflets containing the following were provided for each potential participant. *"If research is involved, disclosures should generally cover the aims and methods of the research, anticipated benefits and risks, any anticipated in-convenience or discomfort, and the subjects' right to withdraw, without penalty, from the research".* (Beauchamp and Childress, 2001).

All participants in the three assessments were of an age and mental capacity to provide informed voluntary consent for participation in the studies. They were not patients of any institution at the time before or during assessment. Thus they were capable of disclosing information that would have excluded them from the assessment and understood the requirements of the assessment prior to their involvement. They all provided informed consent to the investigator (CC). *"For consent to be truly voluntary it should be stressed to the patient that he or she is quite free to refuse to participate without any adverse response or sanction occurring and that the patient can also withdraw during the course of the trial if he wants to"* (Kirk, 1995, p.239). Participants were not coerced, all were aware of their right to withdraw from the study at any time. Neither, monetary or any other inducement to participate was offered to those who conducted the three assessments. All information provided to participants prior to and during each assessment was valid and accurate. Explanation of the study was provided in the information letters given to participants. Prior and during the course of the study, verbal instructions were given to each participant. .

4.4. Haemodynamic Assessment's methodology

Non-invasive procedures were conducted to test the efficiency of the Tromped. It was also beneficial to use non-invasive equipment as recruitment of participants may have become an issue if the procedures were invasive. Duplex ultrasound, Air Plethysmographs and photoplethysmograph machines are used in the medical field to assess valvular competency of the lower limbs, non-invasively (Needham, 2005). All three test categories were researched and both Duplex Ultrasound and photoplethysmography were immediately eliminated.

4.4.1. Duplex Ultrasound

It would have been required to hold an ultrasound probe on either the popliteal vein (which is found at the crease of the back of the knee) or on the skin above the femoral vein at all times during the assessment. There would also have been an associated technical difficulty maintaining adequate contact between the ultrasound transducer and the skin overlying both these areas when the participant would be required to conduct manoeuvres in the seated position. Also Duplex measures velocity and would not provide quantifiable measurements of venous volume or changes in the limb.

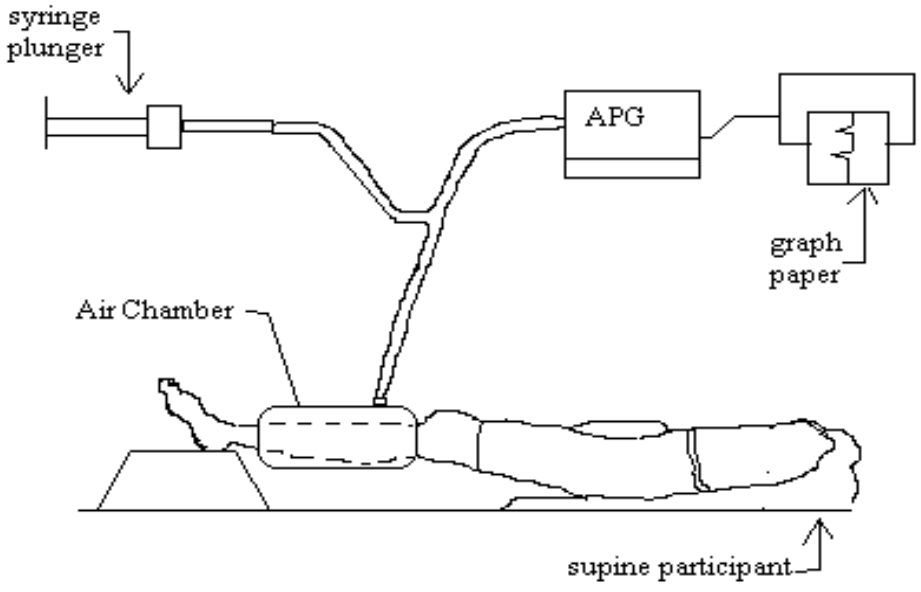
4.4.2. Plethysmography

Air Plethysmographs and photoplethysmographs assess valvular competency by measuring the volume of the lower limbs while the participant stands or remains in the supine position and conducts various foot manoeuvres (Needham, 2005). Photoplethysmography was not ideal as its use has dramatically reduced in the last ten years for testing of valvular efficacy (Needham, 2005) and also the equipment itself was not readily available.

4.5. Air Plethysmography

Air Plethysmography was used to conduct haemodynamic assessments using the Tromped because it is a non-invasive technique it is reproducible, measures calf volume and provides quantifiable results. The technique is used to determine relative volume changes in the lower limbs in response to postural alterations and muscular exercise (Nicolaides and Sumner, 1991). Air Plethysmography is also known as pneumoplethysmography (Schmitz *et al.,* 2006). As the Air Plethysmograph is calibrated, whole leg volume change as a result of exercise can be recorded in absolute

values (ml) and as relative units. Segmental volume changes measured by strain gauge do not represent changes in the whole leg and so this cannot be used with exercise, tiptoe and walking. The Air Plethysmograph consists of a 355mm long tabular polyvinyl chloride air-chamber which surrounds the whole lower limb from knee to ankle (Nicolaides and Sumner, 1991; Needham, 2005). The APG 1000 (ACI Medical, San Marcos, California) is recognised as an accurate evaluation of venous hemodynamics (Criado *et al.*, 1998). It measures volume changes over the region surrounded by an air chamber (calf of a human limb in this instance) as shown in Figure 4.2. *"An increase in volume of the part contained within the plethysmograph causes air to be compressed resulting in a pressure rise"* (Strandness and Sumner, 1975). This rise is then recorded by the transducer, which records the change in volts and then translates and records it as millilitres of blood on the APG plotter (Strandness and Sumner, 1975).



Source: Nicolaides and Sumner, 1991

Figure 4.2. Diagrammatic representation of the APG.

4.5.1. Method of assessing venous function using Air Plethysmography

The chamber was inflated to seven mmHg and connected to a pressure transducer, an amplifier and a recorder, as shown in Figure 4.2. This pressure of seven mmHg ensures adequate contact between the chamber and the leg. The air plethysmograph was calibrated by pressing the syringe plunger which reduced the volume of the system by 100 ml (Nicolaides and Sumner, 1991). The resultant pressure change was stored in the system its purpose was to generate a calibration curve Bays *et al.,* (1994). As the volume change of a gas within a closed system is related to both pressure and temperature a controlled room temperature was necessary (Comerota, *et al.,* 1995).

The plunger was then pulled back to its original position. All of this occurred with the patient in the supine position, with the right leg elevated by 45º and with the right knee slightly rotated, (as shown in Figure 6.1.), which allows emptying of the patient's veins (Nicolaides and Sumner, 1991; Needham, 2005). When the volunteer lies in the supine position, elevation of the leg means that the blood flows to the abdominal and thoracic veins, as a result of gravity, emptying the lower limb veins of blood (Tibbs, 1992).

The volunteer was instructed to stand with all of his/her weight on the left leg. At this time an increase in the right leg standing venous volume (VV) was recorded as a result of the venous filling (Nicolaides and Sumner, 1991; Bays *et al.,* 1994). A wide variety of normal VV values are reported ranging from (80 –170ml) (Bays *et al.,* 1994; Padberg *et al.,,* 2004). Patients presenting with CVI will have values ranging from 100 – 350ml (Nicolaides and Sumner, 1991). However the Venous Filling index is the most important indicator of venous competency as it is an excellent predictor of venous reflux (Criado *et al.,* 1998). It is a measure of the average filling rate. Normal refilling times in a healthy individual is usually greater than 16 seconds (Needham, 2005). A VFI of two ml/s or less occurs in normal limbs with competent veins (Christopoulos *et al.,* 1989; Nicolaides and

Sumner, 1991; Bays *et al.*, 1994). A VFI of 30 mls/s can occur in limbs with reflux (Nicolaides, 2000).

Source: Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 4.3. The APG pressure transducer, amplifier and recorder.

Ambulatory venous pressure (AVP) "is estimated with a tip-toe exercise" (Fukuoka, Okada & Sugimoto, 1998, p. 674). This movement will measure the Ejection Volume (EV), which *"is a measure of the venous pump function and depends on patency of veins and normal venous function"* (Mantoni *et al.*, 2002, p.580). Normal values range between 60-150ml (Bays *et al.*, 1994). The normal ejection volume fraction (EVF) is greater than or equal to 60 percent (Nicolaides and Sumner, 1991; Nicolaides, 1999). Refer to Figure 4.4 to view an EV recorded on the APG trace. The Ejection Volume Fraction (EVF) is the percentage of calf blood volume emptied with a single calf muscle contraction during tiptoe exercise. The Residual Volume (RV) and subsequently the Residual Volume Fraction (RVF) are calculated as a result of the patient conducting ten

consecutive tip-toe movements. The RV is a measurement of the amount of blood remaining in the veins after exercise, in this instance, ten consecutive tiptoes (Nicolaides and Sumner, 1991). The normal residual volume fraction is less than or equal to 35 percent and it is the most useful non-invasive index of the efficiency of the calf muscle pump (Christopoulous *et al.*, 1989).

4.5.2. Standard APG assessment procedure

The standard APG assessment has been described and validated to demonstrate relative volume changes in the lower limbs in response to postural alterations and exercise and thus quantify calf muscle pump function (Christopoulos *et al.*, 1987).

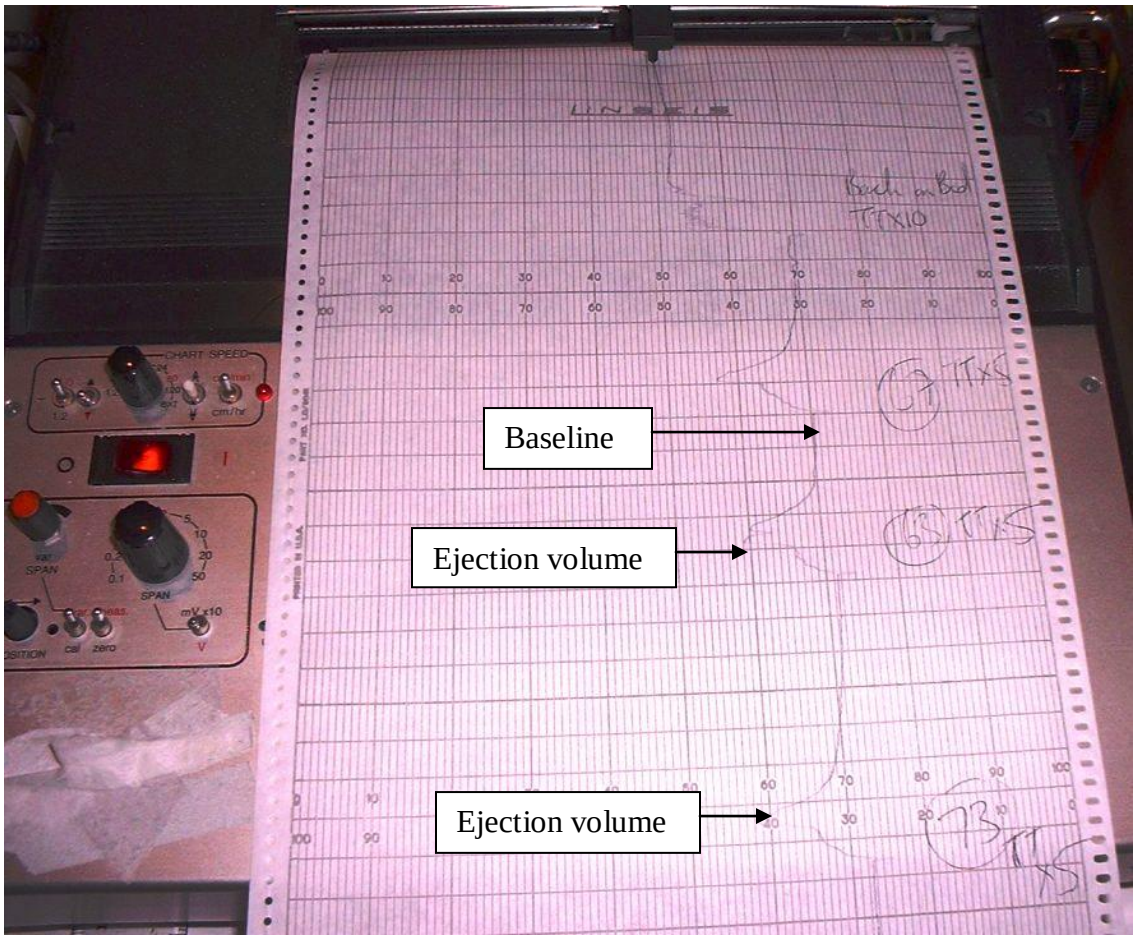
i. The patient was asked to lie in the supine position on an examination couch with a cushion height of 468mm off the ground, to coincide with commercial aircraft seating heights. The volunteer must place their hands by their sides so as not to press on the Inferior Vena Cava (IVC).

ii. The volunteer must remain in this position for at least ten minutes before the test may begin. The room was maintained at a controlled temperature of 20º Centigrade, to obtain equilibrium and prevent vasoconstriction (Cole, 2001b).

iii. The 355mm tubular polyvinyl chloride air chamber was placed around the volunteer's right leg as shown in Figure 6.1. and the APG® was calibrated.

iv. The volunteer was instructed to lie in the supine position with his/her right leg elevated to the 45º angle and right knee slightly bent while the calf veins emptied of blood.

v. After a stable baseline was recorded the volunteer was asked to stand with all of her/his weight positioned on the left leg, with the aid of an orthopaedic frame. An increase in the leg venous volume (VV) was observed.



Source: Non-Invasive Vascular Unit, Beaumont Hospital.

Figure 4.4. Base line and movement recorded on APG trace.

vi. When a steady base line was observed in the standing volunteer, he/she was asked to stand on both tiptoes with all their weight on both legs, holding this position for five seconds. The volunteer then returned to the initial standing position, with all the body weight concentrated on the left leg.

vii. This procedure was repeated until two similar values were recorded on the graph paper. The EV, (the amount of blood propelled up the leg) was recorded as a decrease in volume. The EVF was calculated as a result of calf muscle contraction, as shown in Equation 4.5.

viii. When a steady base line was recorded the volunteer conducted ten consecutive tiptoe movements before returning to the supine position with the

right leg elevated, resting on the support to empty the veins. The volume of blood remaining in the veins after exercise was the residual volume (RV). The RVF is calculated by using equation 4.6.

4.6 Mathematical Modelling

The venous filling index is obtained by using equation 4.4 (Christopoulos *et al.*, 1987):

$$\text{VFI} = \frac{VV(90\%)}{VFT(90\%)} \qquad \textbf{Eqn 4.4.}$$

The EVF was calculated from the following equation (Christopoulos *et al.*, 1987):

$$\text{EVF} = \frac{EV}{VV} \times 100 \qquad \textbf{Eqn 4.5.}$$

The RVF was calculated from equation 6.6 (Christopoulos *et al.*, 1987):

$$\text{RVF} = \frac{RV}{VV} \times 100 \qquad \textbf{Eqn 4.6.}$$

The Mean $\bar{x}$, of each value (for example the standing venous volume obtained from the first assessment), was calculated from equation 4.7 (Reilly, 2000):

$$\bar{x} = \frac{110 + 100 + 150 + 100 + 75 + 130 + 135 + 166 + 70 + 150}{10} \qquad \textbf{Eqn. 4.7.}$$

$\bar{x}$ = 118.6 mls.

This was repeated for each of the different manoeuvre values.

The standard deviation was determined using the following formula (Reilly, 2000):

$$\sigma = \sqrt{\frac{\sum d^2}{n}} \qquad \textbf{Eqn. 4.8.}$$

Where $d = x - \bar{x}$; x is a patients recorded value (standing VV, for example), $\bar{x}$ is the mean of all ten patients values for one particular movement or value (standing VV of the first assessment for example) and n the number of patients.

$\sum d^2$ = [(110-118.6)^2 + (100-118.6)^2 + (150-118.6)^2 + (100-118.6)^2 + (75-118.6)^2 + (130-118.6)^2 + (135-118.6)^2 + (166-118.6)^2 + (70-118.6)^2 + (150-118.6)^2]

$\sum d^2$ = **9646.4**

$$\sigma = \sqrt{\frac{9646.4}{10}} = 31.05$$

The "Student's *t*-test" was used to compare the mean value obtained for each movement in the seated position, standing and walking, to determine if there was any significant statistical difference. The paired Student's *t*-test was used to compare the control manoeuvre to the assessment manoeuvres to determine if a significant difference existed (Reilly, 2000).

The t-test formula (Reilly, 2000) used was $$t = \frac{\overline{x_1} - \overline{x}_2}{\sqrt{\frac{s^2}{n_1} + \frac{s^2}{n_2}}}$$ **Eqn 4.9**.

Where $s^2 = \frac{(n_1 - 1)\hat{s}_1^{\,2} + (n_2 - 1)\hat{s}_2^{\,2}}{n_1 + n_2 - 2}$. **Eqn. 4.9.1**

When $n_1 + n_2 - 2$ = degrees of freedom **Eqn. 4.9.2**

n = the number of patients, therefore n_1 and n_2 both equal 10. s_1 and s_2 were the standard deviation results of the two particular ejection volumes being compared. $\bar{x}_1$ and $\bar{x}_2$ were the mean values of the two ejection volumes being compared.

4.7. Haemodynamic evaluation of the Tromped prototypes

Figure 4.5. represents the order of haemodynamic assessments conducted, involving the various prototypes of the Tromped.

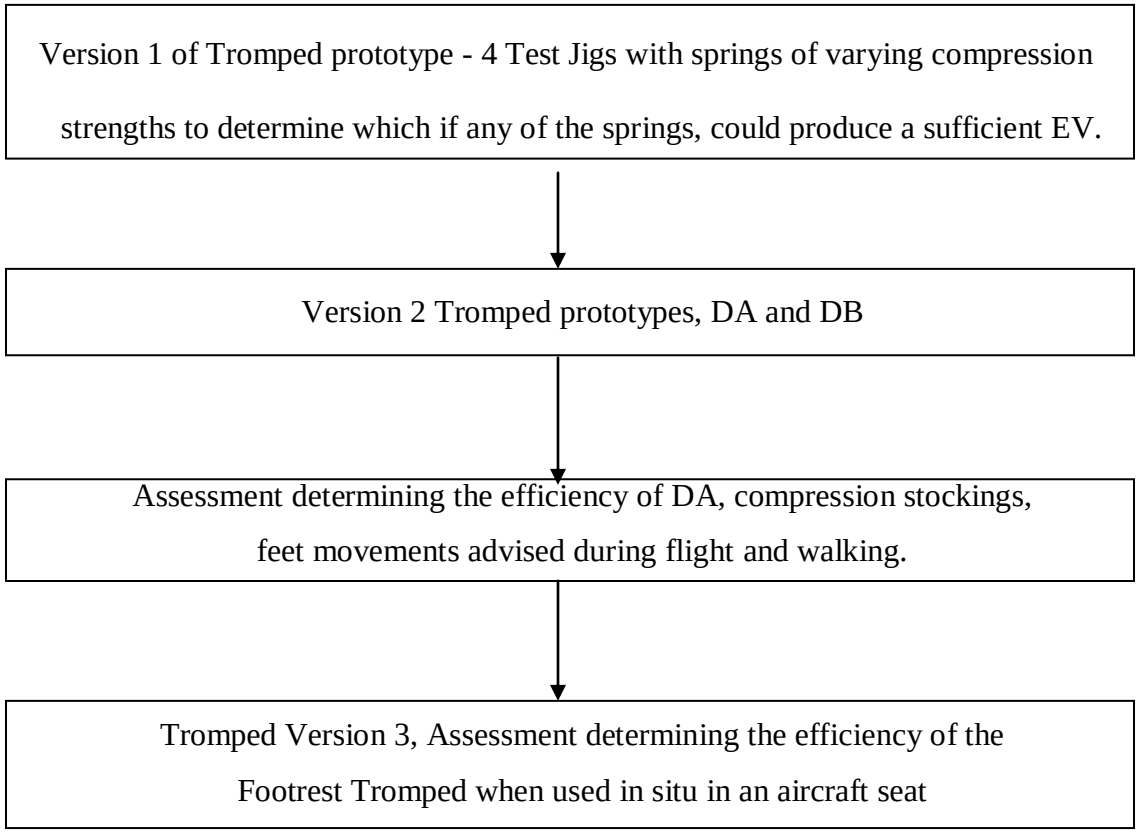


Figure 4.5. Order of Haemodynamic Assessments conducted

4.8. The Tromped and Mediven ® Travel Compression Stocking Sizes

These below knee stockings (UK grade II) had a compression of 18.4 -21.1 mmHg (Hsieh and Lee, 2005). The instructions accompanying them state "Measure the circumference above the ankle at its narrowest part".

Table 4.1. Knee length Mediven® Travel stocking sizes.

Ankle Circumference (mm)	Mediven® travel stocking sizes
180 – 200	Small
200 – 230	Medium
230 – 260	Large
260 – 290	Extra Large
290 – 320	Extra extra large

Source: Mediven® Travel stocking

The size of a participant's right ankle when measured on the day of the study determined which Mediven® knee length travel compression stocking size they required to wear. All ankle measurements were taken using a spring loaded measuring tape.

CHAPTER 5

DEVELOPMENT OF THE TROMPED PROTOTYPES

5.0 Introduction

Development of The Tromped began with a simple design (which established haemodynamic effects in the seated position) and eventually progressed to a commercially viable prototype design for use on board an aircraft. All demonstrator models were assessed to evaluate their ability to effect venous return (when used *in situ*) similar to that achieved in the ambulatory position.

5.1 The first Tromped prototype

The first Tromped demonstrators were produced using aluminium sheet of strength 2024 T4, using conventional fabrication techniques. All four demonstrators produced had the same dimensions. The bases of the demonstrators were 177mm wide and 375mm long. The depth of the demonstrator base was 25mm. The pedals (310 mm long, 106mm wide and 18mm deep) were attached to the base at one end by a hinge and at the front end by the compression spring. Four different springs, selected to provide a range of foot pressures were inserted into each of the demonstrators. Physical parameters of all of the springs were determined following the haemodynamic assessment using a Chatillion Digital Force Gauge (Table 5.1). The displacement of a compression spring is a reliable method of measuring the linear force generated by induced plantar flexion. Compression springs have an automatic stop once fully compressed, which limits stress levels. Compression springs are manufactured from materials suitable to withstand the physical changes experienced during airline travel and exhibit long fatigue lives, suitable for multiple compression cycles (Carlson, 1980).

Once the top of the pedal lined up with the top end of the base the appropriate hinge position could be determined, and so measurements of the hinge's dimensions were transferred to the underside of the pedal and on the upperside of the base.

Table 5.1. Force required to fully compress the Tromped demonstrators.

	Spring height (mm)	Load required to compress the pedal (N)
D1	100	56.94
D2	125	99.21
D3	100	80.97
D4	100	55.16

Source: Collins, 2002-2003.

Holes were drilled into the pedal to coincide with the holes on the hinge, which was then riveted to the underside of the pedal. A hole was also drilled in the upper side of the base to accommodate the hinge measurements and the hinge was riveted to the base (Figure 5.1). Once the pedal was securely attached to the base by the hinge, a gauge setting with an angle of 25º (which provided a reasonable elevation to the foot, without inducing discomfort) was used to determine where the spring should be positioned. Consequently all demonstrator pedals were at the same angle, although some of the springs were of differing heights. Each spring was wire locked to a square shaped mat fashioned from the aluminium sheets. A circle larger in circumference than the spring was cut out of the upper side of the base so that it would allow sufficient clearance for the compression springs. Once in the correct position, the spring mat was riveted to the underside of the base. The upper end of the spring was wired locked to the under side of the pedal. Finally the upper and lower sides of each base were riveted together as were the two sides of each of the pedals. Each demonstrator was marked with its own code to allow identification for experimental purposes (Collins, 2002-2003).

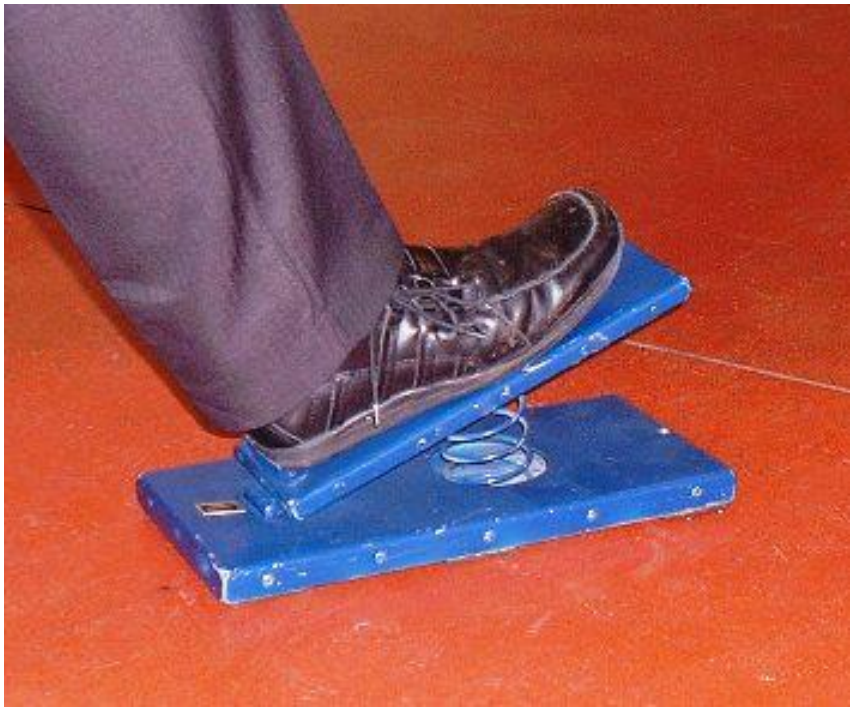


Figure 5.1. The first Tromped demonstrator.

5.2. Hemodynamic Assessment of the first Tromped prototype

Hypothesis: "can any of the springs when compressed in the seated position produce sufficient venous return to mimic normal ambulatory calf muscle pump function, and thus potentially reduce the incidence of FRDVT?"

5.2.1. Location

This assessment was conducted in the Non-Invasive Vascular Unit, Beaumont Hospital, Dublin.

5.2.2. Participants.

The ten healthy volunteers recruited to conduct this assessment comprised of six males and four females. Ages ranged between 20-69 years (mean age 40.2 years ± 17.2 years) were assessed.

5.2.3. Method

The standard APG assessment of calf muscle pump function was performed, requiring the volunteer to move from the supine to the standing position to perform tiptoe manoeuvre to stimulate calf contraction. APG allows non-invasive measurement of changes in volume enabling measurement of calf muscle pump function in terms of EVF. Each demonstrator was assessed in the seated position, with tiptoe movement replaced by compression of the demonstrator pedals. Compression of these pedals required plantar flexion of the ankle, to increase venous return from the deep and superficial system. Plantar flexion requires the volunteer to rise the heel off the ground and place weight on the ball of the foot. As Tromped use mimics dynamic plantar flexion manoeuvre, calf blood flow will increase as the contractions per minute increase.

5.2.4. Normal Values

In the standard APG assessment, a VFI of less than 2ml/s, an EVF of greater than 60 percent and an RVF of less than 35 percent would be considered normal (Christopoulos *et al.*, 1987; Christopoulous *et al.*, 1989).

5.2.5. Results

All of the results are expressed as mean +/- standard deviation, n = 10. EVFs obtained are presented in Figure 5.2 and Table 5.2.

All volunteers had normal venous function, determined by their venous filling index (VFI) and RVF.

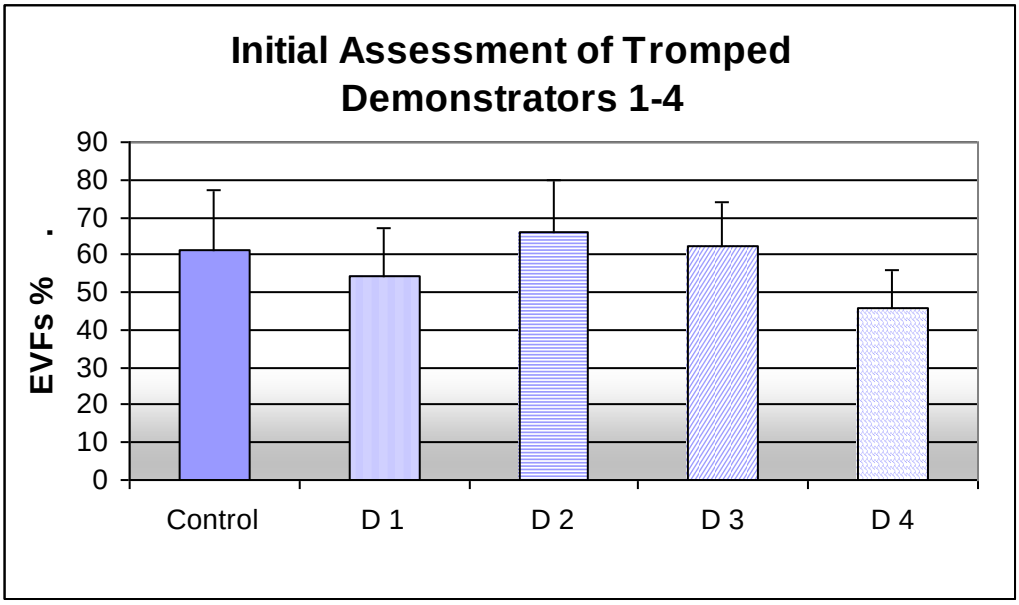


Figure 5.2. EVFs obtained from demonstrators 1 - 4.

Table 5.2. EVFs obtained from demonstrators 1 – 4.

	Control	D 1	D 2	D3	D 4
EVFs (%)	61.02	54.1	65.99	62.17	46.05
SD	16.08	12.83	13.83	11.63	9.84

EVF achieved by control and exercise devices as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

Tip-toe manoeuvre in the standing position acted as control and achieved a mean EVF of 61.01 ± 16.08%. Only demonstrator two (D2) and D3 achieved a greater than 60 percent EVF, which is comparable with normal standing values (Table 5.2., Figure 5.2). Mean RVF of 21.74 ± 11.25 % is achieved by control movements. Demonstrator one, D2 and D3 produced an RVF less than 35 percent, (Table 5.3, Figure 5.3). Even though D2 had a lower RVF (21.54 ± 18.87%) compared to D3 (31.66 ± 22.62%), all ten participants reported D2 to be least user friendly device of all demonstrators. D3 was reported as the

most user-friendly by all ten volunteers and so this spring's compression value was chosen for use in further prototype designs (Collins, 2002-2003).

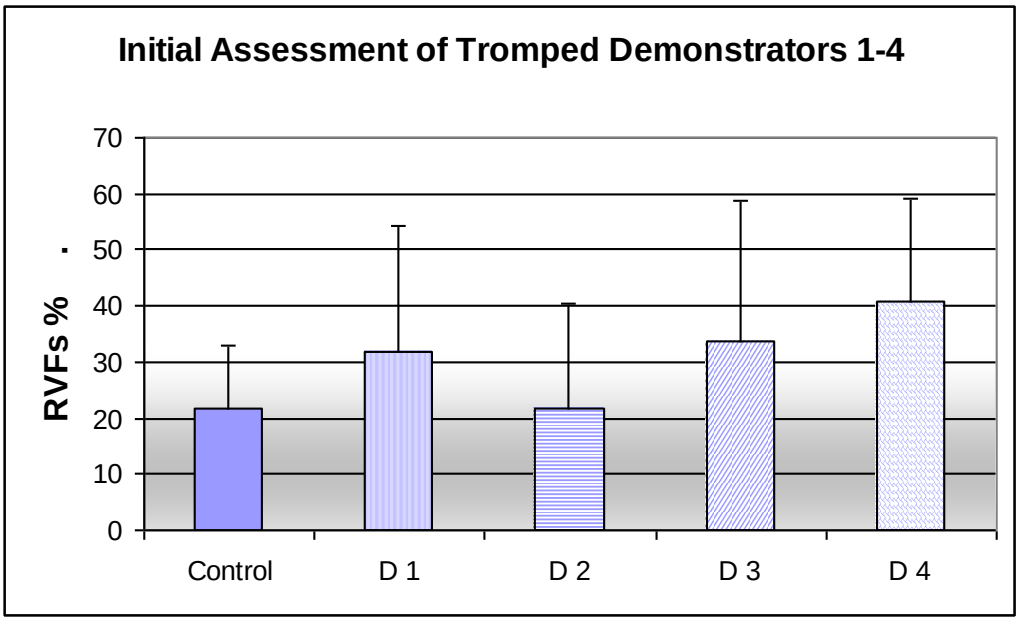


Figure 5.3. RVFs obtained from Demonstrators 1 - 4.

Table 5.3. RVFs obtained from Demonstrators 1 – 4.

	Control	D1	D2	D3	D4
RVFs (%)	21.75	31.66	21.54	33.71	40.75
SD	11.25	22.62	18.87	25.02	18.37

RVF achieved by control and exercise devices as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SDM.

Compression of D2 and D3 produced adequate EVFs while D1, D2 and D3 produced adequate RVFs in the seated position. User preference was for D3. As this device adequately achieved venous emptying in the seated position these parameters were chosen for further investigation.

5.3. Aircraft seat design

The Anthropometric Study to Update Minimum Aircraft Seating Standards was produced by Quigley *et al.,* (2001) of ICE Ergonomics, on the request of the Joint Aviation Authorities (JAA). The aim of this study was to provide regulatory information in areas such as seating dimensions on board. Seat spacing is a safety issue.

The trend in the increase in people's sizes is likely to continue and so the new requirements should take this into account. Recommendations considered a passenger's views on seat access, egress and spacing. Passengers of different heights and weights, ranging in age from 15 to 76 years of age with flight durations from 3.75 hours to 22 hours, seated in all seats were included. Members of the JAA currently do not have regulations regarding aircraft seat spacing, except the UK Civil Aviation Authority Airworthiness Notice 64. This notice regulates the minimum seat space dimensions on aircraft (Table 6.4) over 5700kg MTWA, which holds 20 passengers or more (Quigley *et al.*, 2001).

Table 5.4. The current minimum seat space requirements of the UK Civil Aviation Airworthiness Notice 64.

Dimension	Description	Minimum
A	Minimum distance between the back support cushion of a seat and the back of the seat or other fixed structure in front	660mm (26 inches)
B	The minimum distance between a seat and the seat or other fixed structure in front.	178mm (7 inches)
C	The minimum vertically projected distance between seat rows or between a seat and any fixed structure forward of the seat.	76mm (3 inches)

(Source: Quigley *et al.,* 2001, p. i).

Currently the only EASA regulations covering seat spacing is the minimum seat space requirements of the UK Civil Aviation Airworthiness Notice 64.

- Note: UK AN64 is based on data for fifth percentile (%ile) to 95%ile range of passengers. The report recommends that the range should be increased to one

percentile to 99%ile for safety reasons to allow for the gradual increase in peoples sizes. As a result, this study developed minimum recommendations (fifth and 95%ile) and ideal recommendations (first and 99%ile).

Section 5.0 Evaluation of AN64 states:

"In this section the minimum dimensions in AN64 are assessed against the anthropometric data for UK, European and world populations. The suitability of these dimensions are then tested using a human-modelling CAD system (SAMMIE CAD) and recommendations for revisions to the current and newly identified items are developed. The results of the assessment were used to develop recommendations for both improving and extending AN64 in respect of fit, ease of access / egress, postural flexibility and movement, comfort and the potential for alleviating factors associated with Deep Vein Thrombosis (DVT).

As EASA was responsible for undertaking this report to consider forms of alleviating factors related to DVT, stakeholders of the aviation industry may be considering the legal implications of FRDVT.

UK AN64 only considers aircraft seats when in the upright position.

Recommendations, as stated in the report:

i. Dimension A be increased to at least 711mm 95%ile
ii. Dimension A be increased ideally to 747mm 99%ile.
iii. Dimension A is not sufficient to allow taller passengers to adopt the 'brace' position and should be increased to at least 885mm. The brace position is defined as "the upper body should be bent forward as far as possible with the chest close to the thighs and knees, with the head touching the seat in front" (Quigley *et al.*, 2001, p.41)

iv. Dimension A concerned with the minimum seat space a large passenger can fit in, does not consider if a seat in front is reclined. The reclined seat may use 15-50 mm of space or more, depending on the type of seat back, the amount of rotation and the height from the floor. So when the seat in front is reclined this inhibits the posture of the passenger and may lead to the development of DVT due to a restriction of venous flow, as occurred in the case of Piet Fourie (Section 1.6.) (Quigley *et al.,* 2001).

v. Dimension B at armrest level should be increased to between 228.6mm and 254mm (nine and ten inches) at armrest level and 211.32mm (8.32inches) at cushion level.

vi. Dimension C would need to be increased from 76.2 – 304.8mm (three to twelve inches) to allow a 95%ile passenger to stand without bending. This is impractical from an aircraft design point,

vii. Seventy six point two mm of space hinders the passenger from standing upright, with their knees and ankles being forced forward by position of the seat cushion and their hips being pushed backwards by the top of the seat backs.

viii. Larger build passengers would even be more off balance when trying to access/egress the row of seats.

ix. A shorter passenger will also experience difficulty as his/her buttocks will come into contact with the arm-rests. If the passenger has a large chest it too will be compressed, in this case by the back of the seat in front.

x. This report recommends the consideration of a flip up seat which would increase the amount of space between rows for movement.

xi. To allow sufficient foot clearance to access/egress the seat, a figure of at least 350mm is needed with the ideal foot clearance of 360mm recommended.

This report has found that the seat base heights are too high for smaller female passengers and lowering the seats would cause problems for taller passengers so a foot/leg rest is recommended and a Tromped could be incorporated into this footrest.

5.4. Seat design for Tromped Operation

With the aforementioned seat design parameters in mind primary research on an aircraft to facilitate integration of the Tromped into aircraft cabin structure was conducted. Dimensions of economy class seats, (their height and width etc) on board a Boeing 757 were recorded with a spring loaded measuring tape (Figure 5.4).

i. The height from the floor to the top of the seat cushion was recorded as 457.2mm.

ii. The width of the first row, which consisted of three seats, was 1447.8mm in total.

iii. Cushion width

- The far inner seat had a cushion width of 457.2mm,
- the middle seat a cushion width of 444.5mm
- and the aisle seat width of 457.2mm.

iv. The straight length of the bar under the front row of seats was 1143mm but taking in curvature it was approximately 1219.2mm in length.

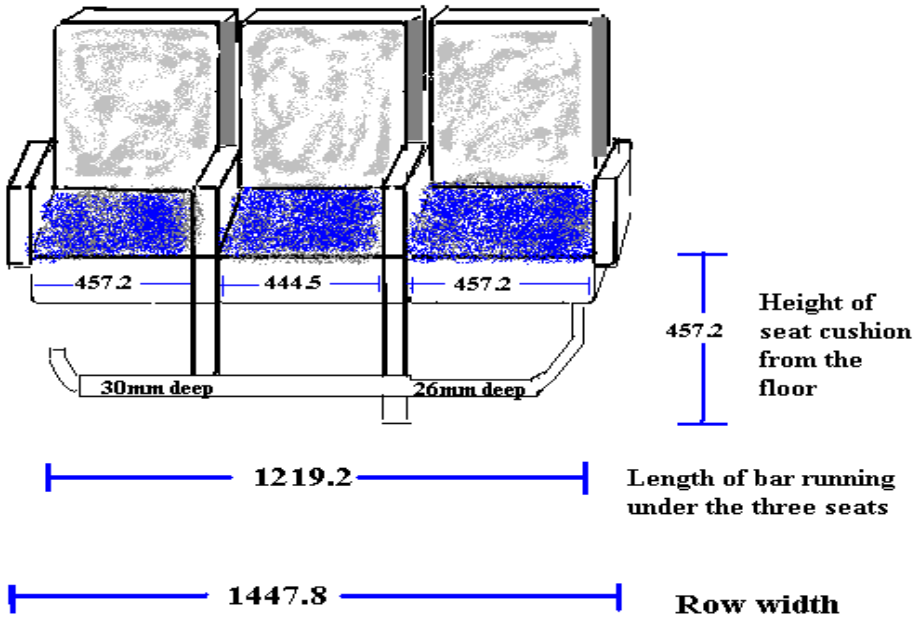


Figure 5.4. Dimensions of the aircraft seats.

This bar was ten mm wide and 26 mm in depth at the outer aisle seat. However in some places, this bar had different dimensions. For example positioned under the middle and inner seat, it increased in size to 20mm width and 30 mm depth. Facing the back end of this aircraft, there were 21 rows of seats on the left side and 20 on the right. The bar under the last eleven rows of seats on the left and ten on the right showed the same increase in size to the measurements underneath the middle and inside seat as discussed. Due to the positioning of both the seat tracking and seat legs on the Boeing Aircraft a swivel type connection will be a necessity, so that the Tromped can be used in the available foot space and in the most comfortable position for the passenger.

5.5. Design Implications

The Main factors which influenced the design of the Tromped were:

i. Commercial practices, i.e. contemplating the most practical way in which a commercial product could be implemented into aircraft design.

ii. Safety, by considering which form would more likely be accepted under the strict regulations and requirements of (EASA), CS-25 and the CFR-25 (section 7.2).

iii. Different markets; different commercial Tromped options i.e. airline installed or purchase by individuals for airline or home use, those immobile due to health reasons or old age or work environment.

A schematic outlining the Tromped prototype development process is shown in Figure 5.5. One obvious implication for Tromped integration is that the connection method to the bar which runs under the seats will have to have two different size fixings. In order for the Tromped to be used by all passengers, (except those seated in the first row of seats), it must be attached to the bar under the seat in front of the user. The design of this bar in respect of its positioning and height off the aircraft floor means that it is not possible to be attached and stored under the seat where the user would sit, without impairing ingress and aggress of that passenger. The design features of the Tromped were incorporated into an aircraft footrest (refer to Section 5.11) an established feature of aircraft design. This report recommends that "The upper surface of a footrest (for smaller passengers) should be about 350mm (14inches) below the front edge of the seat cushion" (Quigley *et al.*, 2001, P.62)**.**

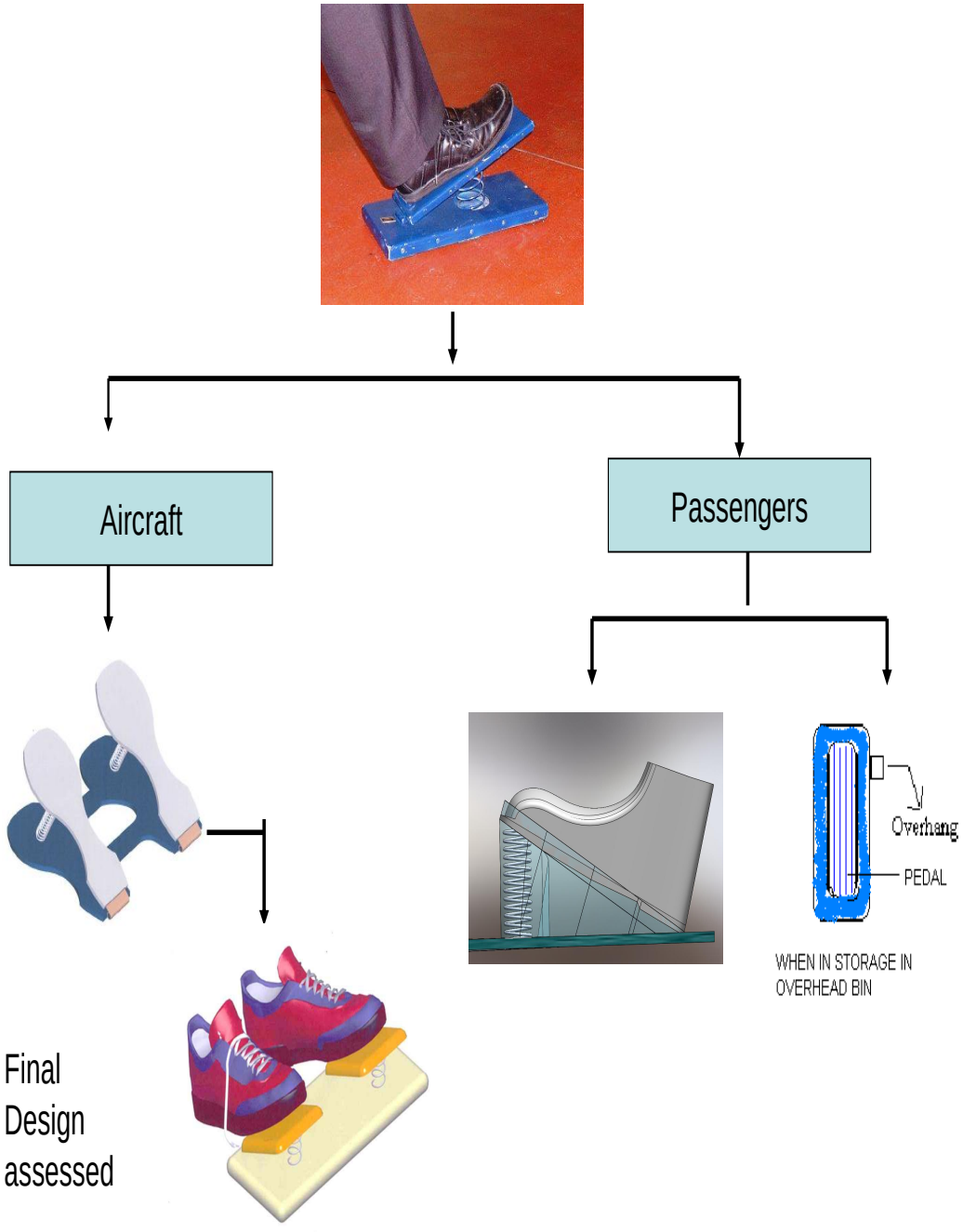


Figure 5.5. Schematic of Tromped design progression.

5.5.1. Tromped version 2, Option I

The aim of the initial "version 2", prototype design concept was to incorporate the Tromped into the aircraft floor frames (Figure 5.6) so that it would be part of the fixtures

and fittings of the aircraft. There is approximately a 508mm gap between two parallel frames of seats. Therefore:

i. The Tromped with its current dimensions would be cumbersome. It could hamper easy access from the seats, especially in the case of the window seat passenger;

ii. Secure bolts would be required at each end of the connections to secure the Tromped to the frame of the seat and it would be difficult to secure two such bolts on one frame;

iii. The length of the carpet panels may not be long enough to allow for two or three devices of this size;

iv. In the event of a crash, the structure of the Tromped attachment may be forced upwards through the floor adding to the potential for serious harm to passengers.

Source: Boeing.com

Figure 5.6 Aircraft seats attached to the floor seat tracking

5.5.2 Tromped version 2, Option II

The second option considered was that the Tromped be permanently fixed to the bar, which runs the length of the seats. The user would pull the Tromped (Figure 5.7) out from under the seat in front of them and fold out the pedals, which would be designed to fold back, when not in use. After use the Tromped would be pushed back under the seat. A special hinge on the connecting bar between the Tromped and the seat would have to be incorporated into this design reducing mobility, both during storage and use. One possible type of connection between the rail under the seats and the tromped could be an R-A-M Strap-On Rail Mounting Ball, which fits all sizes of 19.05mm to 50.8mm round rails. This design is preferable to Option I, as it can be stored under the seat, not hampering access in and out of the seats. This design format would comply with the Ergonomics Report (Quigley *et al.*, 2001). Option II would be marketed to the airlines themselves to purchase and supply to passengers.

Figure 5.7. Diagram of design Option I and II.

5.5.3 Tromped version 2, Option III

Option III considered the Tromped as a stand alone product available for use on aircraft. It could be stored i.e. in an overhead bin for example. It was designed in such a way that the pedals and their corresponding bases would fold over so that the width will halve in size. The problem with this design was that there would be a piece of material (the bar which connects the two pedals) overhanging (refer to Figure 5.8).

The third design was least favoured for this research.

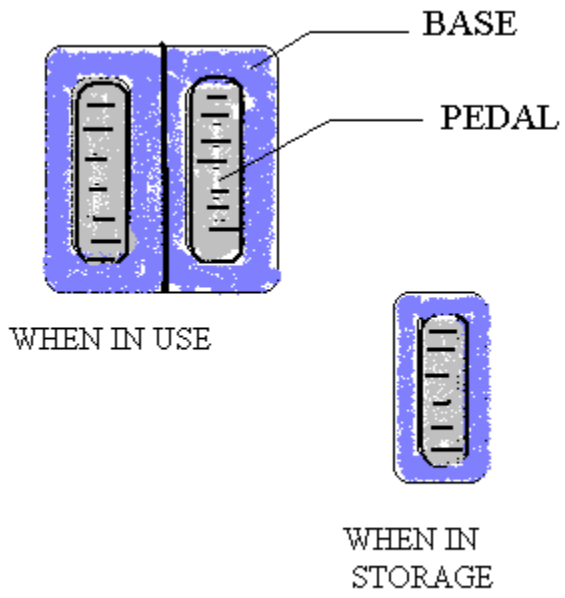


Figure 5.8. Diagram of Tromped design Option III.

5.5.4 Tromped Version 2, Option IV

The fourth concept or design was one of a slipper or shoe. The toe of this shoe permanently positioned at a higher angle than the heel, due to the spring positioned beneath the toe area (refer to Figure 5.9). The user would slip his/her foot into the shoe and press down with the ball of the foot. The base of the shoe could be manufactured from rubber and the shoe itself from a material such as polyester. Option IV could be

stored in an overhead cabin and be marketed by the airline companies. This option could also be offered to the individual traveller who could carry it on board the aircraft and store it in hand luggage when not in operation.

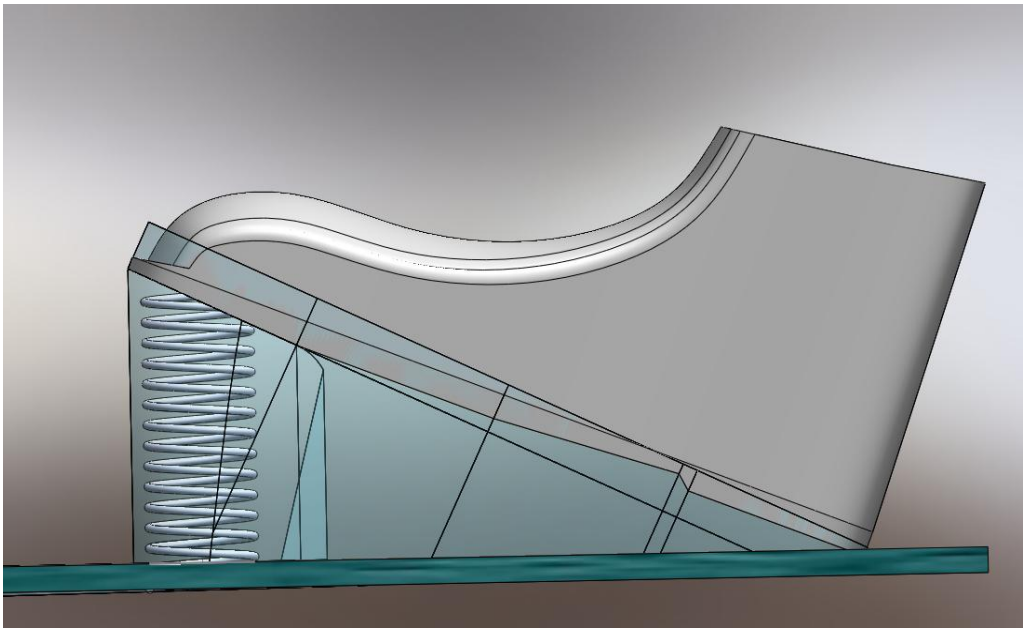


Figure 5.9. Diagram of Tromped design Option IV.

5.5.5. Summary

Tromped design version 2, (Figure 5.7) was considered for use in Option I and Option II. The difference between the two was the method of incorporation into the aircraft fixtures and fittings. Option I was to be incorporated into the seat tracking of the floor, with Option II being attached to the bar which runs under the seats. Design Option III (Figure 5.8) and IV, the Tromped shoe, (Figure 5.9) were designed to be stored in the overhead bins of the aircraft when not in use. It was decided, that the Tromped Option II, be manufactured in prototype form. Further haemodynamic assessments using the Air Plethysmograph with another group of ten healthy volunteers would be conducted.

5.6. Manufacture of the second prototype

A streamlined, light weight version of option II was produced. The shape of both the pedal and the base were modelled on the shape similar to that of a shoe. This reduced the amount of material used so that the finished prototype was both compact and light.

The second Tromped prototypes were designed in 3D and then machined by the Computer Numerical Control (CNC) system. This is "…the automated control of machine tools by a computer and computer program." (Mattson, 2002, p.2). A CNC Vertical Milling machine was used to produce the undersides of the two bases and two pedals after input of a set of instructions into the CNC machine. These instructions were in the form of Numerical symbols (which represented the dimensions of Demonstrator A (DA) and Demonstrator B (DB), the types of tools required to manufacture the devices and choice of coolant (Thyer, 1991; Mattson, 2002).

Two prototypes of differing shoe lengths were designed, to be tested using springs of the same compression value (Figures 5.10 and 5.11). The two prototypes were labelled DA and DB. DA had the larger dimensions of the two demonstrators. Both demonstrator base A and B were made from standard aluminium alloy sections of depth 20mm, width 100mm and length of 600mm. The Tromped pedal bases were made from standard aluminium sections of depth 10mm, width 100mm and length 600mm. The upper plates of both bases A and B and upper plates of pedals A and B were cut out from 3mm deep sheets of Aluminium T4 2024. Sixteen wedges were made from these sheets of aluminium T4 2024 and a hole was drilled in each angle which coincided with the holes drilled in the bases of the two Tromped bases and the two pedal bases. The bases of the Tromped demonstrators were jointed to their upper sides and the pedal bases to the upper sides with self tapping screws. The base and pedal were joined by means of a flap hinge

at the rear end and by the spring at the front edge. Finally a slip proof material (with a sticky underside) was cut out in the shape of the pedals and stuck to their surfaces.

Figure 5.10. Prototype DA and DB.

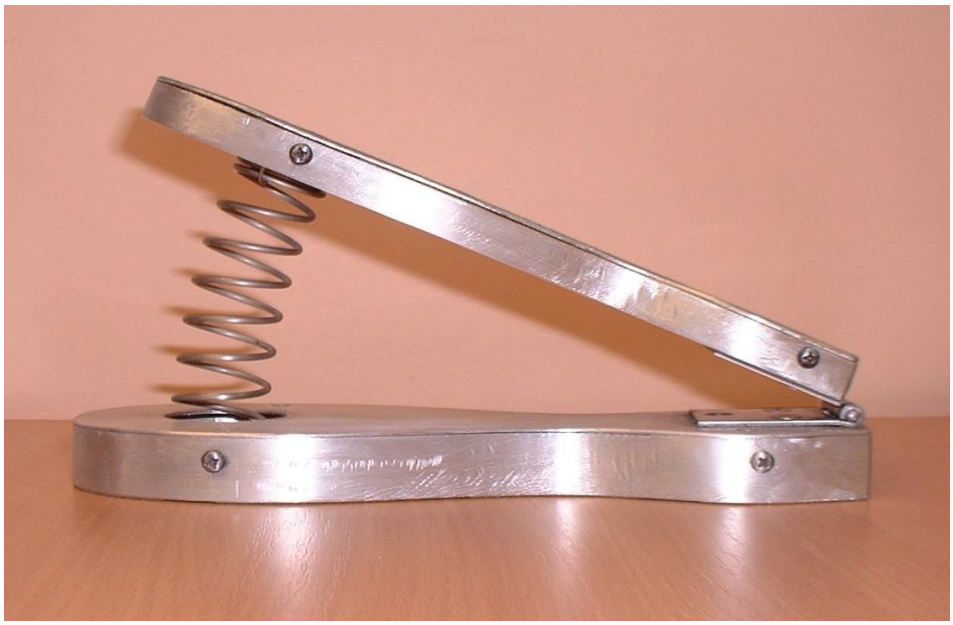


Figure 5.11. Side view of Prototype DA

The demonstrators each consisted of one pedal and base so that it and the spring could be assessed. DA was 242mm long and 100mm at its widest part. The pedal of DA was 230mm long by 80mm wide. DB was 220mm long and 90mm at its widest part. The pedal of DB was 205.5mm long by 85mm wide. As the revised design (Version 2) is smaller in length than the first prototype demonstrator (Version 1), this necessitated a different spring position. The demonstrators of differing dimensions were produced and fitted with one spring each with the same characteristics, to determine if a smaller pedal would have any implications on the EVF and RVF produced. Both springs were positioned 30 mm away from the front edge of the base and pedal. The correct spring characteristics for DA and DB were then determined (section 4.7.3).

5.7. Springs

A spring is defined as an "*elastic body which has the primary function to deflect or distort under load, and to return to its original shape when the load is removed."* (SAE, 1996, p. 131).

5.7.1. Air Springs

Air Springs consist of a contained column of air placed inside an elastomeric bellows or a sleeve. The sleeve or bellows buffer the cyclic motion and provide isolation against vibration. Air springs can be used as primary suspension springs or as a secondary component inside a coil spring.

Advantages of Air Springs over air cylinders or other types of springs:

i. Lower cost than a pneumatic cylinder with the same or nearly the same capabilities

ii. more compact as the minimum height is generally less than the available stroke

iii. Air Springs lack seals or guides and as a result they can be installed more easily than other springs

iv. No form of lubrication is required and so it is a clean operating system with little maintenance required

v. As air springs are designed without seals, there is less friction generated than other forms of springs

vi. An air spring can survive abrasive and corrosive environments better than other springs which require some form of sealing

("About Air Springs" 28/01/04).

5.7.1.1. Air Spring limitations

During flight there is a reduced barometric pressure experienced within the interior of the aircraft cabin as previously described (section 3.16). As an aircraft takes off the cabin air pressure decreases, resulting in the expansion of gases, which could have extreme effects upon air springs. Gases can expand as much as 35 percent within a pressurised aircraft cabin of interior altitude of 2438m (Hinninghofen and Enck, 2006). When the aircraft descends for landing, the cabin air pressure increases so gases will contract (WHO, 2005). Thus, for these reasons air springs were not considered.

5.7.2. Disc Springs

Disc Springs (Beleville Washers) can be made from pretempered material. "They can support heavy loads with small deflections" (Carlson, 1980, p. 121). Belville springs were considered for use in the Tromped Footrest, as the spring parameters (free length,

101.6mm) of DA could not be suitable due to the smaller size of the footrest prototypes (dimensions 145mm ×110mm). DAs pedal was 232mm long compared to 90mm of the Tromped footrest pedal.

Disc springs were investigated for their viability. Eventually which disc spring would produce the required load was determined. The parameters of a Disc Spring are explained below (SAE, 1996, p. 325):

C = Spring Rate, N/mm

D = diameter, mm

E = modulus of Elasticity N/mm^2

F = Force/Load (N)

H = Dish free height, mm

L = overall height = T+H, mm

N = number of Load Cycles,

n = number of disk springs in parallel

I = number of disk springs in series

R = diameter ratio $\frac{D_e}{D_I}$

T = material thickness

W = Energy Storage Capacity

S = Deflection, mm

A Disc spring of D_e = 0 6mm, D_I =3.2mm, T = 0.30mm, Cone Height = 0.15mm, Total Height = 0.45mm, would create a force of 119N if 75 per cent deflection was chosen. An order for 18 of these springs was made, however the smallest order which would be accepted was for 100 of these springs. Upon procurement, it was obvious that these springs were too small to be attached to a pedal which was designed to compress a spring. The sophisticated set up of Disc Springs in series or parallel, within a cylinder and tests to determine their feasibility would have provided no gain in FRDVT knowledge. Therefore it was decided that another form of spring or a different compression spring was the only viable option. Advice was given from a spring

manufacturer to continue using a compression spring of a shorter height for the Footrest Tromped.

5.7.3. Compression Springs

Four different Stainless Steel compression springs were procured (refer to Table 5.4). Six springs with the same physical characteristics were procured and one supplied to Lufthansa Technik for testing. A Chatillion Digital Force Gauge recorded a force of 94.31 N to deflect the spring by a height of 63.39 mm. This differs from the spring used in D3 (Table 5.1), which required a force of 80.97N. Two possible reasons for this difference in compression may exist. Firstly, theoretical equations to determine the deflection height mathematically were conducted. Secondly a certain degree of use or wear and tear may have affected the original spring compression value. It is important to note that the original spring may have been used in an aircraft engine prior to use in the Tromped. Provided it was previously used in its elastic range, this would have no bearing on performance.

Compression Springs made from round wire are the easiest spring to design and produce. They are reliable, and have high fatigue properties. As compression springs have an automatic stop, once they are fully compressed, this prevents over-deflection, limiting stress levels (Carlson, 1980). Different spring materials are used in different environments such as high or low temperatures, vibration, shock loading, high endurance, nonmagnetic capabilities, low hysteresis and a variety of corrosive surroundings (Carlson, 1980).

5.8. Footrest Tromped prototype

Although Tromped version 2, option II, was produced and favourably assessed replicating normal venous haemodynamics in the seated position (Sections 6.2 and 7.2), the design was considered too cumbersome for use on board aircraft. Therefore this option was discounted on the basis of its size related to the bar running beneath the seats. The three seats joined together have a combined width of approximately 1447.8mm. However the bar, which runs underneath the three seats, is only 1219.2mm in length, ending midway of the inner seat, so that it is not long enough to reach the aircraft frame. This bar has two different dimensions varying in thickness, which seems to depend on which seat it is situated under and at which end of the aircraft it is placed. The slimmer bar has dimensions of 10 mm in width and 26mm in depth while the thicker bar has dimensions of 20mm wide, 30 mm deep.

A disadvantage of this design option was the design features of the connecting bar from the Tromped to the seat cannot be standardised. Also the floor width of the aisle seat is smaller in size compared to the middle and window seat and so the aircraft seat legs could also be a factor in determining the actual size of the exercise machine. For these reasons, option II was not considered viable for use on board an aircraft and further thought was expanded into making the Tromped aircraft friendly.

Upon acquisition, it was evident that the free length of the compression springs (101.6mm) used in the first two Tromped prototypes (Figure 5.7) would not be feasible for the third design (Figure 5.8). Thus four springs of smaller dimensions, (Table 5.5) were chosen and sourced.

Table 5.5. Compression spring parameters used in the Footrest Haemodynamic Assessment.

Wire diameter (mm)	Outside diameter (mm)	Free Length (mm)	Minimum Working Length (mm)	Approx. No. of working coils	Load at minimum working length (N)	Rate (N/mm)
1.6	11.6	27.0	13.2	5.5	141.32	10.13
1.6	14.1	36.0	14.1	5.5	112.73	5.19
1.6	14.1	53.5	20.1	8.5	112.73	3.37
2.0	22.0	41.0	13.6	3.5	132.34	4.85

Source, SpringMasters® Spring Directory.

5.9. Material selected to manufacture the Tromped Footrest

For the final Tromped prototype, various materials were investigated to determine which would be best suited for operation in an aircraft environment. Therefore materials which are currently used in the manufacture of aircraft were investigated.

Acrylonitrile Butadiene Styrene (ABS) material was chosen to produce the Tromped footrest prototypes. Acrylonitrile imparts chemical resistance and rigidity, Butadiene ensures the product has impact strength, toughness and is resistant to abrasion, while Styrene contributes to easy processing. Given this balance of properties, ABS copolymers are used increasingly for the manufacture and production of many industrial and domestic products.

ABS is a ductile thermoplastic material, which has the advantage of high impact strength when compared to other thermoplastics, especially in low temperature conditions. One of the material's unique properties is its ability to retain high levels of impact strength at sub zero temperatures. The material exhibits, toughness, resilience, high impact strength, good chemical resistance, non toxicity and it is taint free.

Thermal expansion of ABS is 10.1×10^{-5} m/m °C. All thermoplastics expand at a greater rate than metals. So at the design stage allowance must be made for this. The

working temperature range of ABS is -40°C to +70°C. So, with an increase in temperature, the rigidity of the material will decrease (ABS Material), http://www.eurapipe.com.au/cd/Eurapipe/Material_page1_files/image002.gif

5.10. Manufacturing of the Tromped Footrest

An aircraft footrest (Figure 6.12) was obtained prior to design of the Tromped footrest. Elements such as its size, shape and material type were noted and it was decided to use ABS material for the production of the Tromped footrest.

Figure 5.12. The aircraft footrest.

ABS was acquired in sheet form (material measurements 20mm × 610mm × 1220mm). This sheet of material was used to produce the Tromped footrest prototypes, generated from the AutoCAD diagram of the Tromped Footrest (Appendix D). The underside of both the base and pedals were made separately and had a depth of six mm. The dimensions of the upperside of the base were 290 × 110 × 20 mm. The upperside base

was hollowed out to reduce the weight of the base and a centre web of thirteen mm width was incorporated into the design, for two reasons. Firstly, the APG® assesses blood flow in one leg at a time, thus the need for one foot pedal. Secondly, the centre web would help keep the centre bar in line with the screws, by cutting a hollow in it. Refer to Figure 5.13. to view the hollowed out prototype. So the Tromped footrest was cut in half, along the centre web, creating two prototype bases. The dimensions of the footrest prototypes then became 145mm × 110 × 20 mm.

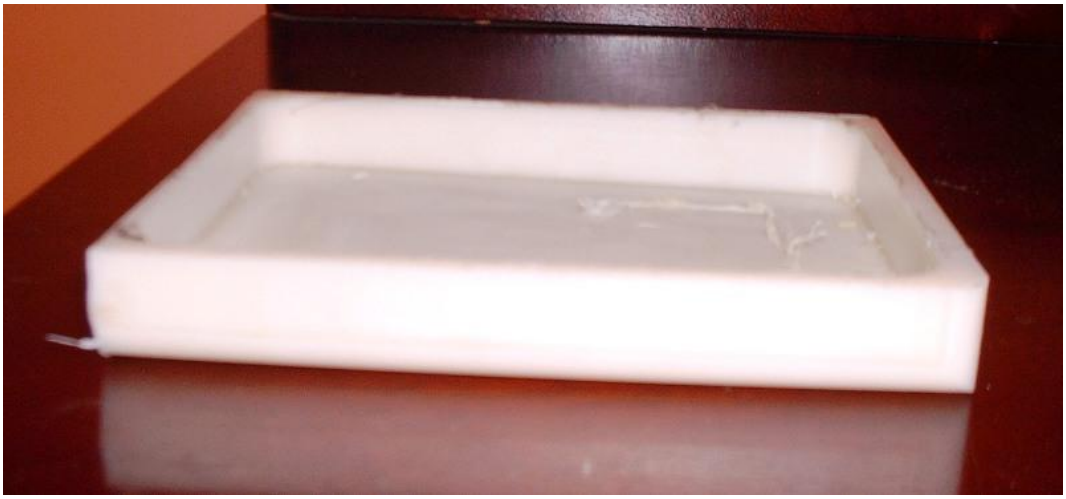


Figure 5.13. The upperside of the hollowed out Footrest prototype.

The design specifications of the Tromped footrest (295 ×115), automatically limited the size of the pedals (90mm × 90mm). This meant that only the ball of the foot would actually compress the pedal (not the heel) unlike the previous two assessments where the foot as a whole was used. As this was the case, the Tromped footrest pedal was not designed to replicate the shape of a foot. Each of the four springs (of different dimensions) were wire locked onto four different aluminium plates of dimension 50 × 50mm (Figure 5.14). It then became apparent that two of these springs would have to be attached to the underside of the base. As the free length of both these springs (53.5mm

and 41mm) were too long to be attached to the upperside of the base and remain in line with the footrest pedal.

Thus the position of these two springs and their mats was determined. The spring of free length 41mm, outside diameter 22 mm was placed on the underside of Prototype I. The "would be" height of the pedal was then determined with the spring positioned at different points on the underside of the base. It was decided that the front edge of this spring (free length 41mm) be positioned 20 mm from the outside front edge of the prototype. To make this possible a square of dimension 50mm × 50mm was cut out of the upperside of the base. Clearance of five mm completely around the spring was cut out of the upperbase so the spring would not foul it.

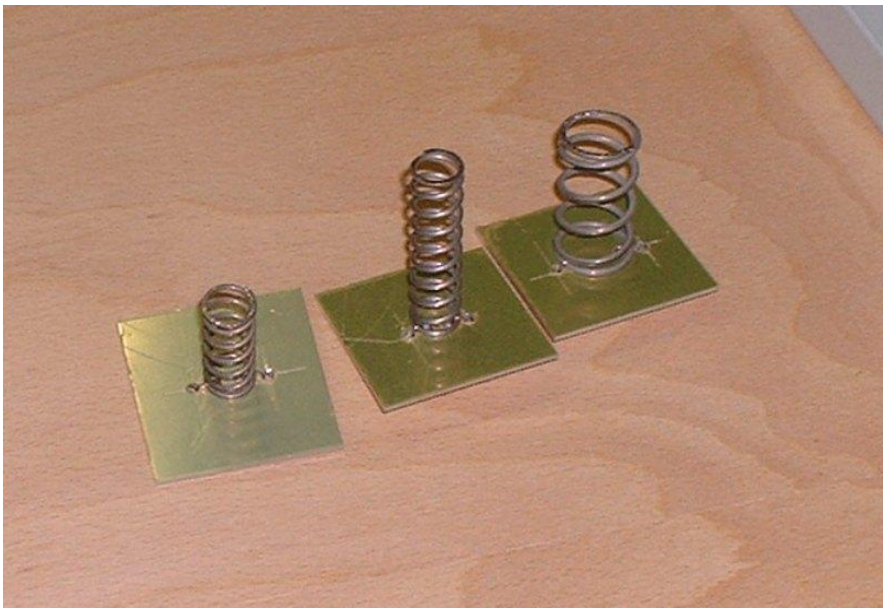


Figure 5.14 Springs wirelocked onto their mats.

The spring of free length 53.5 mm and outside diameter of 14.1 mm also had to be attached to the underside of the base. As this spring had a smaller outside diameter to that previously discussed, the aluminium base plate was reduced in dimension from

50mm × 50mm × 1.5mm to 30mm × 50mm × 1.5mm. Then the spring was positioned 15mm from the outside front edge of the prototype II. The remaining two springs had free lengths of 27 and 36mm respectively, which did not hamper the compression of the foot pedal, when attached to the upperside of prototypes III and IV.

Two test rigs were designed and produced, to contain two of the footrest prototypes (Figure 5.15). As the dimensions of the assessment room were unknown at the time, this seemed a practical option as a bed, aircraft seats and the APG® equipment were to be stored together with the Tromped Footrest rig, some room for manoeuvre would be required.

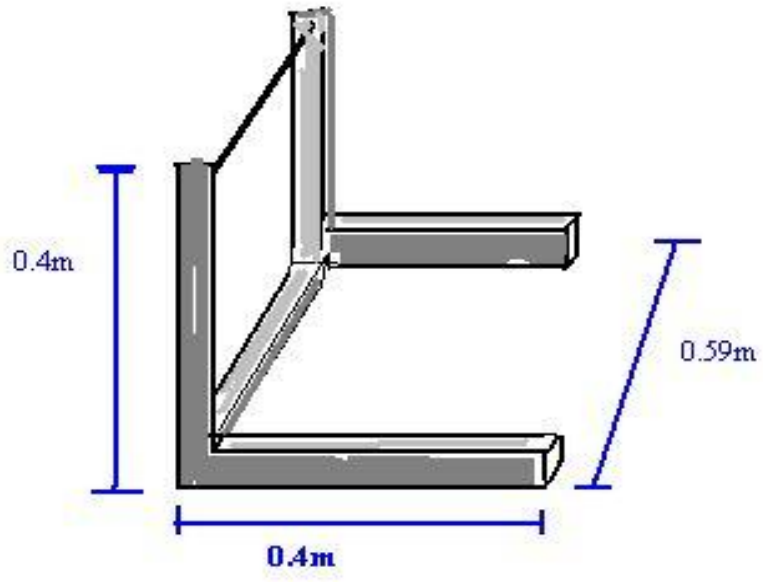


Figure 5.15. Footrest Test Rig Dimensions.

The aircraft footrest (Figure 5.12) had a solid bar running through its centre, which was attached at each end to supportive bars. This design permits the footrest to pivot and the actual device to be moved underneath the seat when not in use. It was decided for the purposes of the medical Footrest assessment (which replicated the seating arrangements

on board a commercial aircraft) it was sensible to achieve this pivot with the Footrest prototypes.

Bars of two differing dimensions were required, to replicate the design of the footrest. Mild steel bars to the following specifications were used:

i. [6mm × 200mm] ×4

ii. [20mm × 4mm × 250mm] × 8.

The centre bar produced had the dimensions 6mm × 157mm. These were then threaded.

The side bars of the Tromped footrest machined had dimensions of 20mm × 4mm × 250mm. The side bar, when inserted onto the centre bar of the rig, the footrest swung constantly on the test jig, hampering test results due to the sensitivity of the APG®. Smaller clearances eliminated this problem.

It was decided that the Tromped footrest, be designed so that it would constantly be at an angle of 60° to the vertical, for ease of use. This choice of inclination was reached after assessing the combined effect of spring free height with perceived passenger comfort and ease of operation. So an angle bar was cut and then welded onto the side bar of the footrest and then screwed into the footrest base. Spacers were attached to the spring plates to ensure that they would remain level once attached to the footrest base. The upper and undersides of the Footrest bases were attached by two five mm countersunk nylock nuts. The base and pedal were attached at one end by a hinge and the other by wire locking the spring to the underside of the pedal, as shown in Figure 5.16. An AutoCAD version of the Tromped Footrest is shown in Figure 5.17.

Following the final assessment Footrest 1 and 2 were detached from the test rig to determine their individual weight. Both footrests were sent to Lufthansa Technik Aermotive Ireland and weighed using an Adventurer Ohaus Weighing Machine. The

weight of Footrest 1 and Footrest 2 (when detached from their side bars) were determined as 0.459kg and 0.4428kg respectively.

As previously determined (section 5.4) a Boeing 757 can have 41 rows of seats. Thus the additional weight of the spring and pedal to the aircraft is 36.97kgs.

Figure 5.16. Tromped Footrest and Rig

Figure 5.17. The Tromped Footrest

5.10.1. Reasons for integrating the Tromped into the aircraft footrest

In conclusion, there were five reasons for integrating this device into a footrest:

i. Not to hamper foot space as this could hinder evacuation time and safety of passengers (section 5.13).

ii. Integration into a standard piece of equipment, previously approved by EASA CS-25 and CFR-25 (which are discussed in the following sections).

iii. Two springs and two foot pedals of a light weight material, added to each footrest, should not significantly affect the aircraft gross take-off weight (AGTW).

iv. The user would be required to place the ball of the foot on the pedals, with the arch of the foot resting on the bottom edge of the footrest. The movement then produced by compressing the footrest pedal should increase the plantar flexing of the foot, which empties the proximal calf pump into the popliteal and femoral veins (Gardner and Fox, 1989) in

comparison to when the whole foot is placed flatly on either of the first two prototype designs. Venous return can be increased by the flattening of the plantar arch, which results in the "lengthening of the venae commitantes of the lateral plantar arch" (Sochart and Hardinge, 1999, p.703).

v. For smaller passengers whose legs are too short to reach the ground, it will alleviate the unwanted pressure which is exerted on the back of the knees (Quigley *et al.*, 2001, p.20).

5.11. Definition of a Medical Device

Prior to assessment of the Tromped and Mediven Travel Stocking Experiment, an application to the Medical Ethics Committee in Beaumont Hospital (site of initial assessment of the Tromped DA) was made. This highlighted the need for classification of the Tromped. Recommendations by the committee (Appendix E) were made to contact the Irish Medicine Board (IMB). The assessment protocol, specifications and photographs of the Tromped prototype TJA, were sent to a Doctor Niall MacAleenan, the medical assessor of the Medical Devices Department of the IMB. He ruled that the Tromped would be classified as a medical device "as its intended use includes medical claims" (Appendix F) and that the Medical Devices Directive (93/42/EEC) and the Statutory Instrument SI 252 of 1994 (Annex I) of the European Communities (Medical Devices) Regulations 1994, be referred to and used as a template to conduct the research. A medical device is defined by the Council Directive (93/42/EEC) concerning medical devices as *"...any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:*

i. *diagnosis, prevention, monitoring, treatment or alleviation of disease,*

ii. *diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*

iii. *Investigation, replacement or modification of the anatomy or of a physiological process,* (93/42/EEC, Article 1, p.4.).

As the Tromped is aimed at the prevention of a disease i.e. FRDVT by replacing a physiological process i.e. venous return it would appear to be a medical device by definition.

Doctor MacAleenan's ruling concluded that as the development of the Tromped (in its current state) is for the purpose of a PhD thesis rather than commercialisation, this research be classified as **non-commercial clinical research of a non-CE marked device** and so therefore no further applications to the IMB would be required. If patents are sought in the future, the European Communities (Medical Devices) Regulations 1994 will be consulted.

The final prototype, the Tromped Footrest is designed so that it can be incorporated into an aircraft. This too will be classed in the same manner as a medical device for the purpose of the Tromped Footrest experiment (Chapter 8).

5.12. Medical Regulations and Aviation Requirements governing the "commercial" Tromped

Article 2 of the Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, refers to entering the medical device into the market for which it is intended (p5 of 37). It basically states that no member state of the EU should act to prevent this occurring, once use of the device will not affect the health of patients or their safety. The device must be properly installed, maintained and used in the manner for which it is

designed. The Tromped footrest prototype was intended for use on board commercial passenger aircraft. Therefore EASA's, Certification Specifications for Large Aeroplanes, CS-25, and the FAA's, Code of Federal Regulations (CFR) Part - 25, are all applicable in terms of installation and use of the Tromped, in compliance with large aircraft requirements.

EASA, CS-25.625 and CFR-25.625, Fitting factors (d), For each seat, berth, safety belt and harness the fitting factor in CS 25.785 (f)(3) apply plus AMC 25.561 (c) for the strength requirements of local attachments of each seat to the structure.

CFR-25.785 is consistent with CS 25.785 (b), which states: *"Each seat, berth, safety belt, harness, and adjacent part of the aeroplane at each station designated as occupiable during take-off and landing must be designed so that a person making proper use of these facilities will not suffer serious injury in an emergency landing as a result of the inertia forces specified in CS 25.561 and CS 25.562"*.

5.13. Application to the Tromped Design

EASA CS-25.561 is concerned with emergency landing conditions of an aircraft. If the aeroplane is damaged in emergency landing conditions on land or water, it is essential that the design protect each occupant under the following conditions.

The structure must give each occupant every reasonable chance of escaping serious injury when proper use is made of seats, belts, and all other safety design provisions. Equipment, cargo in the passenger compartments and any other large masses, must be positioned so that if they break loose they will be unlikely to:

i. Cause direct injury to occupants;

ii. Penetrate fuel tanks or lines or cause fire or explosion hazard by damage to adjacent systems; or

iii. Nullify any of the escape facilities provided for use after an emergency landing.

When such positioning is not practical (e.g. fuselage mounted engines or auxiliary power units) each such item of mass must be restrained under all loads up to those specified in subparagraph (b) (3) of this paragraph, which states that the local attachments for these items should be designed to withstand 1·33 times the specified loads if these items are subject to severe wear and tear through frequent removal (e.g. quick change interior items).

Also seats and items of mass (and their supporting structure) must not deform in any manner that would impede subsequent rapid evacuation of occupants (See IAMC 25.561(d).

EASA CS-25.562 is concerned with dynamic conditions during emergency landing**.**

Part (b) states: With the exception of flight deck crew seats, each seat type design approved for occupancy must successfully complete dynamic tests or be demonstrated by rational analysis based on dynamic tests of a similar type seat, in accordance with each of the following emergency landing conditions. The tests must be conducted with an occupant simulated by a 77kg (170 lb) anthropomorphic, test dummy sitting in the normal upright position.

5.14. Annex 1 the Council Directive 93/42/EEC

5.14.1. General Requirements 1 of Annex I

Essential requirements I. General Requirements I, of Annex I, of the Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, stipulates that a device "…when used under the conditions and for the purposes intended…" will not affect the safety of

its users, and if there are any risks these must be offset against the advantages of its use to the users (in this case airline passengers). It is required, whether there are inherent risks involved, and that the device must have a "high level of protection of health and safety" (93/42/EEC, Annex 1, p.14).

Section 2 states that manufacturers of the said device must ensure that they achieve the subsequent stipulations in the following order:

i. Eliminate or reduce potential risks as much as possible by ensuring a safe design and a safe production process);
ii. Ensure sufficient protection measures are incorporated to raise an alarm or highlight the risks (if any) that cannot be eliminated during use;
iii. Those users are notified of any outstanding risks due to any shortcomings of the protection methods incorporated into the design.

Section 3 points out that the devices design, production and packaging, must be proven to live up to the standards and performance levels as set out by the manufacturers Medical Devices Directive (93/42/EEC). Section 4 of Annex I is concerned with any stresses which can occur during the normal use of the device for which it is designed, inflicting injury or affecting the user or any person in its presence during its use. Section 5 of Annex I relates to the transport and storage of the medical device. It requires that devices "characteristics and performances" during its use will not be adversely affected. This requirement would apply firstly to the transport of the Tromped from its place of production to the aircraft intending to provide this device. Secondly, it would also apply to when the Footrest Tromped would be integrated into the aircraft seats, under which it is designed to be stored, when not in use by passengers.

Section 6 of Annex I is similar to general requirements section 1, where it states that any "undesirable" side-effect of the device during use be weighed against its purpose. In the case of the Tromped, its purpose is to recreate the physiological process of ambulation in the seated position and the possibility of it causing harm is negligible during proper use.

5.14.2. Part II, Requirements regarding Design and Construction

This section is concerned with the chemical, physical and biological properties of the medical device.

Section 7.1., Part II of Annex I, requires that specific attention be spent on:

i. The type of materials chosen, especially if they have toxic or flammable properties.

ii. Ensuring that the medical device's materials are compatible with biological tissues, cells and body fluids, if its intended use means the device will come in contact with any of the above mentioned. As it was used external to the body, the Tromped Footrest is designed to be used by passengers while wearing footwear. If a passenger were to remove his/her shoes and/or stockings, contact with the ABS material, would not provide any health problems.

Section 7.2. of the Medical Devices Directive (93/42/EEC) requires that the risk of contaminants or residues being passed onto any person required to transport, store or use the device, be minimized through its design, manufacture and package procedures.

With ABS there is no risk of any toxic metal substances and it is also taint free (http://www.eurapipe.com . Section, 7.3., states *"The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances*

and gases with which they enter into contact during their normal use or during routine procedures..." (93/42/EEC, Annex I, p. 15). The Tromped footrest would be located in a pressurised aircraft cabin, replicating an altitude between 1,524m and 1829m (5-6000ft) during flight (Bagshaw, 1996). Hence ABS would not react negatively to oxygen, carbon dioxide or nitrogen. Section 7.5 of Annex I stipulates a medical device must be designed and produced so that a risk of any substance leaking from the medical device is kept to a minimum. It is a recommendation of section 7.6 that, if a risk is apparent that a substance could interfere negatively with the device once placed in its intended environment, this risk must be eliminated as much as possible. A spring shield could be placed around the springs, so that nothing could become lodged in either the springs or under the pedals, hindering its efficiency and/or life span. Section 8, is concerned with Infection and microbial contamination. Part one of section 8, states that the design and production of the device must ensure that the risk of infection to the patient, user and/or third parties be eliminated or reduced as much as possible. The medical device should allow ease of handling and minimise risk of contamination by the patient or vice versa. The ABS Tromped Footrest would not have a higher chance of being contaminated than the other materials used on board an aircraft. Also passengers wearing shoes during its use would reduce the risk of cross contamination.

Section 9 is concerned with construction and environmental properties i.e. the operation of the device in the environment for which it is intended for use. If the device is designed in such a way that the use of other devices or equipment in conjunction with the medical device is required then any connections between the devices must be safe and not impair the efficient operation of the combined devices. If there are any restrictions these must be clearly visible on the label and in the instruction booklet.

The Tromped was integrated into a standard piece of aircraft furniture. Its design is modelled on a Boeing 757 footrest, (Figure 5.12).

Section 9.2 requires that:

i. "the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features" be reduced or minimised.

ii. If a risk of a magnetic field, electrical fields, electrostatic discharge, temperature or any variations in pressure or acceleration exist, these must be reduced if possible.

The Tromped was ergonomically designed to minimise risk of injury to aircraft passengers. The Anthropometric study (2001, p. 63) states *"the design of any footrest device might usefully incorporate a capability for a rocking motion…This would allow the passenger to undertake optional and short periods of limited leg muscle 'exercise', which might improve circulation and help to minimise factors causing DVT's.* The study also recommends that the footrest be moved under the seat not to hamper access or egress. Section 9.3. relates to the design and manufacture of a device, which minimises the risk if any, of a fire or explosion occurring whilst in use.

Section 10 of Annex 1, "requirements for devices with a measuring function" also applies to the Tromped footrest, as a counter device to record the number of pedal compressions would have been incorporated into its design, if proven to be efficient at creating substantial venous return. Part one of this section, imposes a requirement that devices with a measuring function, or in the Tromped's case a measuring unit, will provide accuracy and any limits of accuracy must be stated by the producer of the medical device. Section 10.2 states that the "measurement, monitoring and display scale must be designed in line with ergonomic principles, taking account of the intended purpose of the device"

(93/42/EEC, Annex I, p. 16). If the footrest prototypes were as effective as DA when used on a level examination couch then a recommendation of at least 10 compressions of the Tromped Footrest pedals, every half hour, to be recorded on the counter, so that adult passengers could calculate the preferred number of compressions, to prevent venous stasis could be made, as six plantar flexions is sufficient to ensure venous emptying (Needham, 2005). Subsequent testing involving springs of differing resistance is required before this recommendation could be made.

Any measurements made or recorded by a measuring device, must be expressed in legal SI units, according to section 10.3 of Requirements regarding design and construction, Annex II of Council Directive 93/42/EEC, which conform to the provisions of Council Directive 80/181/EEC.

Section, 12, entitled "Requirements for medical devices connected to or equipped with an energy source" is not applicable. The Footrest Tromped will not be powered by any electronic, internal or external source during use, solely by passenger feet. Protection against mechanical and thermal risks, Section 12.7., is applicable to the Tromped Footrest medical device. The device was designed and manufactured so that the user would be protected from resistance and in stability of the device, also taking into account any moving parts, which in the Trompeds case include the spring and foot pedal. Section 12.7.2. requires that both the design and manufacture of the medical device must ensure that a risk of vibration through product use, (unless vibrations are "part of the specified performance") be minimised (Medical Devices Directive (93/42/EEC, p.18). Use of the Tromped does not create vibrations of any kind. Section 12.7.3. requires that the device emits low noise levels, the Tromped will not create noise during its use. Section 12.9 requires that any operating instructions provided on the device must be understandable to the user and/or patient. All participants of the Tromped Medical assessments were given

guidelines on how to use the device prior to the experiments taking place. As at this time, the device is not planned for commercialisation and so Section 13 information supplied by the manufacturer, is not applicable to this research.

5.14.2.1. The Tromped Material

If the commercial footrest Tromped was undergoing certification for approval under CS-25 it would have to undergo dynamic testing or be demonstrated "by rational analysis" to be safe under emergency landing conditions.

The Tromped footrest is manufactured from ABS material, has a spring which is wire locked to the pedal and so will not be the source of any fire while in use. ABS material is not toxic and has good chemical resistance (www.eurapipe.com). The Tromped Footrest was designed with ABS material to ensure minimum weight properties. Also the material's safety and rigid thermoplastic properties were considered, with airline passengers in mind.

5.14.2.2. The Tromped Spring

When not in use, generally aircraft footrests are pushed back under the seats in front of the user, so they do not hamper ingress or egress of passengers. Similar requirements would be necessary for the Tromped Footrest when not in use plus a bell like covering would be required to cover the spring to the underside of the pedal preventing access. The Tromped Footrest cannot through normal use affect the safety of airline passengers. As previously stated a shield could be used to prevent fingers or clothing becoming stuck within the spring.

5.14.2.3. Footrest Attachment

Possibly through constant use the bolts and screws which maintain the Tromped footrest in one piece may exhibit loosening. If the Tromped footrest had been proven successful at recreating normal venous haemodynamics in the seated position in all groups of participants, long-term testing on both the springs and the device would have been conducted.

CHAPTER 6

HAEMODYNAMIC ASSESSMENT I

6.0 Introduction

This assessment was conducted to determine the haemodynamic efficiency of two prototype designs when used in the seated position. Both of these prototypes were developed with the ultimate aim of preventing venous stasis during flight. Hypothesis: to determine if Demonstrators A and B (of differing lengths) achieve adequate venous emptying.

6.1. Air Plethysmography

Once the volunteer stands up and maintains the limb in one position without any muscle contraction, *"...arterial inflow to the limb will steadily fill the veins to maximal capacity at full venous pressure to form a continuous column of blood from the foot up to the level of the heart"* (Tibbs, 1992, p.4).

Air Plethysmography, as previously stated in section 4.5.1, is used to determine EVFs and RVFs, both of which are sensitive indicators of the venous pump function (Nicolaides and Sumner, 1991), with the RVF correlating closely with ambulatory venous pressure measurements (Christopoulos and Nicolaides, 1994). In diseased limbs ambulatory venous pressure remains high as the calf muscle pump function inadequately functions in conjunction with the occurrence of reflux due to valveless deep veins (Tibbs, 1992). The ratios VFI, EVF and the RVF are all reproducible units irrespective of the fact that the venous volume (VV) may vary day to day as it is dependent on venous tone, which is itself variable. Therefore, Air Plethysmography is an ideal test to determine the

effectiveness of the Tromped compression values, constantly producing both a sufficient EVF and RVF (Nicolaides & Sumner, 1991).

Table 6.1. APG Assessments abbreviations key

VV	Venous Volume	
90%VV	Ninety percent of the venous volume	+
VFT	Venous Filling Time	+
VFI	Venous Filling Index	-
EV	Ejection Volume	+
EVF	Ejection Volume Fraction	-
RV	Residual Volume	+
RVF	Residual Volume Fraction	-
TT	Tiptoe	
DA, DB	Demonstrator A, Demonstrator B	
W	Walking	
+	Measured from APG tracing	
-	Calculated derived values	

6.2. Haemodynamic Assessment I

6.2.1. Patients

Ten healthy volunteers recruited by advertisement posters displayed on DIT notice boards, in Bolton Street, February and March of 2005. All healthy males and females between the age of 20 to 70 were eligible. Exclusion criteria included varicose veins or previous surgery, previous DVT and/or recent immobilization including travel of greater than four hours, within previous six weeks.

Five males and five females participated. Ages ranged from 20-68 years. Mean age was 38.7 +/-14.8. The procedure was explained and written informed consent was obtained.

6.2.2. Location

The experiment was conducted in a temperature controlled room of 20º Centigrade in the Non-Invasive Vascular Unit, Beaumont Hospital**.** This achieved equilibrium and

prevented vasoconstriction (Cole, 2001b). The pressure of gas was seven mmHg within the air chamber.

6.2.3. Researcher

The author, CC, was the investigator and performed the assessments under direct medical supervision.

6.2.4. Equipment

The equipment used for the purpose of this assessment consisted of the Air Plethysmograph machine, an examination couch, DA and DB. The couch was placed at a height of 468mm from the ground, in order to imitate the average height of a standard (economy class) aircraft seat, which varies from 457mm – 480mm (Quigley *et al.*, 2001).

6.2.5. Method

i. The volunteers were placed in the supine position, on an examination couch with the appropriate sized calibrated air chamber of the APG surrounding the calf of their right leg (Figure 6.1.). Venous volume was calculated in the seated position as the difference between the volume with the leg elevated in the supine position and the leg dependent in the seated position with the right foot placed on DA.

ii. The standard APG assessment, tiptoe (section 4.5.2) was performed and acted as the control. The EV and RV were measured in millilitres. These values were used to calculate the EVFs and RVFs in the standing position (section 5.6).

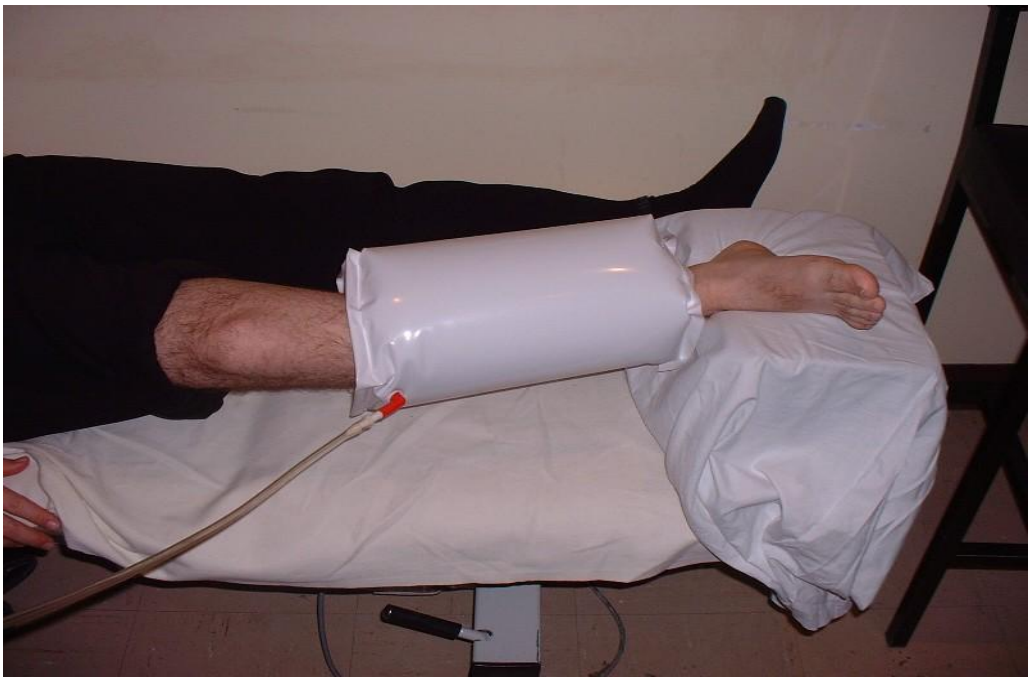


Figure 6.1. Participant wearing APG cuff with his right leg elevated.

iii. At the end of the standard assessment, the two demonstrators, A and B were investigated. In the supine position, once a steady baseline was recorded, the participants were then instructed to sit up on the examination couch and place their right foot on the pedal of DA (Figure 6.2). The increase in venous volume achieved by this postural change was recorded as the sitting venous volume.

iv. Again on achieving a steady baseline the participants were verbally instructed to fully compress the pedal and hold this position for five seconds and then release to the initial position with their foot resting on the uncompressed pedal. This achieved activation of the calf muscle pump and results in a decrease in venous volume equivalent to the EV. This manoeuvre was repeated until two similar EVs were recorded.

v. The volume remaining in the limb after compressing on the pedal of DA ten consecutive times is the RV and is measured as the difference between

the remaining volume and base line achieved when the participant returns to the supine position, with the leg elevated.

vi. The procedures (iii – v) were repeated with DB.

vii. All participants were then instructed to stand up from the examination couch and walk for two minutes in the assessment room, before returning to the supine position on the examination couch. The average EV and RV walking values were then recorded.

viii. The EVF and RVF achieved by DA and DB were then calculated as per standard assessment (section 6.6.).

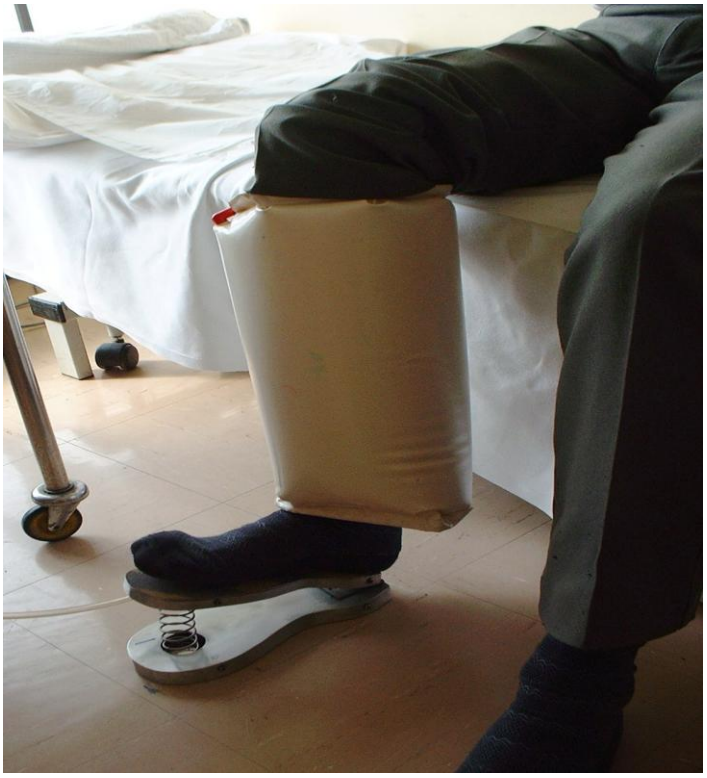


Figure 6.2. Volunteer with right leg resting on DA.

A Diagrammatic representation of the APG tracing conducted is shown in Figure 6.3.

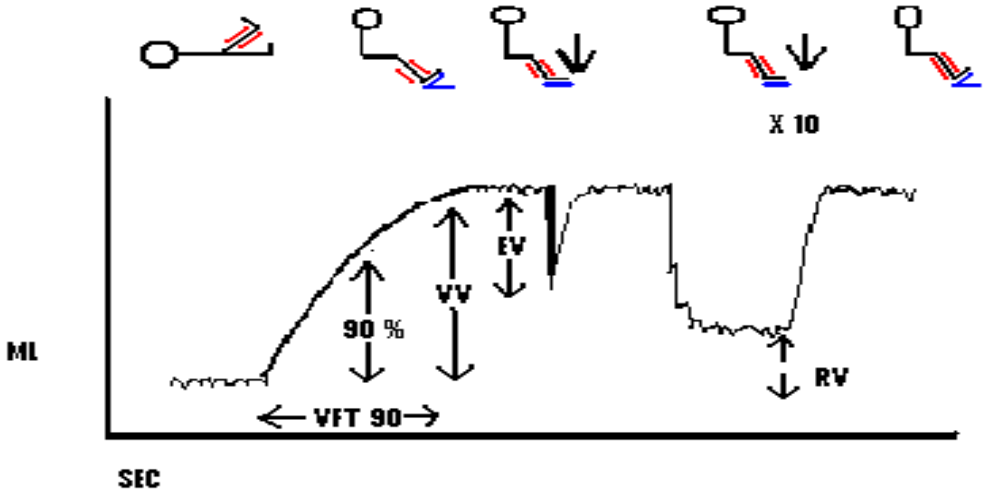


Figure 6.3. Diagrammatic representation of the Air Plethysmograph tracing during Tromped Assessment of Demonstrators (blue) in the seated position.

6.2.6. Statistical Analysis

The statistical analysis was carried out using two formulae (Reilly, 2000); the mean of each result was determined by using equation 4.7, for example by dividing the sum of all ten patients standing venous volume by the number of values. The standard deviation of each result was determined by using equation 4.8. The paired Student's *t*-test was used to determine statistical significance. Statistical significance was accepted at the 95% confidence level ($p \leq 0.05$). With the number of degrees of freedom being 18, the critical value of t is $\pm$ 2.101.

6.2.7. Results

For absolute and derived values obtained from each manoeuvre, of this assessment for each of the ten participants (Appendix G). Mean values are presented in Table 6.2.

Table 6.2. Results.

n=10. Mean age 38.7 +/-14.83		
Standing	Mean+/-Standard deviation	
VV (mls)	118.6 +/-31.05	
90%VV	106.74 +/-27.95	
VFT (sec)	178.75+ /-54.25	
VFI	.679 +/-.144	
TT EV (mls)	72.9 +/-17.98	
TT EVF (%)	64.075 +/-16.918	
TT RV (mls)	21.1 +/-16.04	
TT RVF (%)	16.89 +/-12.7	
Ave Walking EV (mls)	46.8 +/-20.05	
Ave Walking RV (mls)	22.8+/-14.83	
Sitting VV (mls)	107.7+/-31.45	
SITTING		
Mean +/- SD	**DA**	**DB**
EV (mls)	66.6+/-18.97	60.8+/-18.72
EVF (%)	63.05+/-10.62	58.05+/-11.49
RV (mls)	29.5+/-21.41	29.4+/-20.92
RVF (%)	24.83+/-12.75	26.1+/-17.56

The absolute results obtained from Part 1 of the study demonstrate that eight of the ten volunteers had normal VVs within the range of 80 to 170 mls (Bayes *et al.,* 1994). All ten participants had a normal VFI of less than 2ml/sec. Standing VV ranged between 70 and 166 mls, mean 118.6. Sitting VV ranged between 55 and 150 mls, mean 107.7.

6.2.7.1. EVF Results

Standing EVF ranged between 38 and 93.3 mls, mean 64.07. Volunteers two, nine and ten had abnormal EVs of 58 mls, 51mls and 57mls respectively. These reduced EVs could have resulted from the volunteers being nervous and uncomfortable whilst standing and thus tensing the muscles in the cuff leg as a result. DA EVF ranged between 42 and

78.2 mean 63.05. Whereas DB EVF ranged between 44 and 80, mean 58.05. In this procedure only an EV was achieved by walking as no full venous filling occurred between foot movements.

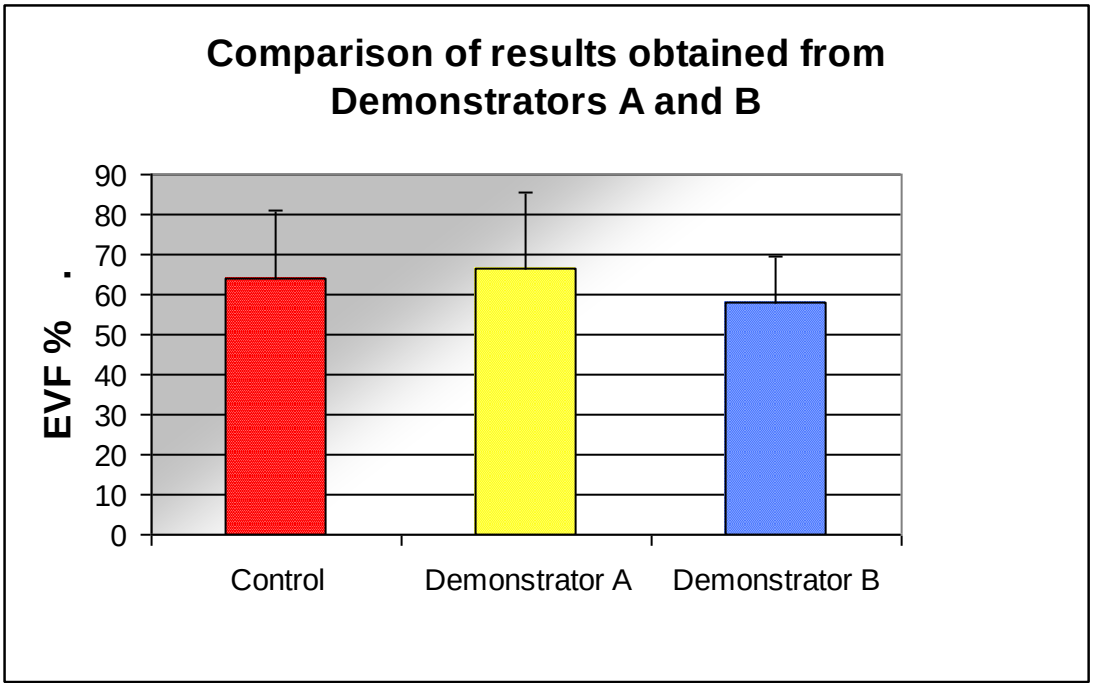


Figure 6.4. EVF obtained by tip-toe (control), DA and DB.

Table 6.3. EVF obtained by tip-toe (control) DA and DB

	Control	DA	DB
EVFs%	64.075	66.6	58.05
SD	16.918	18.97	11.49

EVF achieved by control and exercise devices as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

EVF within the range considered normal was achieved by control and DA. It can be seen (Figure 6.4. and table 6.3.) that DA was the most efficient with an EVF of 66.6 percent. Tiptoe (control) was the second most efficient with an EVF of 64.08 percent. DB was the least efficient producing an EVF, (58.05 percent) below the range considered normal,

greater than or equal to 60 percent as previously stated (Nicolaides and Sumner, 1991; Nicolaides, 1999), hence DB would be deemed inadequate despite the lack of statistical significance. No significant difference at the five percent level, existed between control and DA, control and DB or between DA and DB (Table 6.5).

6.2.7.2. RVF Results

Standing RVF ranged between 4.28 and 20.48 mls, mean 16.89. DA RVF ranged between 6.6 and 46.6, mean 24.83. DB RVF ranged between 6.6 and 67.5, mean 26.1. Only an RV was achieved by walking as no full venous filling occurred between movements.

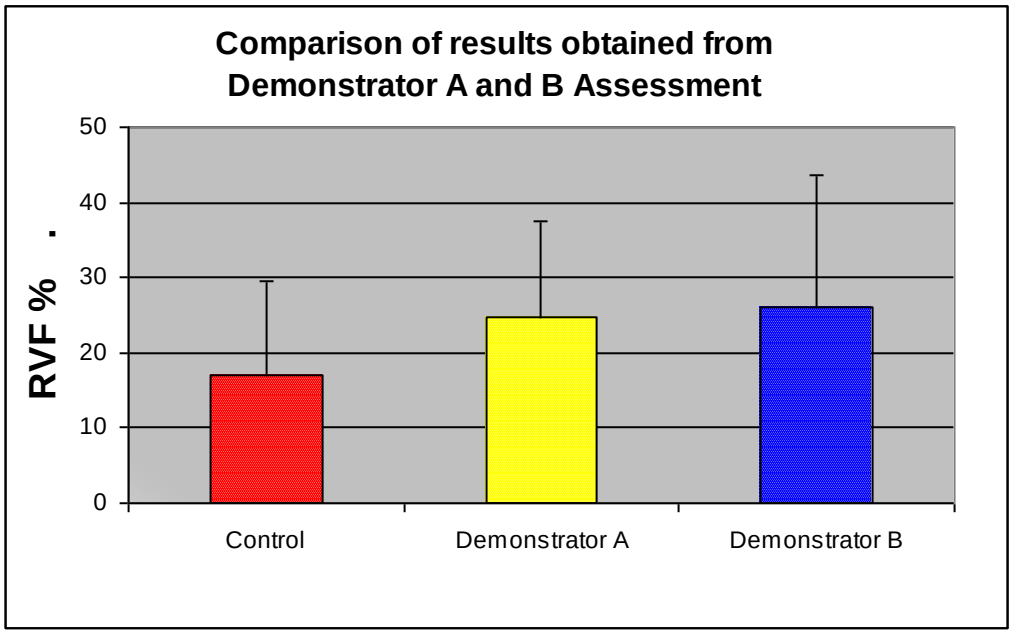


Figure 6.5 RVF obtained by tip-toe (control), DA and DB.

Table 6.4 RVF obtained by tip-toe (control), DA and DB.

	Control	DA	DB
RVFs%	16.89	24.83	26.1
STD	12.7	12.75	17.56

RVF achieved by control and exercise devices as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was achieved by control, DA and DB. It can be seen (Figure 6.5. and table 6.4.) that control was the most efficient with an RVF of 16.89 percent. DA was the second most efficient (RVF of 24.83) and DB the least efficient with an RVF of 26.1 percent. A normal residual volume fraction is less than or equal to 35 percent. No significant difference at the five percent level existed between any of the RVF obtained (Table 6.5).

Table 6.5 Comparison of EV and RV.

Movement	*t* value EV		*t* value RV	
Comparison of tiptoe control V's Ave walking value	3.06	S	-0.246	NS
Comparison of tiptoe control V's DA	0.762	NS	-0.99	NS
Comparison of tiptoe control V's DB	1.47	NS	-0.995	NS
Comparison of Ave walking value V's DA	-2.26	S	-0.813	NS
Comparison of Ave walking value V's DB	-1.61	NS	-0.813	NS
Comparison of DA V's DB	0.688	NS	0.01	NS

Critical value at the five percent significance level = 2.101.

6.3. Discussion

Needham (2005) reported that as little as five or six "cycles" of dorsiflexion or plantar flexion movements will achieve maximum venous emptying. So refilling time in a healthy limb will be quite slow as it is the arteries which will supply the blood rather than reflux in incompetent systems.

In an Air Plethysmography assessment conducted by Grey, (2001), no statistical difference was found when comparing a standing tiptoe movement to walking. Therefore the standing tiptoe movement results produced from the Tromped assessment were used to compare with the sitting movements produced when using DA and DB.

The average walking values were not used in comparison with the DA and DB as the ejection values recorded were produced from one singular movement, which was the foot pressing down on the pedal, holding that position for five seconds. The average walking values were produced by the volunteers continuously taking steps. There was a significant statistical difference in the comparison of the tiptoe standing movement and walking.

6.4. Conclusion

The hypothesis was to determine if DA and DB (of differing lengths) achieve adequate venous emptying. The average tiptoe movement standing was compared with results achieved by both DA and DB. No significant difference existed between tiptoe standing and DA or tiptoe standing and DB. Both demonstrators achieved adequate venous emptying. As previously stated DA achieved an EVF of 66.6 percent and an RVF of 24.83 percent less than 35 percent. DB achieved an EVF of 58.05 percent (less than the required 60 percent) and an RVF of 26.1 percent. Thus if the force required to compress both pedals in DA and DB is responsible for satisfactory EVF and RVF values obtained, the position of the spring relative to the foot is immaterial.

As DA produced more favourable results than DB, it was decided to use DA for further experiments.

CHAPTER 7

THE TROMPED AND MEDIVEN® TRAVEL COMPRESSION STOCKING ASSESSMENT

7.0. Introduction

As travel compression stockings have become more popular with long haul passengers their haemodynamic effects were assessed along with DA and some of the inflight exercises airlines are promoting.

Hypothesis: to determine the effectiveness of the Tromped in comparison to walking, wearing compression stockings and conducting the feet exercises advised by airlines.

7.1. Haemodynamic Assessment II.

7.1.1. Patients

Ten healthy volunteers were recruited by advertising in DIT, Bolton Street (Appendix H, recruitment poster). Healthy males or females between 20 to 35 years were invited to participate.

Exclusion criteria were varicose veins or previous surgery, previous DVT and recent immobilisation including travel of greater than four hours, within previous 6 weeks to the study date.

The ten healthy participants recruited to conduct this assessment comprised of eight males and two females. An information letter was sent to each potential participant (Appendix I) and a questionnaire (Appendix J). Ages ranged between 22 years and 34 years, mean age 27 +/-3.57 years on the day of the study.

All procedures and protocol conformed with the Declaration of Helsinki. All gave written informed consent to participate in this study.

Approval was obtained from the medical ethics committee of Beaumont Hospital.

7.1.2. Location

The study was performed in the Non-Invasive Vascular Unit, Beaumont Hospital. The assessment room was maintained at a controlled temperature of 20º Centigrade, to obtain equilibrium and prevent vasoconstriction (Cole, 2001b)

7.1.3. Researcher

The author, CC, was the investigator and performed the assessments under direct medical supervision.

7.1.4. Equipment

The equipment used for the purpose of this assessment consisted of the Air Plethysmograph machine, an examination couch, a treadmill, DA and Mediven® travel compression stockings.

The couch was placed at a height of 468mm from the ground, in order to mimic the average height of a standard (economy class) aircraft seat, which varies from 457mm – 480mm (Quigley *et al.*, 2001).

7.1.5. Method

i. The volunteers were placed in the supine position, for validation, on an examination couch with a calibrated air chamber surrounding the calf of their right leg. The standard APG assessment, (Control) was performed (section

4.5.2) to measure venous volume (VV), ejection volume (EV), residual volume (RV) in millilitres and used to calculate ejection volume fraction (EVF) and residual volume fraction (RVF) see Figure 7.1.

ii. When a steady baseline was recorded, the participant was asked to walk on to the treadmill at a speed of 2.5km/hr for two minutes duration (Figure 7.2). On completion of the two minutes the participants were then asked to return to the supine position with the leg elevated once again to determine the RV post walking.

iii. When the participant's veins were empty and a steady baseline recorded then she/he was asked to sit up on the examination couch and place his/her right foot on the uncompressed DA. Two similar EVs and the RV were obtained in the same manner as in the first assessment (Section 6.2.5).

iv. Once a steady baseline was again recorded the participant was asked to sit on the edge of the bed, and gently place both feet on the ground however without the right foot bearing any weight. The sitting venous volume was recorded before the participant was asked to conduct the plantar flexion movement (Figure 7.3) (raise his/her right heel off the ground while pressing the ball of the foot against the ground) and hold this position for five seconds. This procedure was repeated until two similar EV values were recorded. The resultant reduction in volume was measured as the EV.

v. When a steady baseline was recorded the participant was instructed to conduct the plantar flexion manoeuvre ten consecutive times before returning to the supine position with the right leg elevated at 45º once again so the RV could be calculated.

vi. When a steady baseline was once again recorded the participant was asked to sit on the edge of the bed, without bearing any weight on the right foot. The sitting VV was recorded before the participant was instructed to conduct the dorsiflexion movement (raise the toes of the right foot off the ground and hold for five seconds) see Figure 7.4. This procedure was repeated until two similar EV values were recorded.

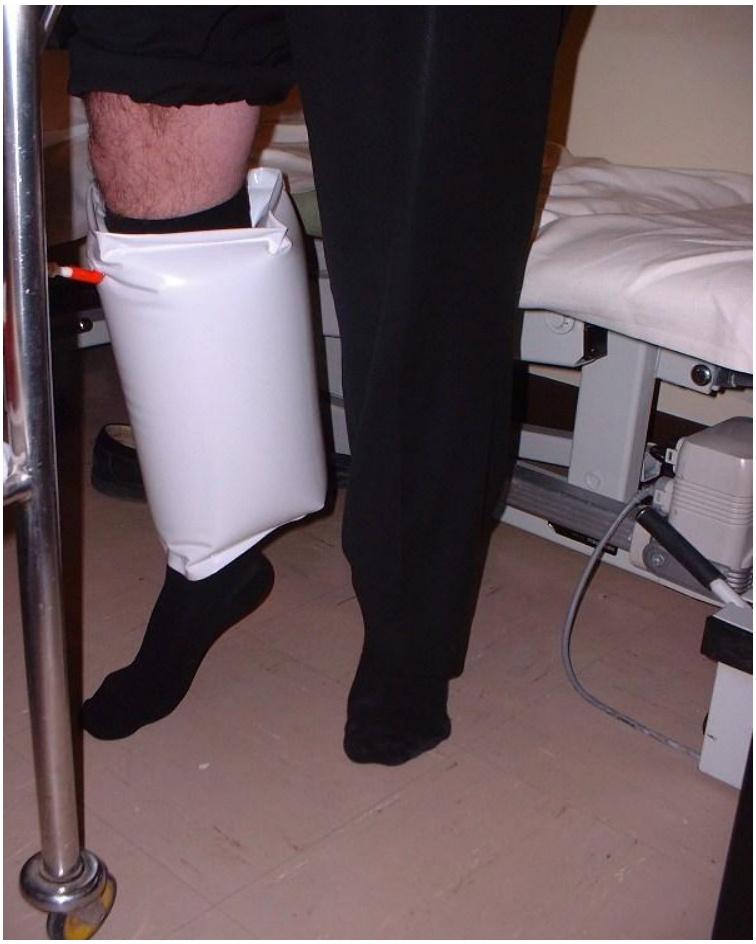


Figure 7.1. Tip-toe manoeuvre in the standing position, with the Mediven® Travel Stocking (black) on the Right limb, underneath the APG Cuff

vii. When a steady baseline was recorded the participant was instructed to conduct the dorsiflexion manoeuvre with the right foot ten consecutive times before

returning to the supine position with the right leg elevated at 45º once again so the RV could be calculated.

Figure 7.2. Participant walking on the treadmill, while wearing the Mediven® Travel Stocking (black) underneath the APG Cuff.

viii. When a steady baseline is recorded the participant was asked to sit on the edge of the bed again, without the right foot bearing any weight. Once the sitting VV and a steady baseline were recorded again, he/she was instructed to raise the right foot slightly off the ground and move the right foot clockwise in a

circular position, 360º once before returning the foot gently to the ground without bearing any weight. This procedure was repeated until two similar EVs were recorded. Then the RV can be calculated once a steady baseline is recorded, by the participant repeating this circular movement ten consecutive times, before returning to the supine position, with the leg elevated, until a steady base line was recorded once again.

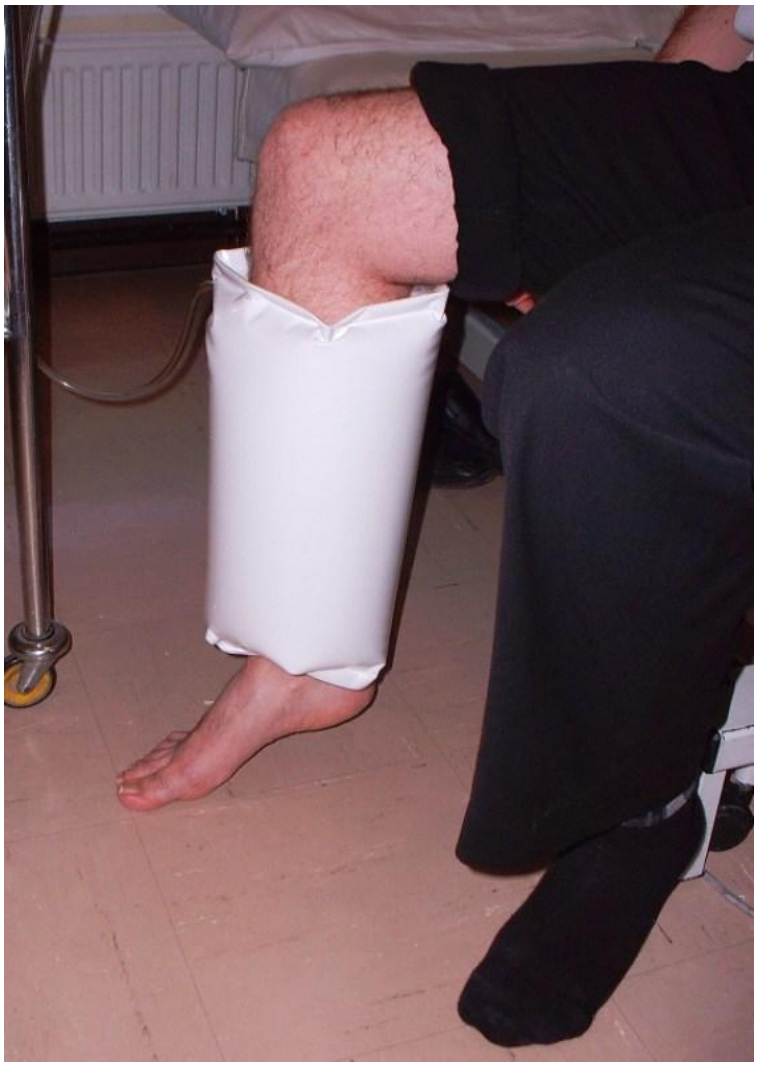


Figure 7.3. Heel up (plantar flexion) of the right foot, in the seated position, without the Mediven® knee length stockings.

ix. The APG machine was then switched off and the cuff removed from the participant's right leg. Participants rested for 15 minutes before his/her right leg was measured to accurately determine the knee length mediven® travel stocking size. The instructions accompanying the stockings state "Measure the circumference above the ankle at its narrowest part". All ankle measurements were taken using a spring loaded measuring tape.

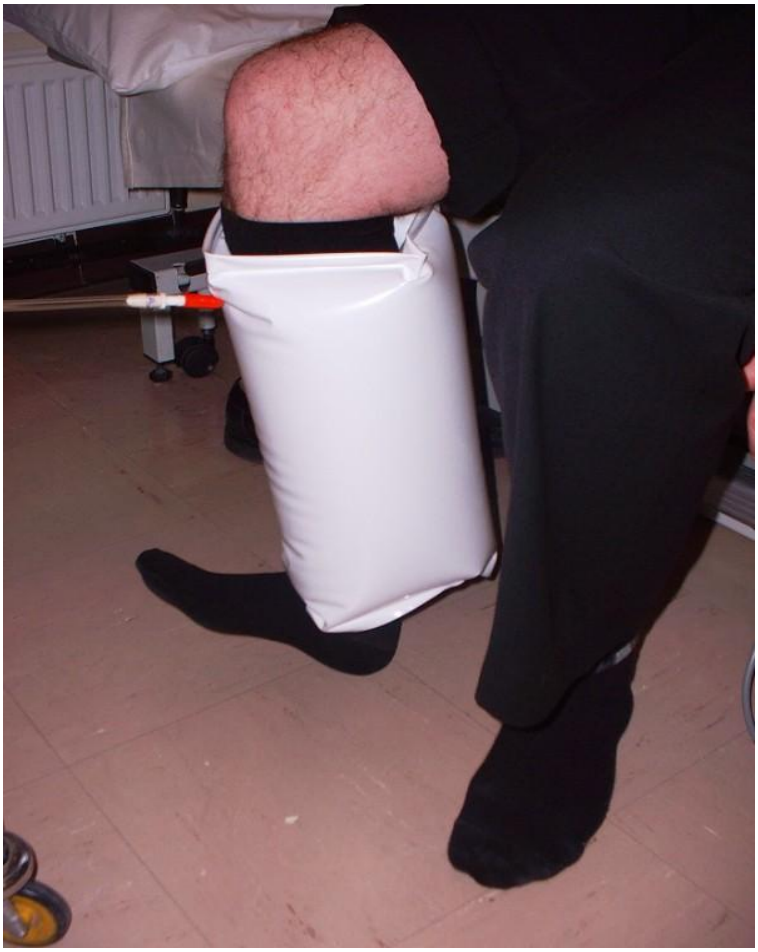


Figure 7.4. Toes up (dorsiflexion) of the right foot, in the seated position, whilst wearing the Mediven® Travel stocking (black).

x. Once the correct stocking size (refer to Section 4.8) was determined for the participant being tested, he/she was asked to place the stocking on the right leg and then return to the supine position on the same examination couch as in

Part 1, remaining in this position for ten minutes in the temperature controlled room.

xi. The APG can be applied over compression stockings (Christopoulos and Nicolaides, 1994). To prevent the APG cuff slipping over the stocking during the various manoeuvres and walking, self adhesive Velcro pads were used to attach the APG cuff and the stocking (Figure 7.5) (Ibegbuna *et al.*, 2003).

xii. The air chamber was then placed around each participant's right calf again and connected to the APG machine and inflated to 7mmHg. The right leg was elevated and the machine calibrated in the same manner as in Part 1 of the experiment.

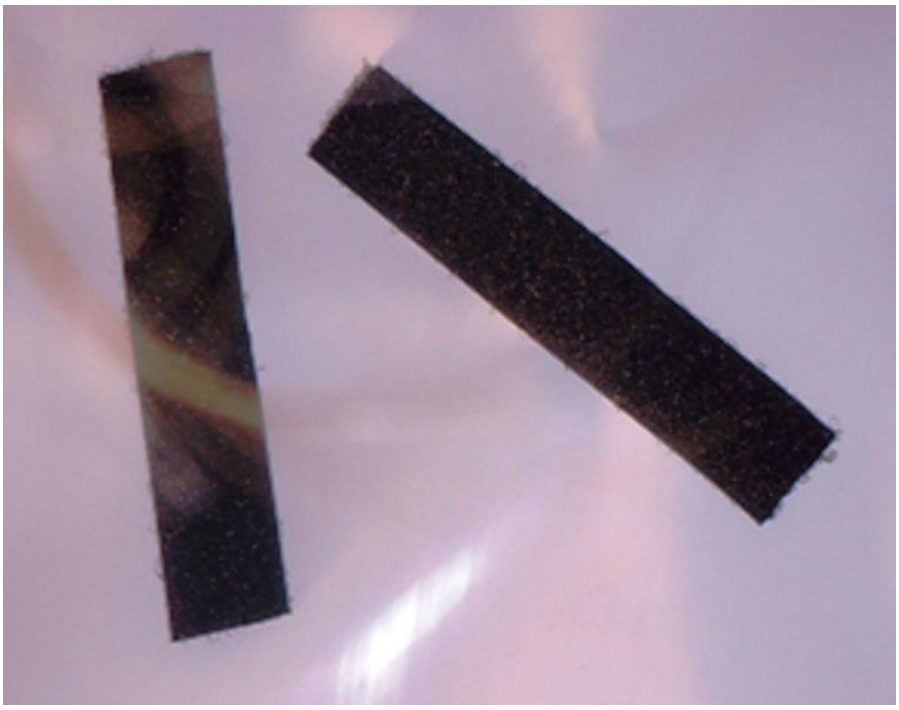


Figure 7.5. Double sided Velcro attached to the underside of the APG Cuff.

xiii. All the procedures from procedure (i) to (viii) of Part 1 of the experiment were repeated and recorded in the same order while the participant wore the mediven® travel stocking underneath the APG cuff.

7.2. Statistical Analysis

The mean of each result was determined by using equation 4.7, for example by dividing the sum of all ten patients standing venous volume by the number of values.

The standard deviation of each result was determined by using the equation 4.8.

The paired Student's *t*-test (equation 4.9) was used to determine the statistical significance between any of the movements mean values when compared both with and without wearing stockings. Statistical significance was accepted at the 95% confidence level ($p \leq 0.05$). With the number of degrees of freedom being 18, the critical value of *t* is $\pm$ 2.101.

7.3. Results

This assessment involved two parts; the first conducting all manoeuvres without wearing the travel stockings (Table 7.1); the second conducting all manoeuvres whilst wearing the travel stockings (7.2). Absolute and derived values were obtained from Part I and Part II of this assessment, from each manoeuvre for each of the ten participants (Appendix K). Mean values are presented in Tables 7.3 and 7.4.

The absolute results obtained from Part 1 of the study, show that all ten participants had a normal standing VV which ranges between 80 and 170mls (Bays *et al.,* 1994) and normal VFIs of less than two ml/sec.

Table 7.1 Mean and Standard deviation results for part I of the assessment, without stockings.

n = 10, mean age 27 +/-3.57				
Standing		Mean+/-Standard deviation		
VV (mls)		**123.3+/-28.85**		
90%VV		**111.96+/-24.95**		
VFT (sec)		**178.65+/-31.56**		
VFI		**0.709+/-0.179**		
TT EV (mls)		**73+/-15.93**		
TT EVF (%)		**51.73+/-14.42**		
TT RV (mls)		**21.6+/-11.72**		
TT RVF (%)		**16.73+/-8.91**		
Ave Walking EV (mls)		**34.4+/-12.18**		
Ave Walking RV (mls)		**21.05+/-13.62**		
Sitting VV (mls)		**98.5+/-20.45**		
SITTING				
Mean +/- SD	**DA**	**Plantar flexion**	**Dorsiflexion**	**Circle**
EV	61.9+/-17.4	45.2+/-18.47	45.3+/-15.01	27.35+/-11.12
EVF	62.36+/-8.13	45.81+/-13.78	47+/-14.419	27.4+/-7.78
RV	28.1+/-12.17	33.6+/-15.71	24.9+/-17.18	33.7+/-22.2
RVF	30.11/-14.58	34.77+/-16.25	26.08+/-16.02	34.98+/-19.64

Table 7.2 Mean and Standard deviation results for part II of experiment with Mediven® stockings.

n=10, mean age 27 +/-3.57				
Standing		Mean+/-Standard deviation		
VV (mls)		**87.4+/-27.64**		
90%VV		**78.66+/-24.88**		
VFT (sec)		**166.85+/-50.65**		
VFI		**0.561+/-0.25**		
TT EV (mls)		**54.4+/-17.03**		
TT EVF (%)		**65.354+/-16.27**		
TT RV (mls)		**25.8+/-14.94**		
TT RVF (%)		**29.62+/-14.53**		
AV Walking EV (mls)		**24.8+/-10.72**		
AV Walking RV (mls)		**24.4+/-15.08**		
Sitting VV (mls)		**71.4+/-24.15**		
SITTING				
Mean +/- SD	**DA**	**Plantar flexion**	**Dorsiflexion**	**Circle**
EV	46.6+/-18.72	40+/-13.28	27.4+/-13.45	24+/-11.21
EVF	64.797+/-13.7	61.64+/-22.71	40.699+/-19.03	35.483+/-16.01
RV	21.7+/-14.53	20.8+/-12.03	17.5+/-15.45	21.15+/-12.94
RVF	33.68+/-21.93	27.79+/-13.16	21.98+/-11.6	29.35+/-16.51

7.3.1. EVF Results, Part I – WITHOUT STOCKINGS

Standing VV ranged between 86 and 160 mls, mean 123.3 mls. Standing EVF ranged between 47.5 and 87.2 mls, mean 51.73 mls (Appendix K). Participants numbered five and seven had abnormal EVs of 54mls and 52mls respectively. All other eight participants had normal tiptoe EVs.

Sitting VV ranged between 62 and 123 mls, mean 98.5 mls. Only an EV was achieved by walking as no full venous filling occurred between steps. DAs EVF ranged between 48.59 and 81.9, mean 62.36. Plantar flexion EVF ranged between 21.1 and 77.58, mean 45.81. Dorsiflexion EVF ranged between 11.92 and 69.44, mean 47 and Circle EVF ranged between 16.05 and 44.9, mean 27.4.

Figure 7.6 and Table 7.3 display EVF results for all manoeuvres conducted without stockings.

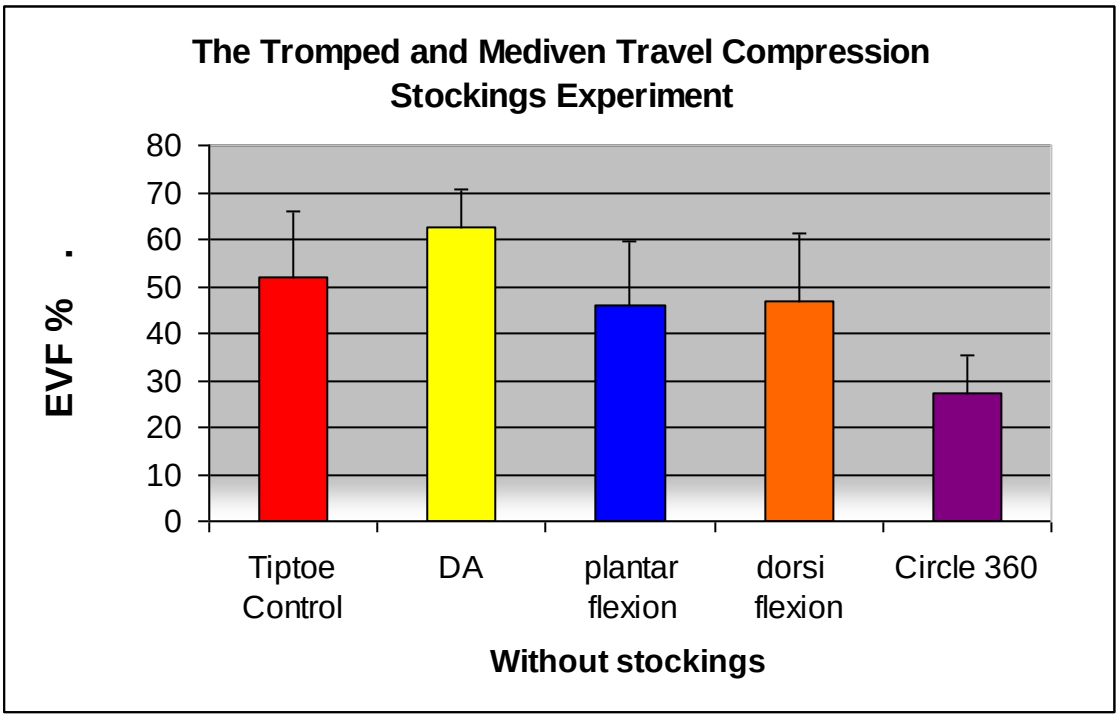


Figure 7.6. EVF obtained by tip-toe (control), use of DA and the three forms of exercise as advised by airlines without stockings.

Table 7.3. EVF obtained by tip-toe (control), use of DA and the three forms of exercise as advised by airlines without stockings.

	Control	DA	Plantar flexion	Dorsiflexion	Circle
EVFs %	51.73	62.36	45.81	47	27.4
SD	14.42	8.13	13.78	14.42	7.78

EVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

Each of the values obtained in Figure 7.6 and in Table 7.3 were derived from participants not wearing Mediven® stockings. EVF within the range considered normal was achieved by only DA (62.36 percent). The standing tiptoe EVF was below 60 percent at 51.73 percent. Both the plantar flexion and dorsiflexion (advised by airlines) produced similar mean EVFs of 45.81 and 47 percent respectively. The final movement required each participant to raise their right foot off the ground and rotate their ankle through 360º in a circle. This produced the lowest EVF, of 27.4 percent. All three exercises, advertised by airlines are not efficient in creating sufficient venous return to the heart to prevent stasis.

A significant difference exists between tiptoe standing EV when compared to each of the following manoeuvres:

i. Plantar flexion;
ii. Toes up (dorsiflexion),
iii. Circle 360º,

No significant statistical difference exists between control and DA. Even though the plantar flexion movement (EVF of 47.83±13.6) did not achieve the required EVF of greater than 60 percent, no significant difference existed when it was compared to DA. A significant difference exists between DA EV when compared to the circle manoeuvre. When Plantar flexions was compared to dorsiflexion, no significant difference was evident. A significant difference existed between Dorsiflexion and circle.

7.3.2. EVF Results Part II – WITH STOCKINGS

The second part of the study involved all ten participants repeating part one's manoeuvres, while wearing Mediven® compression stockings. Standing VV ranged between 42 and 125 mls, mean 87.4 mls (Appendix K). Standing EVF ranged between 31.66 and 102.82 mls, mean 65.35 mls (Table 7.2). Participants numbered three, four, seven, eight and nine produced EVs less than the normal range of 60-150ml (Bays *et al.*, 1994) which again could be as a result of the reduction in VV of the limb due to the compression stockings.

Sitting VV ranged between 35 and 115 mls, mean 71.4 mls. Only an EV was achieved by walking as no full venous filling occurred between steps. DA EVF ranged between 42.87 and 92.59 mls, mean 64.79 mls. Plantar flexion EVF ranged between 13.91 and 100 mls, mean 61.64 mls. Dorsiflexion EVF ranged between 9.25 and 65.62 mls, mean 40.69 mls and circle EVF ranged between 13.63 and 67.56 mls, mean 35.48 mls. Figure 7.7 and Table 7.4 display EVF results achieved with stockings.

EVF within the range considered normal was achieved by all manoeuvres except Dorsiflexion (40.69 percent) and the circle manoeuvre (35.48 percent).

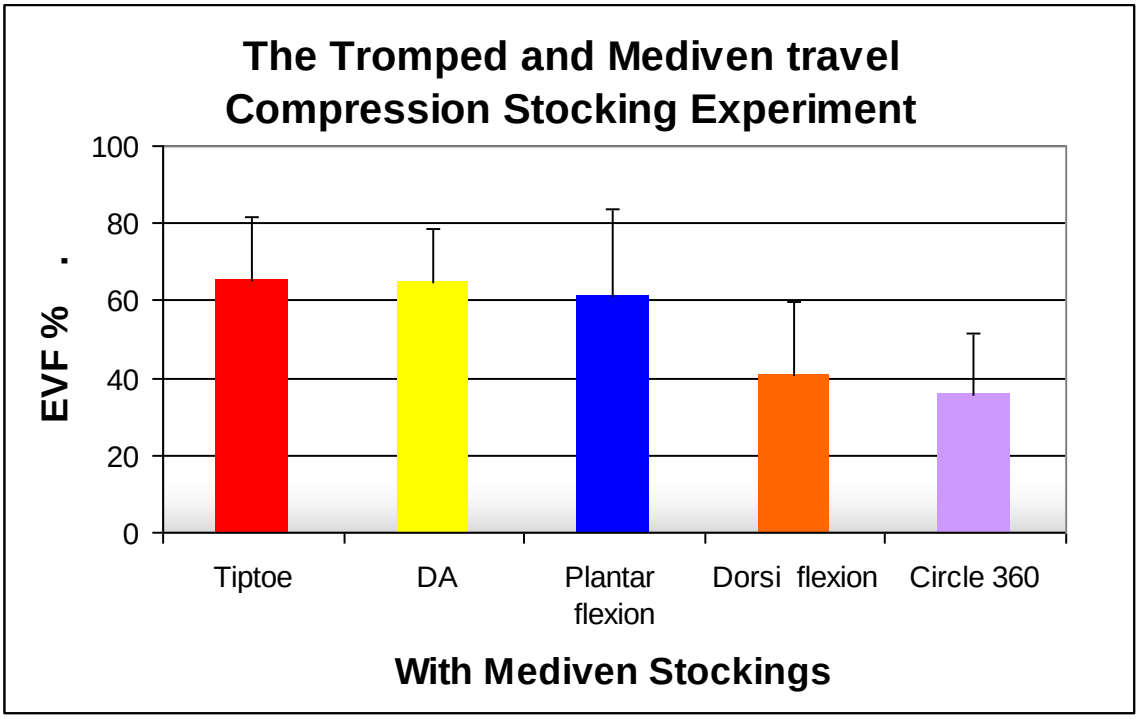


Figure 7.7. EVF obtained by tip-toe, use of DA and the three forms of exercise as advised by airlines whilst wearing the Mediven® stockings.

Table 7.4. EVF obtained by tip-toe, use of DA and the three forms of exercise as advised by airlines whilst wearing the Mediven® stockings.

	Control	DA	Plantar flexion	Dorsiflexion	Circle
EVFs %	65.354	64.79	61	40.69	35.48
SD	16.27	13.7	22.71	19.03	16.01

EVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

No statistical difference exists between control and DA. A significant difference at the five percent level exists between tiptoe standing, when compared to each of the above three manoeuvres; dorsiflexion, plantar flexion and circle. No significant difference exists between plantar flexion compared to DA. There is also a significant difference between DA EV and the circle manoeuvres EV. The circle manoeuvre produced the least

EVF values of 26.75±11.39 with stockings and 24±11.21 with stockings. No significant difference existed between dorsiflexion EV and circle EV.

Table 7.8 and Figure 7.5 display the EVFs achieved when conducting all manoeuvres both with and without the Mediven® Travel compression stockings.

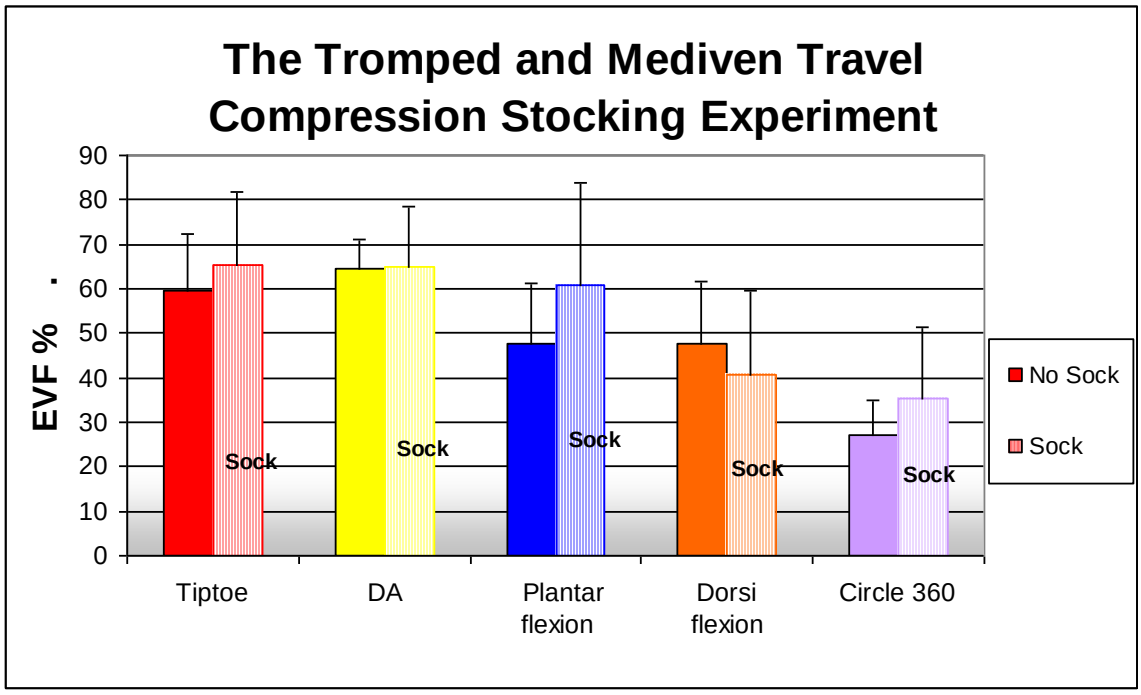


Figure 7.8. EVF values obtained by tip-toe, use of the Tromped and the three forms of exercise as advised by airlines with and without Mediven® Stockings.

Table 7.5. EVF values obtained by tip-toe, use of the Tromped and the three forms of exercise as advised by airlines with and without Mediven® Stockings.

	Without Stockings					With Stockings				
	Control	DA	Plantar flexion	Dorsi flexion	Circle	Control	DA	Plantar flexion	Dorsi flexion	Circle
EVF (%)	51.73	62.36	45.81	47	27.4	65.354	64.79	61	40.69	35.48
SD	14.42	8.13	13.78	14.419	7.78	16.27	13.7	22.71	19.03	16.01

EVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, comparing values obtained with and without Mediven® Compression Stockings. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

Only the Tromped (seated position) produced a mean EVF of greater than 60 percent, in both parts of the study, i.e. with and without wearing the Mediven® graduated compression stockings. All manoeuvres, excepting dorsiflexion, produced a greater EVF when participants wore the stockings than when compared to them conducting manoeuvres without the stockings. A significant statistical difference exists when the tiptoe movement, (without stockings) was compared to tiptoe movement (with stockings). Table 7.4 displays the *t*-values for all compared manoeuvres ejection volumes.

Table 7.6 Comparison of EV values

Manoeuvre	*T* values			
	Without stockings		With stockings	
Comparison of tiptoe control versus DA	1.29	NS	-1.22	NS
Comparison of tiptoe control versus Plantar flexion	3.36	S	-1.93	NS
Comparison of tiptoe control versus dorsiflexion	3.9	S	-0.5	NS
Comparison of tiptoe control versus Circle	7.26	S	-1.52	NS

Critical value at 5% significance level =2.101.

No significant statistical difference exists between Tiptoe (without stocking) versus DA (with stocking). DA is as efficient if used with or without Mediven® stockings, as no significant difference exists between the EV values obtained when participants did and

did not wear Mediven stockings while compressing the Tromped pedal. No significant difference existed between plantar flexion (without stockings) compared with plantar flexion (with stockings) and the Circle manoeuvre (without stockings) compared to the circle manoeuvre (with stockings).

7.3.3. RVF Results Part I – WITHOUT STOCKINGS

Tiptoe (control) RVF ranged between 7.54 and 40, mean 16.73. DA RVF ranged between 9.3 and 53.9, mean 30.11. Plantar flexion RVF ranged between 16.6 and 63.3, mean 34.77. Dorsiflexion RVF ranged between 11.2 and 67.88, mean 26.08 and Circle RVF ranged between 5.17 and 62.38, mean 34.98. Figure 7.9 and Table 7.7 display the RVFs obtained when conducted without stockings.

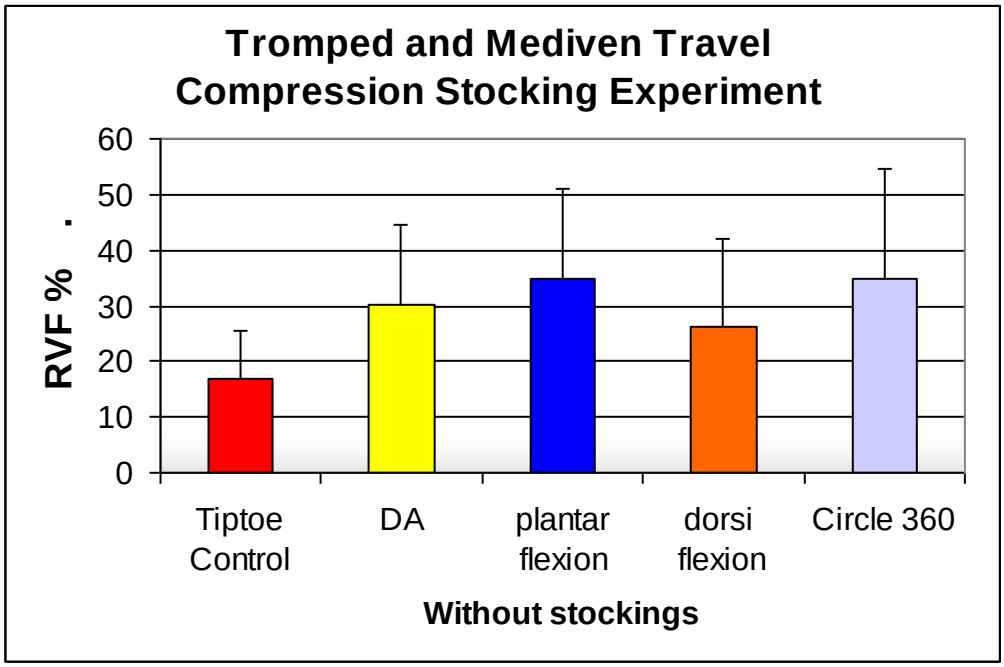


Figure 7.9. RVF obtained by tip-toe (control), use of DA and the three forms of exercise as advised by airlines, without stockings.

Table 7.7. RVF obtained by tip-toe (control), use of the DA and the three forms of exercise as advised by airlines, without stockings.

	Control	DA	Plantar flexion	Dorsiflexion	Circle
RVFs %	16.73	30.11	34.77	26.08	34.98
SD	8.91	14.58	16.25	16.02	19.64

RVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was achieved by all manoeuvres. The tiptoe movement (control) produced the most efficient RVF of 16.73+/-8.91. The dorsiflexion manoeuvre was second to control. It produced a RVF of 26.08±16.02. DA produced an RVF of 30.11±14.58, plantar flexion 34.77±16.25 and circle RVF of 34.98±19.64. No significant difference was detected between control and any of the manoeuvres.

7.3.4. RVF Results Part II of the study

The standing tiptoe RVF (with stockings) ranged between 12.12 and 55.17, mean 29.62. TJA (in the seated position) RVF ranged between 10.71 and 84, mean 33.68. Plantar flexion RVF ranged between 8.1 and 51.85, mean 27.79. Dorsiflexion RVF ranged between 10.6 and 52.17, mean 21.98 and Circle RVF ranged between 9.52 and 71.87, mean 29.35. Figure 7.10 and Table 7.8 display RVFs obtained when conducted with stockings.

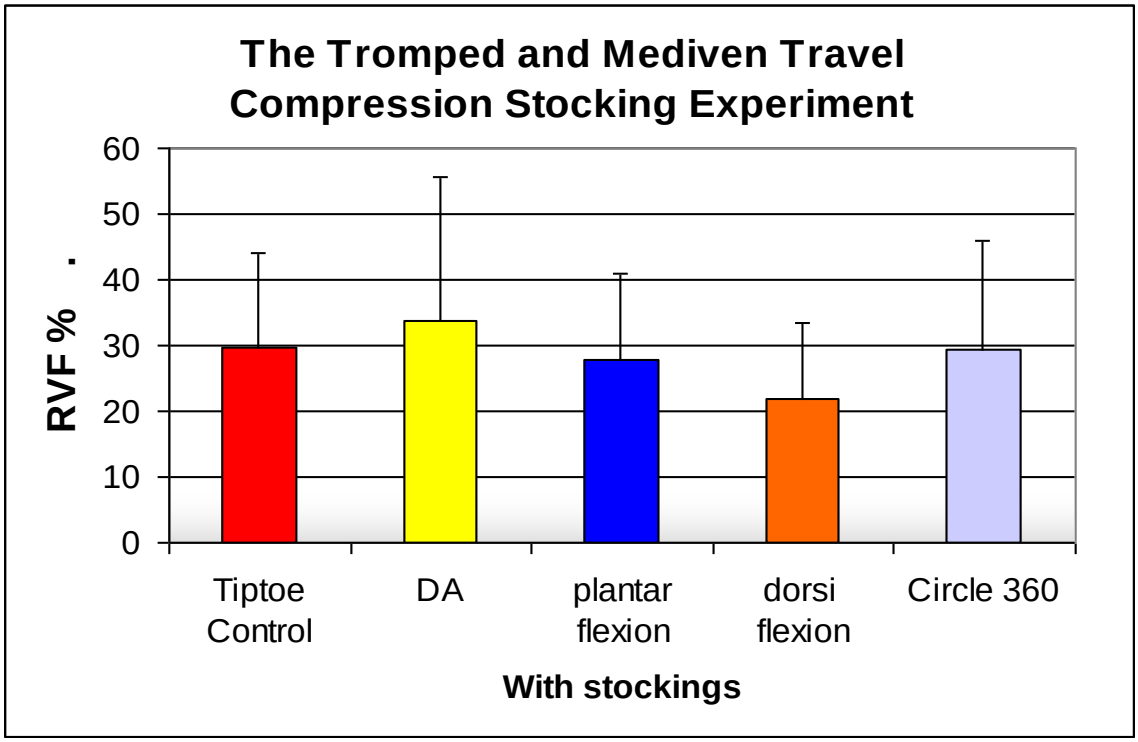


Figure 7.10. RVF obtained by tip-toe, use of DA and the three forms of exercise as advised by airlines whilst wearing the Mediven® stockings.

Table 7.8. RVF obtained by tip-toe, use of TJA and the three forms of exercise as advised by airlines whilst wearing the Mediven® stockings.

	Control	DA	Plantar flexion	Dorsiflexion	Circle
RVFs %	29.62	33.68	27.79	21.98	29.35
SD	14.53	21.93	13.16	11.6	16.51

RVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, as measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was achieved by all manoeuvres assessed. Dorsiflexion produced an RVF of 21.98±11.6. Plantar flexion produced a RVF of 27.79±13.16. The circles manoeuvre whilst seated (29.35±16.51) and the tiptoe control

movement, standing (29.62±14.53). The Tromped produced the least RVF value of 33.86±21.93. Even though the Tromped ranked fifth off all manoeuvres conducted, it still produced an efficient RVF, less than the required 35 percent (Nicolaides and Sumner, 1991), which means it is effective at preventing venous stasis in the lower limbs, even when users wear the Mediven® Compression Stockings. No statistical difference existed between any of the manoeuvres conducted.

Figure 7.11 and Table 7.9 display the RVF achieved when conducting all manoeuvres both with and without the Mediven® Travel compression stockings.

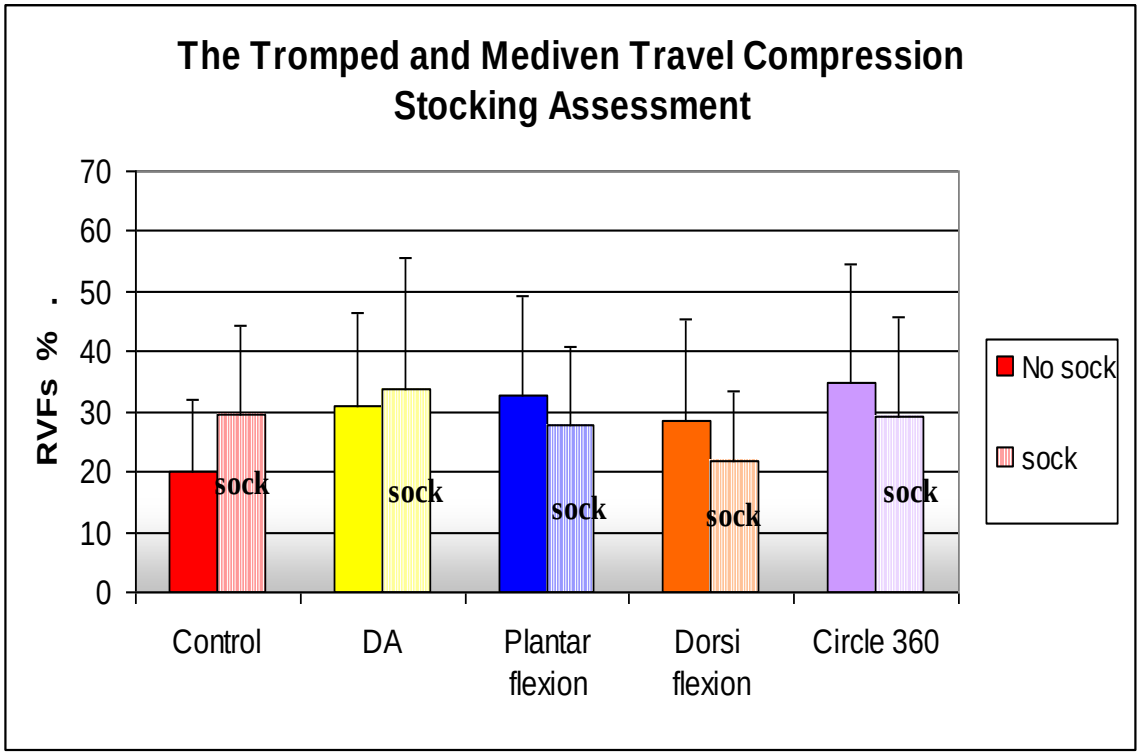


Figure 7.11. RVF values obtained by control, DA and the three forms of exercise as advised by airlines with and without Mediven® Stockings.

Table 7.9. RVF values obtained by control, DA and the three forms of exercise as advised by airlines with and without Mediven® Stockings.

	Without Stockings					With Stockings				
	Control	DA	Plantar flexion	Dorsi flexion	Circle	Control	DA	Plantar flexion	Dorsi flexion	Circle
RVF (%)	16.73	30.11	34.77	26.08	34.98	29.62	33.68	27.79	21.98	29.35
SD	8.91	14.58	16.25	16.02	19.64	14.53	21.93	13.16	11.6	16.51

RVF achieved by control, the Tromped and exercise manoeuvres as advised by airlines, comparing values obtained with and without Mediven® Compression Stockings. Values measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

Results obtained with stockings differed from those of Part 1 of the study which was conducted without participants wearing Mediven® stockings. The circle manoeuvre produced the highest RVF (34.98±19.64), without stockings, however this was still considered within the normal range of less than 35 percent.

Table 7.10 displays the *t*-values for all compared manoeuvres residual volumes.

Table 7.10 Comparison of RV values

Manoeuvre	*t* values			
	Without stockings		With stockings	
Comparison of tiptoe control versus DA	-1.216	NS	0.62	NS
Comparison of tiptoe control versus Plantar flexion	-1.936	NS	0.83	NS
Comparison of tiptoe control versus dorsiflexion	-0.5	NS	1.22	NS
Comparison of tiptoe control versus Circle	-1.52	NS	0.74	NS

Critical value at 5% significance level =2.101.

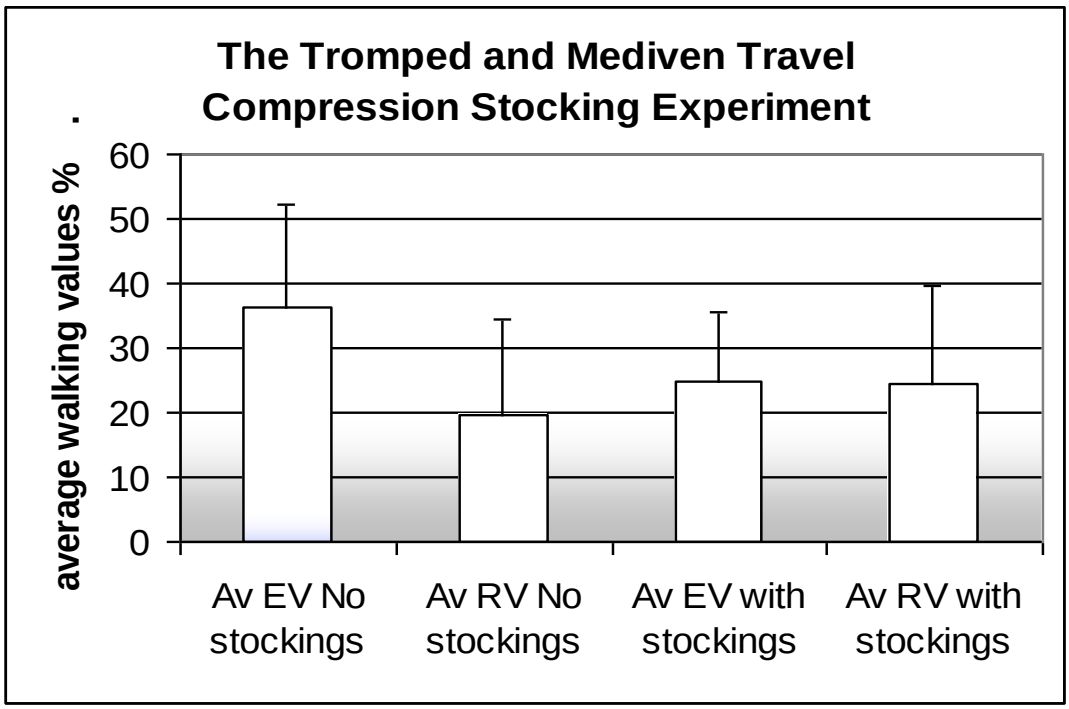


Figure 7.12. Comparison of walking values obtained, with and without wearing stockings.

Table 7.11. Average EV's and RV's achieved by walking.

	Average EV No stockings	Average RV No stockings	Average EV with stockings	Average RV with stockings
Values %	36.4	19.75	24.8	24.4
SD	15.71	14.71	10.72	15.08

Average EV's and RV's achieved by walking, comparing values obtained with and without Mediven® Compression Stockings. Values measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

Walking without stockings produced an average EV of 36.4±15.71 while walking with stockings produced an average EV of 24.8±10.72. An average RV of 19.75±14.71 was recorded without stockings and an average RV value of 24.4±15.08 was produced when participants wore the Mediven Stockings.

A significant difference (Table 7.12) at the five percent level exists between the tiptoe control EV and the average walking EV. However no significant difference was recorded between tiptoe control RV and the average walking RV value.

Table 7.12 Comparison of EV and RV values

Manoeuvre	*t* values			
	Without stockings		With stockings	
Comparison of control EV versus Walking EV	5.97	S	4.65	S
Comparison of control RV versus Walking RV	0.09	NS	0.2	NS

Critical value at 5% significance level =2.101.

7.4. Discussion

The participants results obtained from Part II of the study demonstrate that while wearing the Mediven® Travel Compression Stockings, reduced standing VVs were recorded for four of the participants. This could be due to the fact that compression stockings reduce the cross-sectional area of the limb (Agu *et al.*, 1999; Partsch, 1999; Morris and Woodcock, 2004) so therefore naturally the venous volume of blood should be reduced. All ten participants had a normal VFI.

Each individual has an inherent venous volume, which makes it differ from that of the next individual. Each participant acted as their own control. Once a normal venous system was established for each participant, results derived from the tiptoe manoeuvre were recorded as the control values. As each participant's venous volume varied, so did their ejection volumes and residual volumes for each resulting manoeuvre. There is a wide range of acceptable normal results however once you reach over a certain threshold then it is termed incompetent. Large errors may be due to the fact that some participants

had a more active venous pump, whereas others may have been nervous during the assessment and thus failed to relax the calf muscles of the right leg sufficiently during venous filling thus resulting in varied values.

The medial gastrocnemius is the muscle which does the most work to create the plantar flexion manoeuvre (Quaresima *et al.,* 2001). Thus this muscle is predominantly used during walking and compression of the Tromped pedals.

The average walking values were produced by the volunteers continuously taking steps. Taking 95 percentile $p>0.05$ there was a significant difference in the comparison of the tiptoe standing movement (without stockings) and walking (without stockings) because an average walking value was used. This also applied when the tiptoe standing value with stockings was compared with the walking value while wearing stocking.

The EVF produced as a result of compressing DA's pedal remained the same when conducted with stockings; however the stockings produced greater EVFs for every other manoeuvre conducted, in comparison to manoeuvres conducted without wearing stockings. This was in keeping with the findings of Christopolous *et al.,* (1987). Therefore DA is efficient at activating the venous pump regardless. When the student *t*-test was used to compare EV values obtained by DA with volunteers wearing and not wearing stockings, no statistical difference between the two was calculated. So DA is as efficient when used with or without stockings.

Dorsiflexion and the Circle manoeuvres (advocated by airlines) did not produce EVF within the range considered normal with stockings. This suggests that using Mediven® compression stockings alone, as a form of prophylaxis, is not sufficient to prevent venous stasis and the possibility of preventing FRDVT. This finding is corroborated in several studies, where compression stockings failed to prevent against FRDVT and FRSVT (Belcaro et al., 2001a; Scurr *et al.,* 2001; Hughes *et al.,* 2003).

Only DA achieved the acquired EVF of greater than 60 percent and an RVF of less than 35 percent in the seated position.

Walking with stockings produced EVs smaller than those achieved when walking without wearing stockings. This is because the cross sectional area of the limb and the diameter of the veins would be reduced by the stockings, thus reducing the volume of blood. The RV was greater with stockings than without. This was expected as the purpose of wearing compression stockings is to create venous return.

7.5. Conclusion

The objective of the research for which results are presented in this chapter was to determine the effectiveness of the Tromped in comparison to walking, wearing compression stockings and conducting feet exercises advised by airlines.

The haemodynamic assessments established that DA was more efficient than some of the exercises that the airlines advise their passengers to conduct during flight.

Thus further testing of a new prototype (Tromped footrest) with improved ergonomics designed for use on board an aircraft was planned to prevent stasis and thus the possible onset of FRDVT. This new prototype design would be incorporated into an aircraft footrest so long haul passengers could exercise and promote venous return in the seated position. With this design concept in mind a proposed in-flight assessment was developed which would require the use of an aircraft for four hours or more. The Irish Air Corps and the RFA were contacted to determine if they could facilitate a haemodynamic assessment on board one of their aircraft. However both parties after consideration stated that such an assessment would be impossible. Contact with Purdue University West Lafayette Indiana, America was then made. The college was very

interested in research collaboration however they could not facilitate the assessment requirements either.

Thus after futile attempts to arrange an in-flight assessment it was decided the next natural progression was to conduct the footrest heamodynamic assessment in an aircraft seat without the pressurised chamber of an aircraft cabin.

CHAPTER 8

THE TROMPED FOOTREST ASSESSMENT

8.0. Introduction

The objective of this assessment was to determine if any of the four Tromped footrests, when seated in an aircraft seat, (section 5.10) are as effective as DA and tiptoe control manoeuvre and to determine which gives the greatest venous emptying.

8.1. The Tromped Footrest Assessment

8.1.1. Patients

Eighteen volunteers were recruited by advertising in DIT Bolton Street (Appendix L). Healthy males or females between the ages of 25 to 50 years were invited to participate. Selection criteria included six healthy individuals, six women taking the oral contraceptive pill and six individuals with a BMI of greater than 30. Exclusion criteria were varicose veins or previous surgery, previous DVT and recent immobilization including travel of greater than four hours, within previous six weeks to the study date. Eight males and ten females ranging in ages from 25 to 50 participated. Mean age 35.61±9.58 years on the day of the study. Each volunteer completed a questionnaire (Appendix M) and signed an informed consent form (Appendix N), before commencement of the study. Their height in metres and weight in kilograms were then recorded (Table 8.1).

8.1.2. Location

The assessment was conducted in a temperature controlled room of 20º (as shown in Figures 8.1 and 8.2).

8.1.3. Researcher

The assessment was conducted by one investigator, the author, Carolyn Collins.

Table 8.1. Body Mass Index of each volunteer.

Patient	Date of Birth	Weight (kgs)	Height (m)	BMI (kg/m^2)
1	1/08/58	70	1.64	26.02
2	18/08/81	60	1.53	25.63
3	04/02/71	91	1.6	35.54
4	14/06/67	141	1.83	42.1
5	02/10/60	95	1.79	29.65
6	01/09/63	62	1.74	20.47
7	10/06/79	72	1.8	22.22
8	05/12/56	84	1.8	25.92
9	27/07/63	104	1.83	31.05
10	08/11/79	52	1.6	20.31
11	1/06/73	85	1.8	26.23
12	28/07/80	58	1.57	23.53
13	08/10/56	100	1.87	28.59
14	08/09/56	94	1.77	30.00
15	25/01/82	74	1.7	25.6
16	17/10/81	57	1.64	21.19
17	12/10/78	65	1.71	22.22
18	12/02/77	161	1.82	48.6

8.1.4. Equipment

The APG® machine, a bed, aircraft seat, weighing scales, measuring tape, Footrest prototypes I – IV and DA were the equipment used to conduct this haemodynamic assessment.

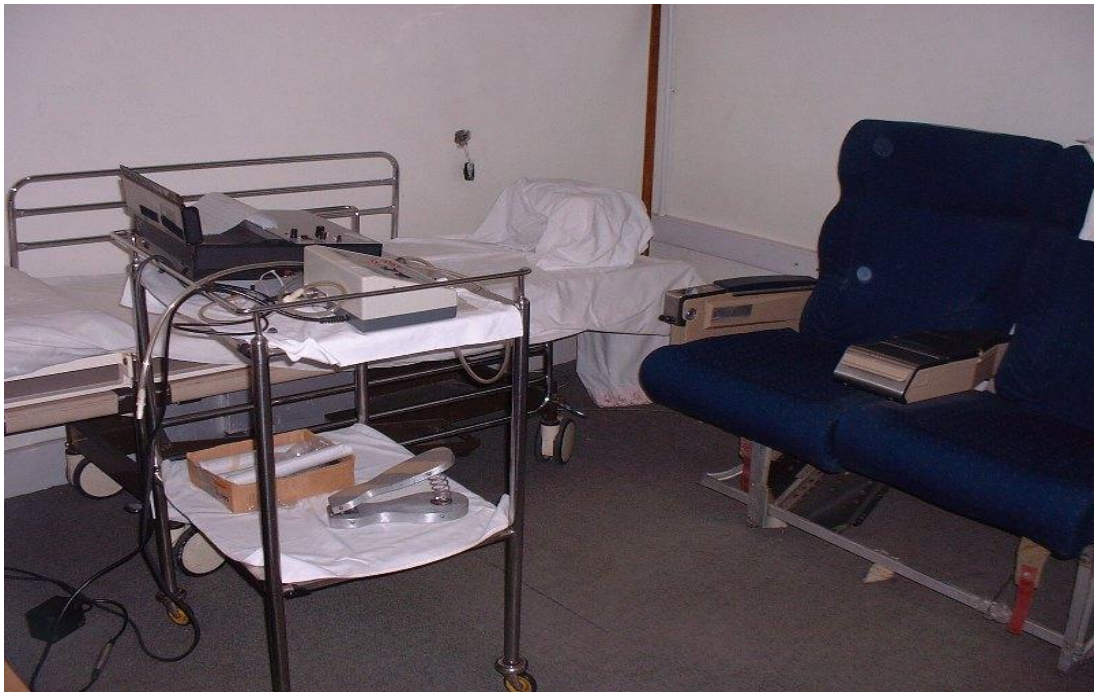


Figure 8.1. Layout of the Tromped Footrest Assessment room.

Figure 8.2. APG Equipment in relation to the aircraft seats and bed.

8.1.5. Method

The assessment protocol and procedures were approved by the DIT ethics committee and conformed to the Declaration of Helsinki.

The footrest prototypes were labelled (I-IV). Footrest I and II were attached to one test rig and footrest III and IV attached to a second test rig. The aircraft seats were positioned beside the examination couch (distance mm to be determined for ease of access to the seat). Taking a seat pitch of 762mm (30 inches), it was determined where the two test rigs should be positioned on the wooden mat (in relation to the aircraft seats) and this was then marked. Using a butterfly screw both test rigs were firmly attached to the wooden mat while in use, to ensure consistency with each test conducted. The APG equipment was placed on a trolley with wheels for manoeuvrability.

i. The standard APG assessment, (Control) was performed to measure venous volume (VV), ejection volume (EV), residual volume (RV) in millilitres and used to calculate ejection volume fraction (EVF) and residual volume fraction (RVF) as explained in detail in section 4.5.2.

ii. When a steady baseline was recorded, the participant was instructed to sit on the aircraft seat, with her or his foot resting on the uncompressed pedal of Footrest I (Figure 8.3). The sitting venous volume was then recorded.

iii. When a steady baseline was recorded, the participant was instructed to depress the pedal with their right foot (a clicking sound donated when the pedal was fully depressed) and maintain this position for five seconds before returning their foot to the initial position of resting it on the uncompressed pedal.

iv. This procedure was then repeated until two similar EV values were recorded.

v. When a steady baseline was again recorded the participant was instructed to compress the pedal ten consecutive times. Upon completion the participant

was asked to return to the supine position on the examination couch with the right leg elevated.

vi. When a steady baseline was again recorded in the supine position, the participant was instructed to sit again in the aircraft seat and place his/her right foot on Prototype II. Procedures (ii-xi) were repeated in that order, for Prototypes II, III and IV, respectively.

vii. The participant was then instructed to return to the supine position, with the right foot resting on the support. Once a steady baseline was recorded, he/she was asked to return to the aircraft seat and place his/her foot on DA, (used in the previous two experiments). Procedures ii to xi were repeated.

viii. The participant was then instructed to return to the supine position, with the right foot resting on the support so that the RV could be recorded.

8.2. Statistical Analysis

The mean of each result (for all 18, obese, normal and contraceptive group) was determined by using equation 4.7, for example by dividing the sum of all 18 patients standing venous volume by the number of values. The standard deviation of each result (for all four groups) was determined by using equation 5.8.

The paired Student's *t*-test (equation 5.9) was used to determine the statistical significance of any comparison between any of the movements mean values. Statistical significance was accepted at the 95% confidence level ($p \leq 0.05$). With the number of degrees of freedom being 34, (for all 18 participants) the critical value of t is ± 2.032.

For the individual groups of six, with a 95% confidence level ($p \leq 0.05$), the number of degrees of freedom being ten, (for all six participants) the critical value of t is ± 2.228.

Figure 8.3. Participant resting her foot on Footrest one, whilst sitting on the aircraft seat.

8.3. Results

8.3.1. Absolute and derived results of all 18 participants

The absolute and derived values for each of the 18 participants were calculated (Appendix O). Mean values are presented in Table 8.2.

The standing VV ranged between 40 and 193 mls, mean 116.16 mls. All 18 participants had a normal VFI of less than two ml/sec.

Table 8.2. Results of all 18 volunteers.

n = 18, Mean age 35.61+/-9.58					
Standing	Mean+/-Standard deviation				
VV (mls)	116.16+/-43.76				
90%VV	104.27+/-38.18				
VFT (sec)	138.83+/-33.08				
VFI	0.89+/-0.39				
TT EV (mls)	67.22+/-37.39				
TT EVF (%)	67.22+/-17.2				
TT RV (mls)	31.11+/-20.12				
TT RVF (%)	27.94+/-18.96				
Sitting VV (mls)	94.55+/-27.07				
SITTING					
Mean +/- SD	**Footrest 1**	**Footrest 2**	**Footrest 3**	**Footrest 4**	**DA**
EV	49.61+/-30.24	44.5+/-25.5	18+/-34.54	18+/-38.69	54.27+/-26.63
EVF	49.63+/-22.09	45.81+/-18.16	42+/-19.59	44.01+/-21.3	55.65+/-19.5
RV	18+/-33.81	45.05+/-17.49	40.66+/-17.03	35.16+/-19.12	42.77+/-19.14
RVF	53.81+/-20.12	50.27+/-20.9	42.49+/-18.31	38.83+/-24.15	47.64+/-24.29

8.3.2. EVF Results of all 18 participants.

Standing EVF ranged between 37.27 and 97.95 mls, mean 67.22. Seven of the 18 participants had reduced standing EVs (less than 60mls). These were participants one, two, six, seven, 15, 16 and 17. They had EVs of 53mls, 41mls, 45mls, 53mls, 48mls, 50mls and 20mls respectively.

Sitting VV ranged between 50 and 140 mls, mean 94.55 mls. Footrest I EVF ranged between 16 and 93.93 mls, mean 49.63. Footrest II EVF ranged between 17.5 and 71.64 mls, mean 45.81 mls. Footrest III EVF ranged between 12 and 70.9 mls, mean 42 mls. Footrest IV EVF ranged between 4.21 and 89.09 mls, 44.01 mls. TJA EVF ranged between 26.59 and 94.54 mls, mean 55.65 mls

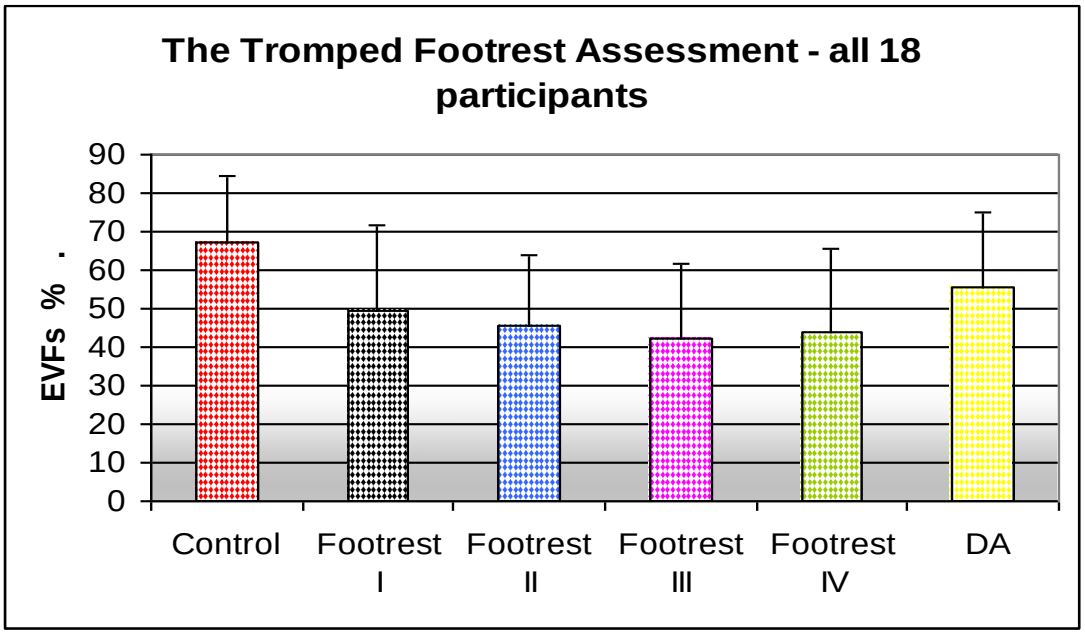


Figure 8.4. EVF obtained by tip-toe, Footrest I – IV and DA of all 18 volunteers.

Table 8.3. EVF obtained by tip-toe, Footrest I – IV and DA of all 18 volunteers.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
EVFs %	67.22	49.63	45.81	42	44.01	55.65
SD	17.2	22.09	18.16	19.59	21.3	19.5

EVF achieved by control, Footrest I – IV and DA in all 18 volunteers. Values measured by Air Plethysmograph represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

EVF within the range considered normal was only achieved by the control (tiptoe) manoeuvre which produced an EVF of 67.22±17.2. DA produced an EVF of 55.65±19.5 however this and all other devices for this study group produced results less than the range considered normal. Therefore a statistical difference was observed when control was compared to all four footrests and DA. No statistical difference exists between Footrest I and DA. However a significant difference was not observed between Footrest

I when compared to both Footrest III and Footrest IV. A significant difference was observed when Footrest II was compared to both Footrest III and Footrest IV, however no statistical difference existed when it was compared to DA. No significant difference was observed between Footrest III and Footrest IV however a significant difference existed between Footrest III and DA, also Footrest IV and DA.

8.3.3. RVF Results of all 18 participants

Standing RVF ranged between 4.44 and 87.36 mls, mean 27.94 mls. Footrest I RVF ranged between 31.81 and 90.76 mls, mean 53.81 mls. Footrest II RVF ranged between 13.2 and 93.75 mls, mean 50.27 mls. Footrest III ranged between 4.716 and 78.94 mls, mean 42.49 mls. Footrest IV ranged between 4.716 and 90.52 mls, mean 38.83 and TJA RVF ranged between 14.15 and 88.88 mls, mean 47.64 mls.

RVF within the range considered normal was only achieved by control (tiptoe) with a value of 27.94±18.96. A significant difference exists between control and Footrest I. Even though Footrest II, III and IV and DA produced RVFs which are not considered within the normal range, no significant difference exists between them and control.

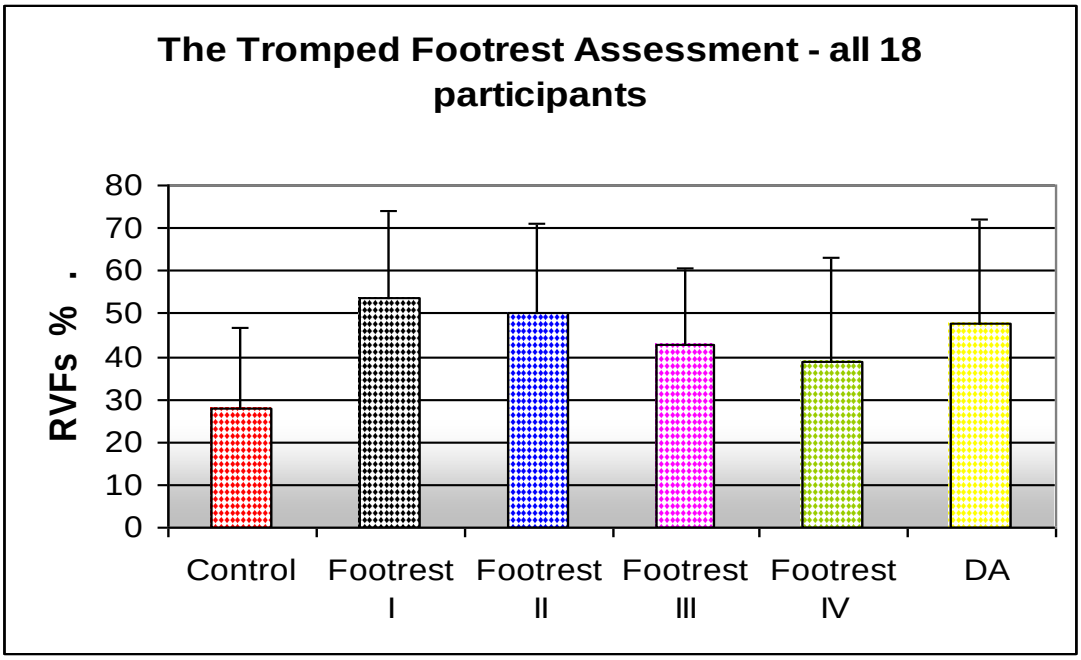


Figure 8.5. RVF obtained by tip-toe, Footrest I – IV and DA of all 18 volunteers.

Table 8.4. RVF obtained by tip-toe, Footrest I – IV and DA of all 18 volunteers.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
RVFs %	27.94	53.81	50.27	42.49	38.83	47.64
SD	18.96	20.12	20.9	18.31	24.15	24.29

RVF achieved by control, Footrest I – IV and DA in all 18 volunteers. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

A significant difference at the five percent level exists between Footrest I when compared to Footrest II, III, IV and DA. No significant difference was observed between all other device results when compared (Table 8.5).

Table 8.5. Comparison of EV and RV for all 18 participants.

Maneouvre	*t* value EV		*t* value RV	
Comparison of tiptoe standing V's Footrest I	2.597	S	1.413	NS
Comparison of tiptoe standing V's Footrest II	3.238	S	-2.218	S
Comparison of tiptoe standing V's Footrest III	5.088	S	-1.537	NS
Comparison of tiptoe standing V's Footrest IV	4.813	S	-0.619	NS
Comparison of tiptoe standing V's Test Jig A	2.29	S	-1.78	NS

Critical value at 5 percent significance level = 2.032

8.3.4. Results of the Normal Group

The absolute and derived values for the Normal study group can be found in Appendix P.

Mean values are presented in Table 8.6.

Table 8.6. Results of the Normal study group

n=6, Mean age 41.83+/-8.85					
Standing	Mean+/-Standard deviation				
VV (mls)	**135.66+/-42.11**				
90%VV	**121.26+/-38.9**				
VFT (sec)	**129.16+/-24.61**				
VFI	**1.041+/-0.293**				
TT EV (mls)	**94.66+/-49.72**				
TT EVF (%)	**65.74+/-16**				
TT RV (mls)	**31.5+/-8.13**				
TT RVF (%)	**26.3+/-12.91**				
Sitting VV (mls)	**95.33+/-28.56**				
SITTING					
Mean +/- SD	**Footrest 1**	**Footrest II**	**Footrest III**	**Footrest IV**	**DA**
EV	56.5+/-32.96	45+/-24.7	44.33+/-20.97	45+/-18.01	51.83+/-25.55
EVF	59.27+/-23.06	46.57+/-17.98	47.97+/-18.26	48.79+/-15.5	53.89+/-19.5
RV	48.33+/-13.73	45.66+/-13.09	44.5+/-10.22	30.33+/-12.14	45.5+/-14.77
RVF	54.24+/-16.89	51.99+/-21.71	39.66+/-16.52	35.84+/-18.93	52.48+/-22.43

Standing VV ranged between 87 and 193 mls, mean 135.66 mls. All participants had normal VFIs.

8.3.4.1. EVF Results of the Normal Group

Standing EVF ranged between 48.62 and 93.26 mls, mean 65.74 mls. Participants one, six, seven and 13 had abnormal EVs of 53 mls, 45 mls, 53 mls and 180 mls respectively. Sitting VV ranged between 54 and 132 mls, mean 95.33 mls. Footrest I EVF ranged between 27.65 and 93.93 mls, mean 59.27 mls. Footrest II EVF ranged between 23.4 and 70.45 mls, mean 46.57 mls. Footrest III EVF ranged between 17.02 and 70.31 mls, mean 47.97 mls. Footrest IV EVF ranged between 24.46 and 67.18 mls, mean 48.79 mls and DA EVF ranged between 26.59 and 90.56 mls, mean 53.89 mls.

EVF within the range considered normal was only achieved by the control (tiptoe) manoeuvre. Footrest I produced an EVF of 59.27±23.06, however this is slightly less than the range considered normal which is greater or equal to 60 percent. DA produced an EVF of 53.89± 19.5, which is less than the normal range. A statistical difference at the 5 percent level was observed between control and Footrest III and control and Footrest IV.

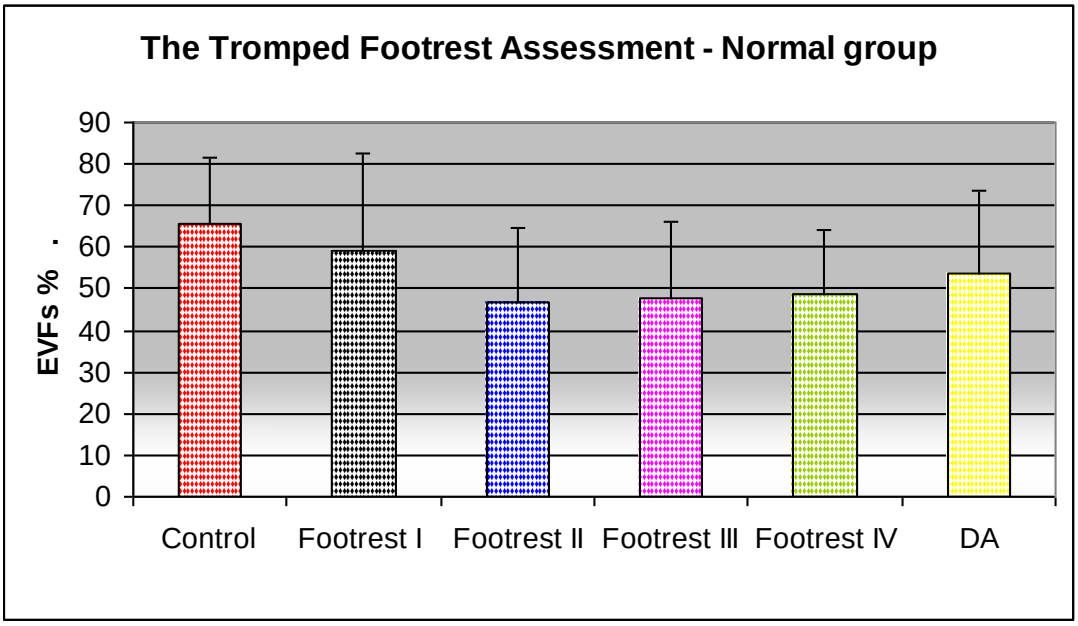


Figure 8.6. EVF obtained by tip-toe, Footrest I – IV and DA in the Normal group.

Table 8.7. EVF obtained by tip-toe, Footrest I – IV and DA in the Normal group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	TJA
EVFs %	65.74	59.27	46.57	47.97	48.79	53.89
SD	16	23.06	17.98	18.26	15.5	19.5

EVF achieved by control, Footrest I – IV and the Demonstrator A in the Normal study group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

8.3.4.2. RVF Results of the Normal Group

Standing RVF ranged between 12.95 and 52.87 mls, mean 26.3 mls. Footrest I RVF ranged between 27.27 and 78.72 mls, mean 54.24 mls. Footrest II RVF ranged between 27.27 and 93.75 mls, mean 51.99 mls. Footrest III RVF ranged between 34.09 and 67.02 mls. Footrest IV RVF ranged between 9.52 and 66.66 mls, mean 35.84 and DA RVF ranged between 20.32 and 88.88 mls, mean 52.48 mls.

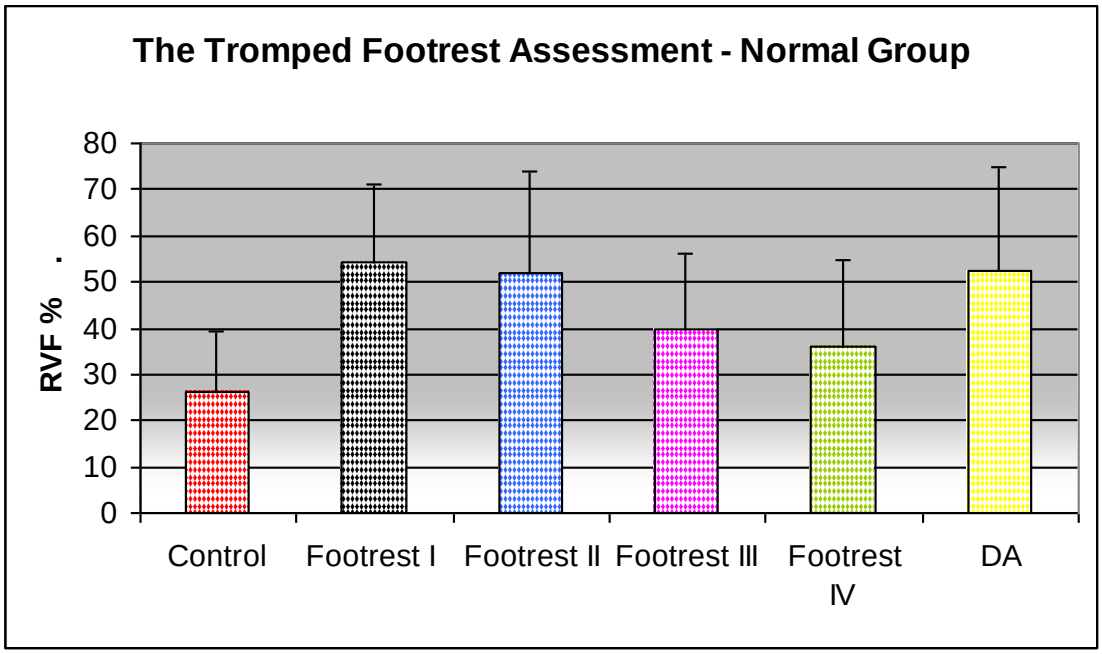


Figure 8.7. RVF obtained by tip-toe, Footrest I – IV and DA in the Normal group.

Table 8.8. RVF obtained by tip-toe, Footrest I – IV and DA in the Normal group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
RVFs %	26.3	54.24	51.99	39.66	35.84	52.48
SD	12.91	16.89	21.71	16.52	18.93	22.43

RVF achieved by control, Footrest I – IV and DA in the Normal study group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was only achieved by the control (tiptoe) manoeuver. Footrest IV produced a RVF of 35.84±18.93 however this is slightly greater than the range considered normal which is less than 35 percent. A statistical difference at the five percent level was observed between control and Footrest I, control and Footrest II, control and Footrest III and between Footrest I and Footrest IV (Table 8.9).

Table 8.9. Comparison of EV and RV for the Normal group.

Maneouvre	*t* value EV		*t* value RV	
Comparison of tiptoe standing V's Footrest I	1.56	NS	-2.58	S
Comparison of tiptoe standing V's Footrest II	2.19	NS	-2.25	S
Comparison of tiptoe standing V's Footrest III	2.28	S	-2.44	S
Comparison of tiptoe standing V's Footrest IV	2.3	S	0.196	NS
Comparison of tiptoe standing V's DA	1.876	NS	-2.03	NS

Critical value at 5 percent significance level = 2.228

8.3.5. Results of the Obese Group

The absolute and derived values for the obese group can be found in Appendix Q. Mean values are presented in Table 8.10. Standing VV ranged between 81 and 175 mls, mean 116.16 mls. All six of the obese study group had a normal VFI.

8.3.5.1. EVF Results of the Obese Group

Standing EVF ranged between 54.28 and 97.5 mls, mean 67.22 mls. All six of this study group had normal standing EVs ranging between 60 and 96 mls, mean 85.83 mls. The sitting VV ranged between 80 and 146 mls, mean 107.83 mls. Footrest I EVF ranged between 37.89 and 76.36 mls, mean 58.53 mls. Footrest II EVF ranged between 21.05 and 69.09 mls, mean 49.44 mls. Footrest III EVF ranged between 14.75 and 70.9 mls, mean 47.72 mls. Footrest IV EVF ranged between 4.21 and 89.09 mls, mean 46.68 mls and DA EVF ranged between 38.75 and 94.54 mls, mean 62.71 mls (Figure 8.8 and Table 8.11).

Table 8.10. Results of the Obese Study Group

n = 6, Mean age 39+/-7.02, Mean BMI of 36.15+/-7.03	
Standing	Mean+/-Standard deviation
VV (mls)	**117.33+/-36.25**
90%VV	**105.6+/-32.63**
VFT (sec)	**151.66+/-43.46**
VFI	**0.8946+/-0.498**
TT EV (mls)	**85.83+/-13.92**
TT EVF (%)	**77.148+/-16.46**
TT RV (mls)	**22.16+/-21.59**
TT RVF (%)	**19.328+/-12.29**
Sitting VV (mls)	**107.83+/-20.03**

SITTING					
Mean +/- SD	**Footrest 1**	**Footrest 2**	**Footrest 3**	**Footrest 4**	**DA**
EV	63.16+/-16.98	55.16+/-25.8	51.66+/-22.87	52.66+/-32.98	68.33+/-24.53
EVF	58.53+/-12.61	49.44+/-17.07	47.22+/-18.76	46.68+/-26.01	62.71+/-19.54
RV	43.66+/-16.74	45.66+/-23.66	38.16+/-24.34	42.33+/-28.08	37.33+/-23.52
RVF	40.75+/-14.94	42.05+/-22.44	35.31+/-23.19	39+/-27.59	33.51+/-17.25

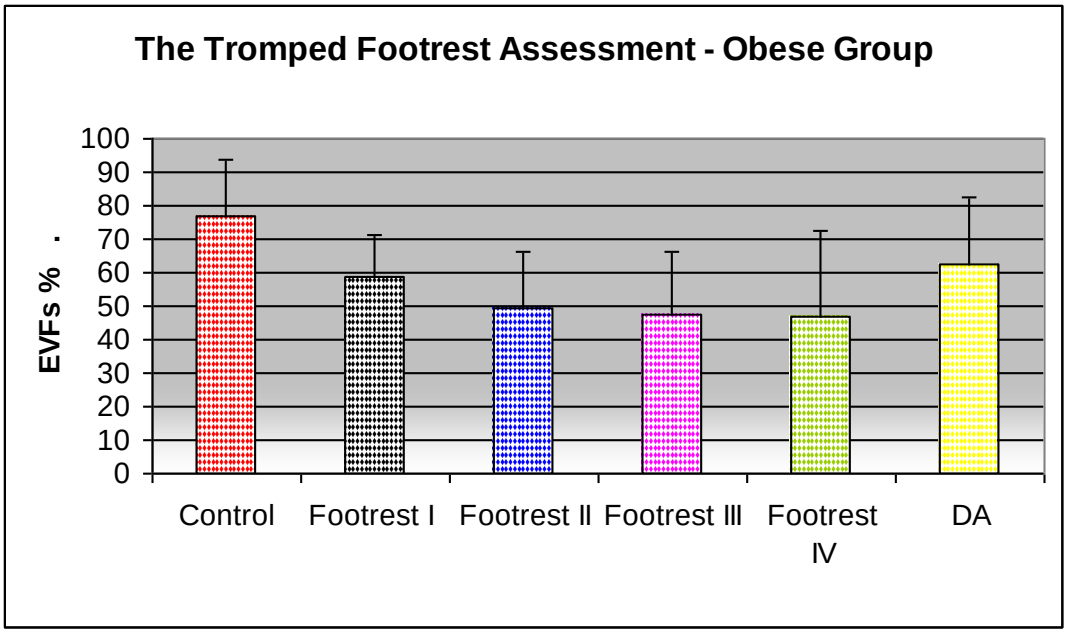


Figure 8.8. EVF obtained by tip-toe, Footrest I – IV and DA in the obese group.

Table 8.11. EVF obtained by tip-toe, Footrest I – IV and DA in the obese group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
EVFs %	77.148	58.53	49.44	47.22	46.68	62.71
SD	16.46	12.61	17.07	18.76	26.01	19.54

EVF achieved by control, Footrest I – IV and Demonstrator A in the Obese group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

EVF within the range considered normal was achieved by the control (tiptoe) manoeuver and DA. DA produced an EVF of 62.71±19.54. Footrest I produced an EVF of 58.53 ± 12.61, which is less than the range considered normal. Therefore a significant difference at the five percent level between control and each of the four Footrests was observed. However no statistical difference between control and DA was observed. A statistical difference at the five percent level was observed between Footrest I and Footrest III and Footrest III and DA (Table 8.13).

8.3.5.2. RVF Results of the Obese Group

Standing RVF ranged between 4.44 and 31.42 mls, mean 19.328 mls. Footrest I RVF ranged between 18.86 and 68.42 mls, mean 40.75 mls. Footrest II RVF ranged between 13.2 and 83.15 mls, mean 42.05 mls. Footrest III RVF ranged between 4.716 and 78.94 mls, mean 35.31 mls. Footrest IV RVF ranged between 4.716 and 90.52 mls, mean 39 and DA RVF ranged between 14.15 and 56.84 mls, mean 33.51 mls.

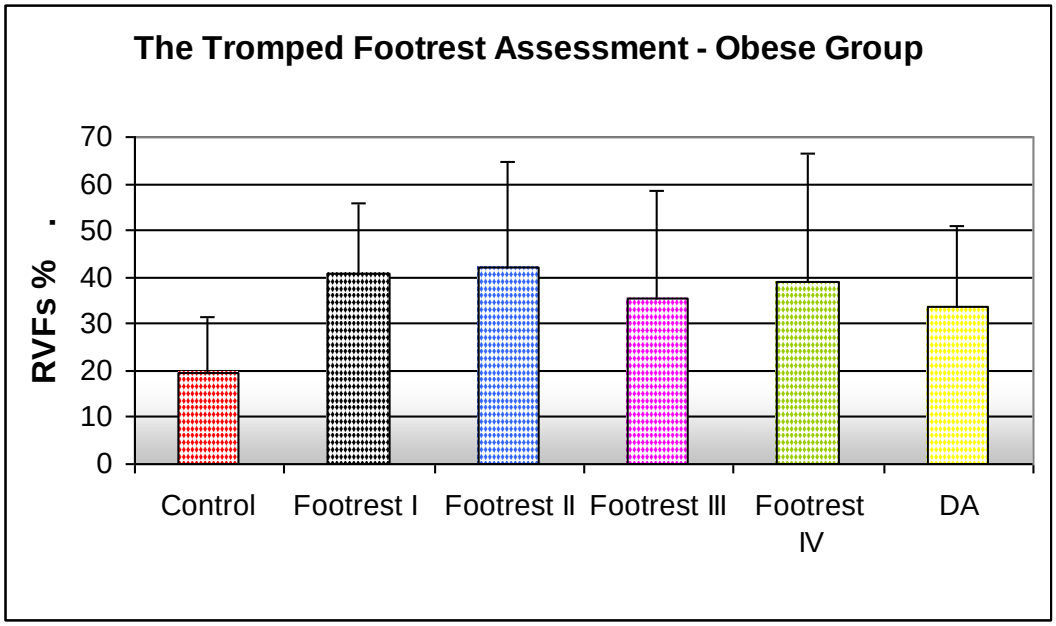


Figure 8.9. RVF obtained by tip-toe, Footrest I – IV and DA in the obese group.

Table 8.12. RVF obtained by tip-toe, Footrest I – IV and DA in the obese group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
RVFs %	19.328	40.75	42.05	35.31	39	33.51
SD	12.29	14.94	22.44	23.19	27.59	17.25

RVF achieved by control, Footrest I – IV and D A in the Obese group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was achieved by the control (tiptoe) maneouver and DA. The most efficient maneouver to control was DA with an RVF of 33.51±17.25. Footrest III produced an RVF of 35.31 ± 23.19, which is slightly greater than the normal range of less than 35 percent. No significant difference at the five percent level between any of the devices was observed (Table 8.13).

Table 8.13. Comparison of EV and RV for the Obese group.

	t value EV values		*t* value RV values	
Comparison of tiptoe standing V's Footrest I	2.529	S	-0.191	NS
Comparison of tiptoe standing V's Footrest II	2.56	S	-1.797	NS
Comparison of tiptoe standing V's Footrest III	4.6	S	-1.204	NS
Comparison of tiptoe standing V's Footrest IV	2.269	S	-1.394	NS
Comparison of tiptoe standing V's DA	1.519	NS	-1.163	NS

Critical value at 5 percent significance level = 2.228

8.3.6. Results of the Oral contraceptive group

The absolute and derived values for the oral contraceptive group can be found in Appendix AIII. Mean values are presented in Table 8.11. Standing VV ranged between 40 and 165 mls, mean 95.5 mls. All participants had normal VFIs.

8.3.6.1. EVF Results of the Oral contraceptive group

Participants ten and 17 had abnormal EVs of 165 and 40 mls respectively. This is not surprising as oestrogens (contraceptive pill) induce hypercoagulation (Tibbs, 1992). Participant ten's abnormality may be attributed to the pill. Participant 17 appears to have been nervous or had balance which resulted in her tensing her muscles impairing venous flow.

Standing EVF ranged between 37.27 and 80 mls, mean 58.78 mls. Sitting VV ranged between 50 and 130 mls, mean 80.83 mls. Footrest I EVF ranged between 16 and 67.69 mls, mean 31.14 mls. Footrest II EVF ranged between 17.5 and 66 mls, mean 41.14 mls. Footrest III EVF ranged between twelve and 65.38 mls, mean 30.91 mls. Footrest IV EVF ranged between 22.38 and 76.92 mls, mean 36.55 mls and TJA EVF ranged between 27.69 and 81.25 mls, mean 50.36 mls.

Table 8.14 Results of the Oral Contraceptive study group.

n = 6, Mean age 26+/-1.35.					
Standing	Mean+/-Standard deviation				
VV (mls)	**95.5+/-46.02**				
90%VV	**85.95+/-34.18**				
VFT (sec)	**135.66+/-53.82**				
VFI	**0.734+/-0.327**				
TT EV (mls)	**56.66+/-27.13**				
TT EVF (%)	**58.78+/-13.76**				
TT RV (mls)	**39.66+/-22.99**				
TT RVF (%)	**41.92+/-20.75**				
Sitting VV (mls)	**80.83+/-25.68**				
SITTING					
Mean +/- SD	**Footrest 1**	**Footrest 2**	**Footrest 3**	**Footrest 4**	**Test Jig A**
EV	29.16+/-26.81	33.33+/-20.87	28.66+/-25.99	33.33+/-30.21	42.66+/-23.11
EVF	31.14+/-16.75	41.14+/-17.64	30.91+/-17.5	36.55+/-18.93	50.36+/-17.25
RV	51.5+/-16.13	43.83+/-13.56	39.33+/-12.28	32.83+/-19.58	45.5+/-16.83
RVF	66.27+/-19.4	56.5+/-14.77	49.38+/-11.66	41.65+/-24.75	56.87+/-14.11

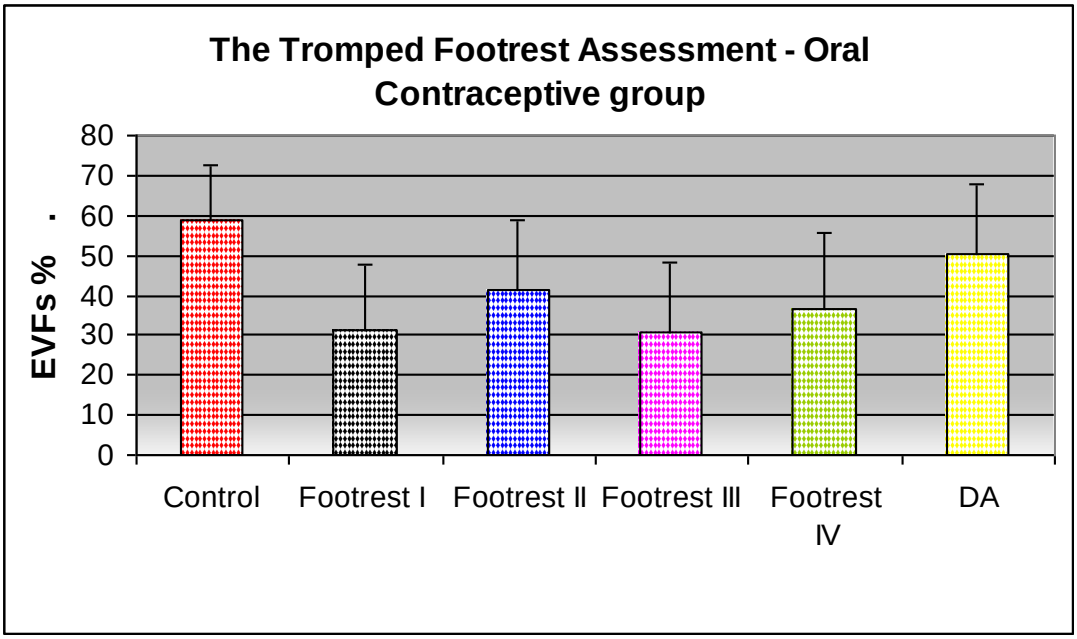


Figure 8.10. EVF obtained by tip-toe, Footrest I – IV and DA in the Oral Contraceptive group.

Table 8.15. EVF obtained by tip-toe, Footrest I – IV and DA in the Oral Contraceptive group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	DA
EVFs %	58.78	31.14	41.14	30.91	36.55	50.36
SD	13.76	16.75	17.64	17.5	18.93	17.25

EVF achieved by control, Footrest I – IV and the Tromped Demonstrator A by the Oral contraceptive group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

EVF within the range considered normal was not achieved by any of the manoeuvers, including control. Control did achieve an EVF of 58.78±13.76, which is less than the range considered normal (greater than 60 percent). No significant difference at the five percent level between control and the five devices was observed (Table 8.17).

8.3.6.2. RVF Results of the Oral contraceptive group

Standing RVF ranged between 27.27 and 87.36 mls, mean 41.92 mls. Footrest I RVF ranged between 38.8 and 90.76 mls, mean 66.27 mls. Footrest II RVF ranged between 33.07 and 74.19 mls, mean 56.5 mls. Footrest III RVF ranged between 34.61 and 62.68 mls, mean 49.38 mls. Footrest IV RVF ranged between 7.69 and 70 mls, mean 41.65 mls and DA RVF ranged between 40.76 and 80.64 mls, mean 56.87 mls.

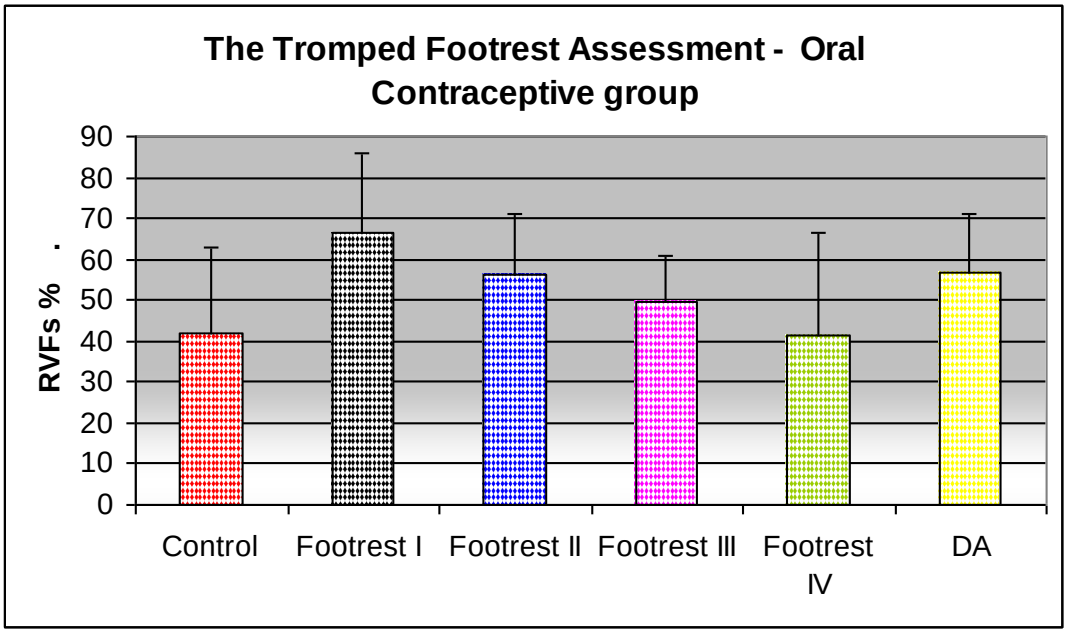


Figure 8.11. RVF obtained by tip-toe, Footrest I – IV and DA in the Oral Contraceptive group.

Table 8.16 RVF obtained by tip-toe, Footrest I – IV and DA in the Oral Contraceptive group.

	Control	Footrest I	Footrest II	Footrest III	Footrest IV	TJA
RVFs %	41.92	66.27	56.5	49.38	41.65	56.87
SD	20.75	19.4	14.77	11.66	24.75	14.11

RVF achieved by control, Footrest I – IV and the Tromped Test Jig A in the Oral contraceptive group. Values measured by Air Plethysmograph are represented as a fraction of the venous volume and expressed in percentage (%) and reported as Mean +/- SD.

RVF within the range considered normal was not achieved by any of the manoeuvers, including control. No statistical difference between control and the five devices was observed (Table 8.17).

Table 8.17 Comparison of EV and RV for the Oral Contraceptive group.

	t value EV values		*t* value RV values	
Comparison of tiptoe standing V's Footrest I	1.76	NS	-1.032	NS
Comparison of tiptoe standing V's Footrest II	1.66	NS	-0.3826	NS
Comparison of tiptoe standing V's Footrest III	1.82	NS	0.031	NS
Comparison of tiptoe standing V's Footrest IV	1.4	NS	0.554	NS
Comparison of tiptoe standing V's DA	0.962	NS	-0.502	NS

Critical value at 5 percent significance level = 2.228

8.3.7. Results of all four study groups

8.3.7.1 EVF Results comparing all four study groups

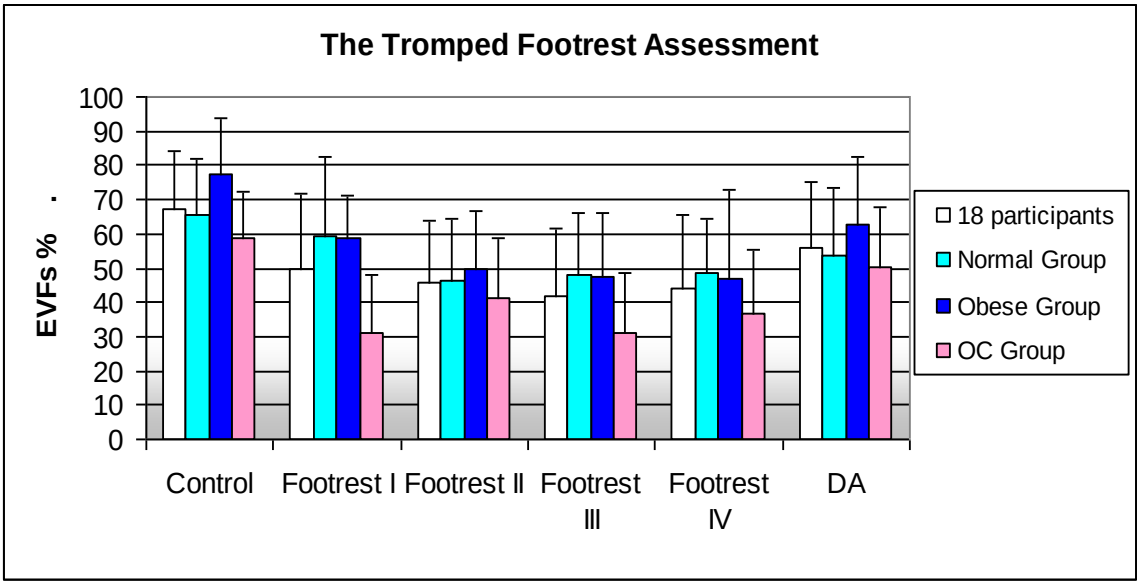


Figure 8.12. Comparison of the four groups EVFs for control, Footrest I – IV and DA.

The control (tiptoe) movement produced a mean EVF of 67.22±17.2 in all eighteen volunteers. As can be seen from all the results (except in the case of the obese group) neither of the four Tromped footrests, or DA produced an EVF greater than 60 percent.

8.3.7.2. RVF Results of all four study groups

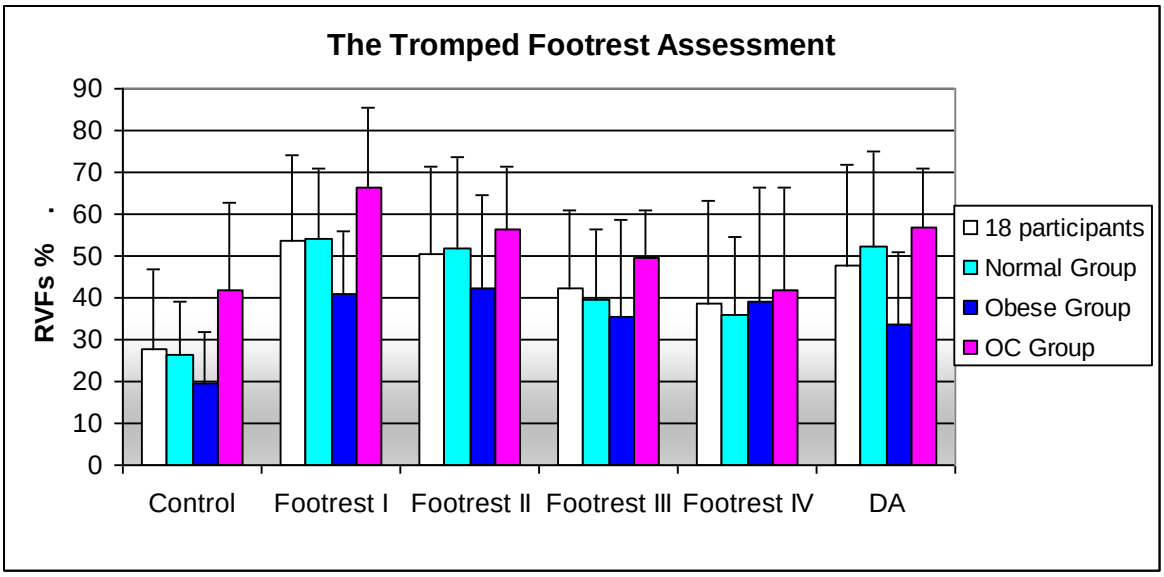


Figure 8.13. Comparison of the four groups RVFs for control, Footrest I – IV and DA.

The control (tiptoe) movement produced a mean RVF of 27.94±18.96in all eighteen volunteers. As can be seen from all the results (except in the case of the obese group) neither of the four Tromped footrests, or DA produced a RVF less than 35 percent.

8.4. Discussion

The standing tiptoe movement acted as control, as they did in the previous experiments, and were used to compare the results obtained from all four footrests and DA, to determine if any of the footrest prototypes were as efficient as tiptoe and the Tromped.

As previously stated, both the calf muscle pump (refer to section 2.6.3) in conjunction with respiratory muscle pump (section 2.3.2) facilitate the return of blood to the heart Miller *et al.*, (2005). Sitting in an aircraft seat can affect the blood flow in the lower extremites in a negative way, due to the incline in the aircraft seat.

The previous two assessments conducted with DA produced adequate results, all ten participants were required to sit on the examination couch which had a level surface while using DA. The only difference with this experiment was that the examination couch was replaced with aircraft seats. These aircraft seats had a width of 560mm, the distance from the front edge of the seat to the back cushion was 550mm. Owing to the design of the seat incline (Figure 8.14), the participants knees were 40mm higher than the underneath of their buttocks. It is hypothesised that this incline of 40mm prevented normal return of blood to the heart, therefore, affecting normal respiration while restricting the gastrointestinal transit and normal blood circulation of all the 18 participants who took part in this assessment (Hinninghofen & Enck, 2006).

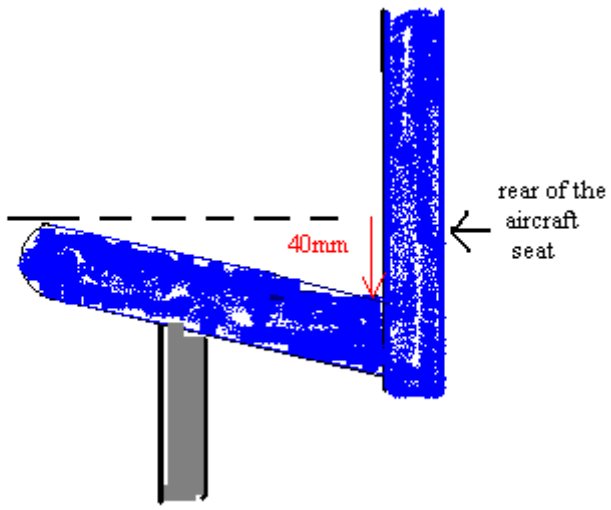


Figure 8.14. Incline of the Aircraft Seat.

Further research conducted to compare venous return in various seat designs both with and without using the Footrest Test Jigs in the seated position is recommended.

The obese group produced a control mean EVF of 77.148±16.46 and a mean RVF of 19.328±12.29. Footrest Pedal I produced a mean EVF of 58.33±12.61 which was

promising however the mean RVF of 40.75±14.94 was not satisfactory as it was above the required value of 35 percent. Tromped footrests II to IV were not efficient at creating sufficient venous return. DA was efficient for this group alone when used *in-situ* in an aircraft seat, at promoting sufficient venous return. It produced a mean EVF of 62.71±19.54 and an adequate mean RVF of 33.51±17.25.

The aircraft seat may not have interfered in venous return of obese people, as they would have larger buttocks and larger thighs than the other participants, thus reducing the angle of decline in the seat and the affect of poor circulation the other participants experienced.

8.5. Conclusion

The objective of the assessment was to determine if any of the four Tromped footrests (section 4.10) are as effective as DA and tiptoe control manoeuver and to determine which gives the greatest venous emptying.

Activation of the CMPF did achieve venous return from the calf area, however only as far as the thigh area, which could predispose a passenger to proximal DVT.

CHAPTER 9

CONCLUSIONS & RECOMMENDATIONS

9.0. Conclusions

Death resulting from long haul flight has been established. This dissertation describes research to produce and evaluate an in-flight exercise device to alleviate FRDVT. Airlines recommend in-flight exercises during flight. These consist of plantar flexion (pressing the balls of ones feet against the ground) and dorsiflexion (raising the toes off the ground). Thus a spring loaded novel prototype device "The Tromped" was envisaged which would allow the user to replicate both of these manoeuvres when used on board commercial aircraft but gain greater benefit from being required to do more work. This research hypothesised that compression of a spring loaded pedal, while seated, would activate the calf muscle pump initiating venous return.

An attempt to conduct an in-flight assessment was unsuccessful. Airlines, the Irish Air Corps, the Royal Air Force and an American University were all lobbied towards this aim. Unfortunately none of the airlines were interested as they will not accept liability for this life threatening syndrome. The Irish Air Corp, the RAF and Perdue University exhausted all measures in an attempt to collaborate with this research. However flight duration and access to a hospital with ultrasound machinery and specialised medical requirements posed a problem.

It is important to realise that DVT may be symptomatic and asymptomatic. It is as a result of the latter, that it is impossible to determine a specific incidence of FRDVT. Travellers may have a DVT for up to two to three weeks after a flight before they become

aware of their condition. Other travellers may develop an embolus, which can then kill if it becomes lodged in an artery of the lung.

This body of research could be used to increase FRDVT awareness as set out in the Research objectives, section 1.1.2. and has led to these conclusions:

i. FRDVT is a real problem, one which is killing air passengers and will continue to do so if some form of prophylaxis is not developed for commercial use on commercial aircraft;

ii. Plantar flexion against a predetermined resistance of 94.31 N to deflect the spring by a height of 63.39mm, when seated on a level seat can effectively replicate normal venous ambulation in healthy individuals. However when used in an aircraft seat, it only appears efficient at promoting sufficient venous return in the obese. Therefore this research has established that FRDVT has a third causative factor, in the configuration of the aircraft seat.

iii. If a form of in-flight prophylaxis is one day available on board commercial aircraft, its design will be influenced by aircraft design requirements, legislation, medical evidence and both airline and consumer acceptance. Ruling out commercial and social factors to alleviate this problem is impossible.

iv. Compression of the Tromped footrest pedal with springs of Force ranging from 112.73N to 141.32N and free lengths of 27-53.5mm in an aircraft seat, cannot replicate normal venous ambulation and so recommendations for further research in this area is necessary.

FRDVT is a real problem and knowledge of its true incidence is required.

In the context of FRDVT prophylaxis, mechanical methods would seem most attractive, however no ideal device has of yet been described. Air volume systems, Lym Gym, Airogym and Veinguard were all investigated. However as each of these devices aim to increase flow in the seated position by movement of air in a partially inflated system, they are unsuitable for use in flight. The changes in air pressure which occur with different altitudes result in inconsistent work achieved by movements. This increases the difficulty quantifying the amount of work required to effectively achieve the CMPF, thus reducing venous stasis adequately.

The Skywalker's pedals are not securely attached to the base. The semi-circular pivot is detachable which means the design does not conform to aviation standards. A device such as the Novamedix A V impulse system, in its present form is unsuitable for use during flight due to the air compressor. Hence the need for a more suitable in-flight device along mechanical lines that will adequately activate the calf muscle pump function and result in sufficient venous return.

Proprietors, executives of airlines and every court in the world, need to be informed that an episode of DVT may lead to death by PE, and that every survivor of a DVT is at risk of life long health problems. If an airline passenger suffers from a first event of DVT they may suffer the consequences of this for the rest of their lives in the form of chronic venous disease. This will not only inhibit the distance that they can walk due to pain and swelling (Neglén, 2003, Padberg *et al.*, 2003,) and IC (Tibbs, 1992), but could lead to complications such as ulceration possibly (Ramaswamai and Nicolaides, 1994; Meissner, 2002), and the increased chance of developing recurrent thrombi, which could kill eventually.

9.1. Recommendations

Further research should be conducted. It is proposed that it concentrates on the following four areas:

i. Various seat types, (to be used on board commercial aircraft) especially ones with no dip in the seat cushion, or possibly with dips of only ten or 20mm, should be assessed with the APG and volunteers of varying weight, height, age and medical status should be used to determine which is optimal for normal venous return;

ii. Re-conduct the Tromped Footrest assessment, with springs of stronger stiffness to determine if this design could be effective for use on board commercial aircraft;

iii. Investigate the efficiency of the Tromped in new study groups; such as those with genetic defects associated with thrombi development, obese women, obese women on the pill, groups of various height such as under 1.5m and over 1.9m;

iv. Conduct an in-flight assessment with an optimised Tromped footrest.

This body of research has led to the following general recommendations:

i. Some form of prophylaxis should be made available to the general flying public by the airlines to prevent against FRDVT.

ii. It is necessary that a system of logging incidences of medical DVT and PE and FRDVT and PE into a database becomes compulsory. This must be conducted at national and international level, as the full extent of the seriousness of DVT and PE will never be realised until this recommendation is put into effect. Factors such as number of flights flown, dates of travel,

duration of flights taken and hours spent in airports as well as if economy or business class flown should be documented.

iii. It should be mandatory world wide that all medical episodes or instances which occur on board an aircraft be documented in full. Where a death may occur on an aircraft or in the airport grounds, a post mortem should be mandatory, with the results of the post mortem then logged into the system.

iv. In-depth research should be conducted to redesign aircraft seats so that they can be both comfortable and conducive to facilitating venous return to the heart.

v. An international minimum standard size passenger space of at least 760mm (30 inches) should be made obligatory, out of a duty of care to passengers for both safety reasons and comfort levels.

vi. Government spending both at a national and international level is recommended in conjunction with airline spending to tackle the medical problems associated with flying both short haul and long haul flights.

REFERENCES

About Air Springs (28/01/04). [Online]. Available:http://mechanical-components.globalspec.com/LearnMore/Mechanical_Components/Springs/ (at 2/04/04)

ABS Material, http://www.eurapipe.com.au/cd/Eurapipe/Material_page1_files/image002.gif (2/11/04)

Advisory Council for Aeronautics Research in Europe (ACARE). (2002). *Strategic Research Agenda, Volume 2.*

Aerospace Medical Association (AMA). Medical Guidelines Task Force. (2nd ed). (2003). "Medical Guidelines for Airline Travel". *Aviation, Space and Environmental Medicine.* 74 (5), II, A-A18. [Online]. Available: http://www.asma.org.pdf/publications/medguid.pdf (at 25/1/07).

Agu, O., Hamilton, G., Baker, D. (1999). "Graduated compression stockings in the prevention of venous thromboembolism" *B J Surg*, 86, 992-1004.

Airogym™ [Online]. Available: (http://www.airogym.com/whatisit.php).

"Airogym™ DVT Exercise Cushion – Clinical Trials". (2007). [Online]. Available: http://www.airogym.com/trials.php (at 17/02/07).

Anderson, F. A., Spencer, F. A. (2003). "Risk Factors for Venous Thromboembolism", *Circulation*, 107, I-9 – I-16.

Anderson, F. A., Audet, A. M. (1998) *Best Practices- Preventing Deep Vein Thrombosis and Pulmonary Embolism. A practised Guide to Evaluation and Improvement.* Centre for Outcomes Research, University of Massachusetts Medical School. [Online] Available: http://www.outcomes-umassmed.org/dit/best-practice/manual.cfm (at 23/08/05)

Arsov, T., Miladinova, D., Spiroski, M. (2006). "Factor V Leiden is Associated with Higher Risk of Deep Venous Thrombosis of Large Blood Vessels". *Croat Med J.* 47, 433-9.

Aryal, K. R., Al-khaffaf, H. (2006). "Venous Thromboembolic Complications Following Air Travel: What's the Quantitative Risk? A Literature Review". *Eur J Vasc Endovasc Surg*. 31, 187-199.

Aznar, J., Vayá, A., Estellés, A., Mira, Y., Segí, R., Villa, P., Ferrando, F., Falcó, C., Corella, D., Espańa, F. (2000). "Risk of venous thrombosis in carriers of the prothrombin G20210A variant and factor V Leiden and their interaction with oral contraceptives". *Haematologica* 85 (12), 1271-76.

Bagshaw, M. (1996). "Jet leg, pulmonary embolism, and hypoxia". *The Lancet* 348, p.415.

Bagshaw, M. (2001). "Travellers thrombosis: a review of deep vein thrombosis associated with travel". *Aviat Space Environ Med*. 72 (9), 848-51.

Baron, J. A., Gridley, G., Weiderpass, E., Nyrén, O., Linet, M. (1998). "Venous thromboembolism and cancer". *The Lancet*. 351, 1077-80.

Barton, M., Dubey, R. K. and Traupe T. (2002). "Oral contraceptives and the risk of thrombosis and atherosclerosis". *Expert Opin. Investig. Drugs* 11, (3), 329-332.

Bastounis, E. A., Karayiannakis, A. J., Makri, G. G., Alexiou, D., Papalambros, E. L. (1996). "The incidence of occult cancer in patients with deep venous thrombosis: a prospective study". *Journal of Intern Med*. 239, 153-56.

Bays, R. A., Healy, D. A., Atnip, R. G., Neumyer, M., Thiele, B. L. (1994). "Validation of air plethysmograph, photoplethysmograph, and duplex ultrasonography in the evaluation of severe venous stasis" *J Vasc Surg*, 20, 721-7.

Beauchamp, T. L., Childress, J. F. (5^{th} ed). (2001). *Principles of Biomedical Ethics*. New York. Oxford University Press, Inc.

Belcaro, G., Nicolaides, A. N., Veller, M. (1995). *Venous Disorders A Manual of Diagnosis and Treatment.* London. W. B. Saunders Company Ltd.

Belcaro, G., Geroulakos, G., Nicolaides, A. N., Myers, K. A., Winford, M. (2001a). "Venous thromboembolism from Air Travel, LONFLIT Study" *Angiology* 52 (6) 369-374.

Belcaro, G., Geroulakos, G., Nicolaides, A. N., Myers, K. A., Winford, M. (2001b). "Venous thromboembolism from Air Travel, LONFLIT Study 2: Prospective, Randomised Evaluation of the Effect of Elastic Compression to Prevent Flight DVT" *Angiology* 52 (6) 371-374.

Belcaro, G., Cesarone, M. R., Shah, S. S. G., Nicolaides, A. N., Geroulakos, G., Ippolito, E., Winford, M., Lennox, A., Pellegrini, L., Brandolini, R., Myers, K. A., Simeone, E., Bavera, P., Dugall, M., Di Renzo, A., Moia, M. (2002). "Prevention of edema, flight microangiopathy and venous thrombosis in long flights with elastic stockings. A randomized trial. The LONFLIT 4 Concorde Edema-SSL Study". *Angiology*. 53 (6) 635-645.

Belcaro, G., Cesarone, M. R., Nicolaides, A. N., Ricci, A., Geroulakos, G., Acerbi, G., Candiani, C., Griffin, M., Bavero, P., Dugall, M., Brandolini, R., Renzo, A. Di., Ricci, A., Ippolito, E., Winford, M., Golden, G. (2003a). "The LONFLIT 4 – VENORUTON Study A Randomized Trial Prophylaxis of Flight-Edema in Normal Subjects". *Clin Appl Thromb Hemost*. 9 (1), 19-23.

Belcaro, G., Cesarone, M. R., Nicolaides, A. N., Ricci, A., Geroulakos, G., Shah, S. S. G., Ippolito, E., Myers, K. A., Bavera, P., Dugall, M., Moia, M., Renzo, A. Di., Erichi, B. M., Brandolini, R., Dugall, M. (2003b). "Prevention of Venous Thrombosis with Elastic Stockings During Long-Haul Flights: The LONFLIT 5 JAP Study". *Clin Appl Thromb Haemost*. 9 (3), 197-201.

Belvís, R., Masjuan, J., García-Barragán, N., Cocho, D., Martí-Fàbragas, J., Santamaría, A., Leta, R. G., Martínez-Castrillo, J. C., Fernández-Ruiz, L. C., Gilo, F., Martí-Vilalta,

J. L. (2005). “Stroke and pulmonary thromboembolism after a long flight”. *European Journal of Neurology* 12: 732-34.

Bergqvist, D. (2003/2004). “Assessment of the Risk and the Prophylaxis of Venous Thromboembolism in Surgical Patients”. *Pathophysiol Haemost Thromb*. 33, 358-61.

Blombery, B. and McGrath, B. (2000). “Chronic venous insufficiency in post-thrombotic patients”*Clinical Science* 98, 445-47.

BMA (2004). “The impact of flying on passenger health: a guide for healthcare professionals” [Online]. Available: http://www.bma.org.uk/ap.nsf/AttachmentsByTitle/PDFFlying/$FILE/Impactof flying.pdf (at 07/01/06).

Bockenstedt, P. (2003). “D-Dimer in Venous Thromboembolism”. *N Eng J Med*. 349 (13), 1203 – 1204.

Boeing.com (2008). *Aircraft seats attached to the floor seat tracking.* [Online]. *Available:* http://www.boeing.com/companyoffices/gallery/images/commercial/767400-27.html (at 19/11/08).

Bongiovanni, C. M. (2002). “Venous Disease: Lifestyle and Other Risk Factors”. *J Vasc Tech.* 26 (3), 213 -217.

Browse, N. L., Burnand, K. G., Lea Thomas, M. (1988). *Diseases of the Veins Pathology, Diagnosis and Treatment.* Great Britain. Edward Arnold.

BTS Guidelines. (2003). “British Thoracic Society guidelines for the management of suspected acute pulmonary embolism”. *Thorax* 58, 470-84.

Bucciarelli, P., Rosendaal, F. R., Tripodi, A., Mannucci, P. M., De Stefano, V., Palareti, G., Finazzi, G., Baudo, F., Quintavalla, R. (1999). “Risk of Venous Thromboembolism and Clinical Manifestations in Carriers of Antithrombin, Protein C, Protein S

Deficiency, or Activated Protein C Resistance A Multicenter Collaborative Family Study". *Arterioscler Thromb Vasc Biol*. 19, 1026-33.

Bullock, B. L. (4th ed.). (1996). *Pathophysiology Adaptations and Alterations in Function.* New York. Lippincott-Raven Publishers.

Burnand, K., Waltham, M., Smith, A. (2001). "Travel and risk of venous thrombosis". *The Lancet*, 357, 553-54.

Butenas, S., Mann, K. G. (2002). "Blood Coagulation" *Biochemistry (Moscow)* 67 (1), 3-12 [Online]. Available: http://www.springerlink.com/content/q57532p1129341g7/ (at 01/08/2006).

Caillard, G., Clerel, M. (2001). "Travel and Risk of venous thrombosis". *The Lancet*, 357, (9255), 554-5.

Cannegieter, S. C., Doggen, C. J. M., van Houwelingen, H. C., Rosendaal, F. R. (2006). "Travel-Related Venous Thrombosis: Results from a Large Population-Based Case Control Study (MEGA Study)". *PLoS Medicine*. 3 (8) e307, 1258-1265. [Online]. Available: http://www.plosmedicine.org (at 3/12/06)

Caprini, J. A., Traverso, C. I., Arcelus, J. I. (1994). "Intermittent pneumatic compression" in Bergqvist, D., Comerota, A. J., Nicolaides, A. N., Scurr, J. H. (eds). *Prevention of Venous Thromboembolism.* London. Med-Orion Publishing company.

Carlson, H. (1980). *Springs : Troubleshooting and Failure Analysis, Volume 1.*. New York: Marcel Dekker, Inc.

Carruthers, M., Arguelles, A. E., Mosovich, A. (1976). "Man in transit: biochemical and physiological changes during intercontinental flights". *The Lancet* 1, 977-81.

Caruana, M. F., Brightwell, R. E., Huguet, E. L., Whitear, P., Hodgkinson, D. W., Osman, I. S. (2003). "Calf exercise in the seated position using a new dynamic biped

device increases femoral vein peak velocity up to eight-fold". *Phlebology*. 18 (2): 70-72.

Cesarone, M. R., Belcaro, G., Nicolaides, A., Incandela, L., De Sanctis, M.T., Geroulakos, G., Lennox, A., Myers, K. A., Moia ,M., Ippolito, E., Winford, M. (2002). Venous Thrombosis from Air Travel: The LONFLIT3 Study-Prevention with Aspirin vs Low-Molecular-Weight Heparin (LMWH) in High-Risk Subjects: A Randomized Trial. *Angiolog.* 53 (1), 1-6.

Cesarone, M. R., Belcaro, G., Nicolaides, A. N., Ricci, A., Geroulakos, G., Ippolito, E., Brandolini, R., Vinciguerra, G., Dugall, M., Griffin, M., Ruffini, I., Acerbi, G., Corsi, M., Riordan, N., Stuard, S., Bavera, P., Dugall, M., Di Renzo, A., Kenyon, J., Errichi, B. M. (2003a). "Prevention of Venous Thrombosis in Long-Haul Flights with Flite Tabs: The LONFLIT-FLITE Randomized, Controlled Trial". *Angiology* 54, T1-T9.

Cesarone, M. R., Belcaro, G., Nicolaides, A. N., Geroulakos, G., Lennox, A., Myers, K. A., Moia, M., Ricci, A., Brandolini, R., Ramaswami, G., Bavera, P., Dugall, M., Ippolito, E., Winford, M. (2003b). "The Lonflit4 – Concorde – Sigvaris Traveno Stockings in Long Flights (EcoTraS) Study A Randomised Trial" *Angiology* 54 (1); 1-9.

Cho, Y. P., Lee, D. H., Jang, H. J., Kim, J. S., Han, M. S. Lee, S. G. (2002). "Peripheral arterial insufficiency associated with protein C deficiency". *Br J Rad.* 75, 843-46.

Christopoulos, D. C., Nicolaides, A. N., Szendro, G., Irvine, A. T., Bull, M., Eastcott, H. H. G. (1987). "Air- plethysmography and the effect of elastic compression on venous haemodynamics of the leg". *J Vasc Surg* 5:148.

Christopolous, D.C., Nicolaides, A. N., Cook, A. Irvine, A. Galloway, J. M. D., Wilkinson, A. (1989). "Pathogenesis of venous ulceration in relation to the calf muscle pump". *Surgery.* 106, 829-35.

Christopoulos, D., Nicolaides, A. (1994). "Air Plethysmograghy" in in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Clain, A. (16th ed). (1980). *Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery.* Bristol: John Wright and Sons Ltd.

Clarke, M., Hopewell, S., Juszczak, E., Eisinga, A., Kjeldstrøm, M. (2006). "Compression stockings for preventing deep vein thrombosis in airline passengers (Review). *Cochrane Database of Systematic Reviews*. 2, 1-31. [Online]. Available: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004002/pdf_fs.html (at 18/01/07)

Clevland Clinic. (2007). Deep and Superficial Anterior Veins of the leg (2008). [Online]. Available: http://content.revolutionhealth.com/contentimages/cc-legcirculation.jpg (at 03/05/2007)

Code of Federal Regulations, Part 25 – Airworthiness Standards: Transport Category Airplanes, (CFR-25).

Cogo, A., Lensing, A. W. A., Koopman, M. M. W., Piovella, F., Siragusa, S., Wells, P. S., Villalta, S., Büller, H. R., Turpie, A. G. G., Prandoni, P. (1998). "Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: prospective cohort study. *BMJ*, 316, 17-20. [Online]. Available: http://www.bmj.bmjjournals.com/cgi/reprint/316/7124/17 (at 7/11/05).

Colbert, D. (2004). Deep venous thrombosis and air travel. *Irish Medical Times.* Friday, August 6 2004, p.18.

Cole, S. E. A. (ed) (2001a). *Vascular Laboratory Practice IPEM, Part II – Extra and Intracranial Arterial Assessment*. England. Institute of Physics and Engineering in Medicine.

Cole, S. E..A (ed). (2001b). *Vascular Laboratory Practice, IPEM, Part IV*. England, Institute of Physics and Engineering in Medicine.

Collins, C. (2002 – 2003). *The Tromped A Solution for Flight Related Deep Vein Thrombosis* (Dissertation, BSc). Department of Transport Engineering, Dublin Institute of Technology.

Comerota, A.J. (1994a). "Operative Venous Dilation and its Relationship to Postopertive Deep Vein Thrombosis" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Comerota, A. J. (1994b). "DVT: Diagnostic Tests in the Screening of Asymptomatic Patients" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Comerota, A. J., Harada, R. N., Eze, A. R., Katz, M. L. (1995). "Air Plethysmography: a clinical review" *International Angiology*, 14, 1, 45-52.

Comerota, A. J. (2000). " Thrombolytic Therapy for Iliofemoral Deep Venous Thormbosis: An Opportunity Missed?" in Ansell, J. E., Weitz, J. I., Comerota (eds). Advances in Therapy and the Management of Antithrombotic Drugs for Venous Thromboembolism. *American Society of Hematology*, 266-284.

Cook, D., Meade, M., Guyatt, G., Griffith, L., Granton, J., Geerts, W., Crowther, M. (2004). "Clinically important deep vein thrombosis in the intensive care unit: a survey of intensivists". *Crit Care*. 8, R145-R152. [Online]. Available: http://ccforum.com/content/8/3/R145 (at 17/10/05).

Criado, E., Farber, M. A., Marston, W. A., Daniel, P. F., Burnham, C. B., Keagy, B. A. (1998) "The role of air plethysmograph in the diagnosis of chronic venous insufficiency". *J Vasc Surg*. 27 (4), 660-70.

Crowther, M. A., Kelton, J. G. (2003). "Congenital Thrombophilic States Associated with Venous Thrombosis: A Qualitative Overview and Proposed Classification System". *Ann Intern Med,* 138, 128-134.

Cummin, A, R. C., Nicholson, A. N. (2002). *Aviation Medicine and the Airline Passenger.* London: Arnold Publishers.

Dai, G., Tsukurov, O., Chen, M., Gertler, J. P., Kamm, R. D. (2002). "Endothelial nitric oxide production during in vitro simulation of external limb compression". *Am J Physiol Heart Circ Physiol*. 282, H2066-75. [Online]. Available: http://www.ajpheart.physiology.org (8/11/05).

Dalen, J. E. (2003). "Economy Class Syndrome, Too Much Flying or Too Much Sitting?". *Arch Intern Med* 163, 2674-76.

Damjanov, I. (2002). *Pathology Secrets.* Philadelphia. Hanley and Belfus, Inc.

Declaration of Helsinki (1964), Ethical Principles for Medical Research involving Human Subjects adopted by the 18th World Medical Assembly in Helsinki, Finland in 1964. [Online]. Available: http://www.wma.net/e/policy/pdf/17c.pdf (at 5/01/04).

Derry, S., Loke, Y. K. (2000). "Risk of gastrointestinal haemorrhage with long term use of aspirin: meta-analysis". *BMJ* 321, 1183-87. [Online]. Available: http://www.bmj.bmjjournals.com (at 18/10/2004).

Dixon, K. A. (2001). "The non-invasive diagnosis of pulmonary embolus, The pretest probability helps determine the best imaging method." *BMJ* 323, 412-3.

Desmarais, S., de Moerloose, P., Reber, G., Minazio, P., Perrier, A., Bounameaux, H. (1996). "Resistance to activated protein C in an unselected population of patients with pulmonary embolism". *The Lancet,* 347, 1374-5.

De Visser, M. C. H., Rosendaal, F. R., Bertina, R. M. (1999) "A Reduced Sensitivity for Activated Protein C in the Absence of Factor V Leiden Increases the Risk of Venous Thrombosis" *Blood*. 93 (4), 1271-6.

Dobrin, P. B. (1997). "Physiology and Pathophysiology of Blood Vessels" in Sidawy, A. N., Sumpio, B. E., DePalma, R. G. (eds) *The Basic Science of Vascular Disease*. New York. Futura Publishing Company, Inc.

Osman, I. S., Hodgkinson, D. W., Whitear, P. (2006). "Doctors Testimonials" Lym Gym. [Online]. Available: http://www.lymgym.com/pages/index.cfm?FuseAction=ShowPage&sec=1&page=165 (at 05/09/06).

European Aviation Safety Agency (EASA), Certification Specifications For Large Aeroplanes, (CS-25),

Eklof et al., (1996) Venous thromboembolism in association with prolonged air travel. *Dermatol Surg*. 22, 637-641.

Eklof B, Maksimovic, D., Caprini, J. A., Glase, C. (2005). "Air Travel-Related Venous Thromboembolism". *Disease-a-Month*, 51 (2), 200-207.

Ferrari, E., Chevallier, T., Chapelier, A. Baudouy, M. (1999). "Travel as a Risk Factor for Venous Thromboembolic Disease: A Case-Control Study", *Chest*, 115, (2), 440-444. [Online]. Available: http://www.chestjournal.org (at 1/12/05).

Ferrari, E., Morgan, G. (2001). "Travel and risk of venous thrombosis". *The Lancet*, 357, 553-54.

Fleming, P., Fitzgerald, P., Devitt, A., Rice, J., Murray, P. (2000). "The effect of the position of the limb on venous impulse foot pumps". *J Bone Joint Surg [Br]* 82-B (3) 433-4.

Flores, R. J., Sandur, S. (2006). "Massive Hemoptysis". *Hospital Physician*, 37-43. [Online]. Available: http://www.turner-white.com (at 17/2/07).

Fowkes, F. G. R., Lee, A. J., Evans, C. J., Bradbury, A. W., Ruckley, C. V. (2001). "Lifestyle risk factors for lower limb venous reflux in the general population: Edinburgh Vein Study". *International Journal of Epidemiology* 30, 846-852.

Fox, S. I. (5th ed.). (1996). *Human Physiology*. The McGraw-Hill Companies, Inc. United States of America.

Fukuoka, M., Okada, M., Sugimoto, T. (1998). "Foot venous pressure measurement for evaluation of lower limb insufficiency". *J Vasc Surg*. 27, 671-6.

Gallagher, G. L., Sumpio, B. E. (1997). "Endothelial Cells" in Sidawy, A. N., Sumpio, B. E., DePalma, R. G. (eds) *The Basic Science of Vascular Disease*. New York. Futura Publishing Company, Inc.

Galili, Y., Bass, A. (2002). "Long Distance Flights and the Risk of Venous Thromboembolism – A Real Threat or Just Another Flight Hysteria?" *IMAJ*. 4, 1020-22.

Gardner, A. M. N., Fox, R. H. (1989). *The Return of Blood to the Heart: venous pumps in health and disease.* London: John Libbey & Company Ltd.

Gardner, A. M. N., Fox, R. H. (2001). *The Venous System in Health and Disease.* The Netherlands. IOS Press.

Geerts, W., Selby, R. (2003). "Prevention of Venous Thromboembolism in the ICU". *Chest* 124 (6), 357S – 363S. [Online]. Available: http://www.chestjournal.org (at 7/11/05).

Ginsberg, J.S., Greer, I., Hirsh, J. (2001), "Use of Antithrombotic Agents During Pregnancy". *Chest*, 119, (1) 122S-131S.

Giordano, J. M. (5th ed). (2000). "Embryology of the Vascular System" in Rutherford R.B. Cronenwett, J. L., Gloviczki, P., Johnston, K. W., Kempczinski, R. F., Krupski, W. C. (eds). *Vascular Surgery, Volume 1*. USA. W. B. Saunders Company

Gispert, P., Drobnic, M. E., Vidal, R. (2006). "Economy Class Syndrome or Immobile Traveler's Syndrome? Case Report". *Arch Bronconeumol* 42 (7), 373-5. [Online]. Available http://www.archbronconeumol.org (at 19/12/06).

Goldhaber, S. Z. (1998). "Pulmonary Embolism". *NEJM*. 339, (2), 93-104.

Goldhaber, S. Z., Elliot, C. G. (2003). "Acute Pulmonary Embolism: Part 1, Epidemiology, Pathophysiology and Diagnosis." *Circulation.* 108:2726-9.

Goldhaber S. Z. (2004). "Pulmonary embolism". *The Lancet*, 36, 1295-30.

Goldhaber, S. Z., Fanikos, J. (2004). "Prevention of Deep Vein Thrombosis and Pulmonary Embolism". *Circulation*. 110, e445-e447. [Online]. Available: http://www.circulationaha.org (at 27/02/07).

Gorshtein, A., Levy, Y., Shoenfeld, Y. (2002). "Air Flights and Venous Thromboembolism - A Preventable Condition". *IMAJ*. 4, 1080-1.

Grand'Maison, A., Bates, S. M., Johnston, M., McRae, S., Ginsberg, J. S. (2005). ""ProC Global": A functional screening test that predicts recurrent venous thromboembolism". *Thromb Haemost*, 93, 600-4.

Gray, H. (2001). *Gray's Anatomy A Facsimile*. United Kindom. Grange Books Ltd.

Greer, I.A., Walker, I. D. (2004). "Hormone Replacement Therapy and Venous thromboembolism. Guideline No. 19". *Royal College of Obstetricians and*

Grey, C. (2001). Air Plethysmography Test, unpublished experiment, Non-Invasive Vascular Unit, Beaumont Hospital, Dublin 9.

Günay, A., Öztürk, A., Budak, T., Özbek, U., Üskent, N. (2001). "Activated Protein C Resistance in Polycythemia Vera". *Turk J Heamatol*. 18, (3), 157-164.

Hansson, P.O., Welin, L., Tibblin, G., Eriksson, H. (1997). "Deep vein thrombosis and pulmonary embolism in the general population. 'The Study of Men Born in 1913'". *Arch Intern Med* 157, 1665-70.

Harding, J. R. (1990). "Liquid crystal thermography in the investigation of suspected DVT". *Br J of Rad*, 63:993-4.

Harper D, Nelson E, Gibson B, Prescott R, Ruckley C. (1995). "A prospective randomised trial of Class 2 and Class 3 elastic compression in the prevention of venous ulceration". *Phlebology*; **1**: 872-73.

Harper-Deacon, J. (2006). "What's the Alternative?" Style, Sunday Times. Sunday, April 23 2006, p.49.

Haas, S., Haas, P. (1994). "The efficacy of low molecular weight heparins" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Heit, J. A., Melton III, L. J., Lohse, C. M., Petterson, T. M., Silverstein, M. D., Mohr, D. N. O'Fallon, W. M. (2001). "Incidence of Venous Thromboembolism in Hospitalized Patients vs Community Residents". *Mayo Clin Proc*. 76, 1102-10.

HELP AT HOME (2002). Worried about the Risk of DVT On Long Journeys? These Cushions Can Provide Useful Exercise. Winter, 23*.

Hinninghofen, H., Enck, P. (2006). "Passenger well-being in airplanes". *Autonomic Neuroscience: Basic and Clinical.* 129, 80-85.

Hirsh, J. Hull, R. D. (1987). *Venous Thromboembolism: Natural History, Diagnosis and Management*. Florida. CRC Press, Inc.

Hirsh, J. (1990). *Clinical Haematology, Antithrombolic Therapy*. London. Baillière Tindall W. B. Saunders.

Hirsh, J., Dalen, J. E., Anderson, D. R., Poller, L., Bussey, H., Ansell, J., Deykin, D. (2001a). "Oral Anticoagulants: Mechanism of Action, Clinical Effectiveness and Optimal Therapeutic Range. *Chest*. 119,8S-21S.

Hirsh, J., O'Donnell, H. J. (2001b). "Venous thromboembolism after long flights: are airlines to blame?" *The Lancet* 357, 1461-2.

Hodkinson, P. D., Hunt, B. J., Parmar, K., Ernsting, J. (2003). "Is mild normobaric hypoxia a risk factor for venous thromboembolism?". *J Thromb Haemost.* 1, 2131-33.

Hodson, M. (2002) Don't let them off the hook. *The Sunday Times*, Sunday February 17 2002, p. 8.

Hommes, D. W., Büller, H. R., Brandjes, D. P. M., ten Cate, J. W. (1994). "Preoperative risk factors in the prediction of postoperative venous thromboembolism" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Hsieh, H-F., Lee, F-P. (2005). "Graduated compression stockings as prophylaxis for flight-related venous thrombosis: systematic literature review". *Journal of Advanced Nursing.* 51 (1): 83-98.

Hughes, R. J., Hopkins, R .J., Hill, S., Weatherall, M., Van de Water, N., Nowitz, M., Milne, D., Ayling, J., Wilsher, M., Beasley, R. (2003). "Frequency of venous thromboembolism in low to moderate risk long distance air travellers: the New Zealand Air Traveller's Thrombosis (NZATT) study". *The Lancet* 362, 2039-2043.

Hughes, R., Thomson, K., Hopkins, R., Weatherall, M., Wiltshire, C., Wilsher, M., Beasley, R. (2005). "Determinants of plasma D-dimer levels in a travelling population". *Journal of Thrombosis and Hemostasis* 3, 2445-48.

Hughes, R., Heuser, T., Hill, S., Ryder-Lewis, S., Weatherall, M., Hopkins, R., Beasley, R. (2006). "Recent air travel and venous thromboembolism resulting in hospital admission". "*Respirology* 11:75-79.

Hull, R. D. Raskob, G.E. Hirsh, J. (1986). "Prophylaxis of venous thromboembolism. An overview". *Chest* 89, 3745-835.

Hyers, T. M. (1999). "Venous Thromboembolism". *Am J Respir Crit Care Med*, 159, 1-14.

Ibegbuna, V., Delis, K. T., Nicolaides, A. N., Aina, O. (2003). "Effect of elastic compression stockings on venous hemodynamics during walking" *J Vasc Surg.* 37, 420-5.

IEH (2001). "A Consultation on the Possible Effects on Health, Comfort and Safety of Aircraft Cabin Environment". United Kingdom. Institute for Environment and Health. [Online]. Available: http://www.silsoe.cranfield.ac.uk/ieh/pdf/w5.pdf (at 12/02/03)

International Air Transport Association (IATA). (2004). *Environmental Review 2004*. Montreal-Geneva. [Online]. Available: http://www.iata.org/NR/rdonlyres/B73AF136-9824-4149-80F2-E5A5BAD0C89E/34687/IATAEnvironmentalReview2004.pdf (at 11/2/06).

"International First Class Explained and Compared". (2007). [Online]. Available: http://www.seatguru.com/charts/intl_first_class.php (7/07/07).

Jameson, B. (2001). "GPs urged to offer prophylaxis to patients going on long-haul flights". *Irish Medical Times*, Friday May 11 2001.

Jeppesen A&P Technician Airframe Textbook. (2nd ed). (2002). Colorado, Jeppesen Sanderson Inc.

Johnson, R. V., Evans, A. D. B. (2001). "Venous thromboembolic disease in pilots". *The Lancet.* 358, 1734.

Johnson, A. O. C. (2003). "Chronic obstructive pulmonary disease •11: Fitness to fly with COPD". *Thorax*. 58, 729-732.

Johnston A. (21/10/03). *The Pill that Prevents DVT*. [Online]. Available: http://www.aviation-health.org/Newspage.asp?ArtID=222. (at 11/24/03).

Joung, S., Robinson, B. (2002). "Venous thromboembolism in cancer patients in Christchurch, 1995-1999". *NZMJ* 115 (1155), 1-8. [Online]. Available: http://www.nzma.org.nz/journal/ (at 17/10/05).

Kahn, S. R., Solymoss, S., Lamping, D. L., Abenhaim, L. (2000). "Long-term Outcomes After Deep Vein Thrombosis: Postphlebitic Syndrome and Quality of Life". *J Gen Intern Med*, 15, 425-429.

Kakkar, V. V., Cohen, A. T. (1994). "Low dose heparin with and without dihydroergotamine" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds). *Prevention of Venous Thromboembolism*. London. Med-Orion Publising Company.

Keeling, D. M., Mackie, I. J., Moody, A., Watson, H. G., The Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology. (2004). "The diagnosis of deep vein thrombosis in symptomatic outpatients and the potential for clinical assessment and D-dimer assays to reduce the need for diagnostic imaging".

Kelman, C. W., Kortt, M. A., Becker, N. G., Li., Z., Mathews, J. D., Guest, C. S., Holman, C. D. J. (2003). "Deep vein thrombosis and air travel: record linkage study". *BMJ*, 327, 1072-1076.

Kester, T., Rosendaal, F. R., de Ronde, H., Briët, E., Vandenbrouche, J. P., Bertina, R. M. (1993). "Venous thrombosis due to poor anticoagulant response to activated protein C: Leiden Thrombophilia Study" *Lancet*. 342:1503-6.

Kesteven, P. L. J. (2000). "Traveller's thrombosis". *Thorax.* 55, (1), S32-S36. [Online]. Available at: http://www.thorax.bmjjournals.com (at 22/5/2005)

Killewich, L. A., Sandager, R. N., Nguyen, A. H., Lilly, M. P., Flinn, W. R. (1995). "Venous hemodynamics during impulse foot pumping". *J Vasc Surg*, 22, 598-605.

Kingman C. E. C., Economides, D. L. (2002). "Air travel in pregnancy" *The Obstetrician and Gynaecologist*. 4, 188-92.

Kirk E. (1995) "Research and Patients" in Tingle J., Cribb, (eds) A *Nursing Law and Ethics*. Oxford., Blackwell Science Ltd.

Klatsky, A. L., Baer, D. (2004). "What Protects Asians from Venous Thromboembolism?" *Am J Med.* 116, 493-5.

Klauser, A., Schirmer, M., Frauscher, F. (2004). "Venous thromboembolism in long-distance air travellers". *The Lancet* 363, 896-7.

Köppel, H. Renner, W., Brodmann, M., Pabst, E., Pilger, E. (2001). "Correlation between Activated Protein C-Resistance and Factor V Leiden Mutation". *J ClinBasic Cardiol*, 4, (1), 73-4.

Kraaijenhagen, R. A. Haverkamp, D., Koopman, M. M. W., Prandoni, P., Piovella, F., Büller, H. R. (2000). "Travel and risk of venous thrombosis". *The Lancet.* 356, 1492-3.

Krupski, W. C. (1997). "Platelets" in Sidawy, A. N., Sumpio, B. E., DePalma, R. G. (eds) *The Basic Science of Vascular Disease*. New York. Futura Publishing Company, Inc.

Kumar, V., Abbas, A. K., Fausto, N. (7^{th} ed). (2005). *Robbins and Cotran Pathologic Basis of Disease*. Elsevier Saunders.

Kumar, P., Clark, M. (5^{th} ed), (2002). *Clinical Medicine*. United Kingdom. WB Saunders.

Labelle, C. A., Kitchens, C. S. (2005). "Disseminated intravascular coagulation: Treat the cause, not the lab values". *Cleveland Clinic Journal of Medicine*. 72 (5), 377-97.

Labropoulos, N., Giannoukas, A., Delis, K., Kang, S. S., Mansour, A., Buckman, J., Katsamouris, A., Nicolaides, A. N., Littooy, F. N., Baker, W. H. (2000). "The impact of isolated lesser saphenous vein system incompetence on clinical signs and symptoms of chronic venous disease". *J Vasc Surg*. 32 (5), 954-60.

Laffan, M. (1998). "Pulmonary embolism". *Thorax* 53, 698-702.

Lapostolle, F., Surget, V., Borron, S. W., Desmaizières, M., Sordelet, D., Lapandry, C., Cupa, M., Adnet, F. (2001). "Severe Pulmonary Embolism associated with air travel". *N Engl J Med*, 345 (11), 779-783.

Lee, A. J., Evans, C. J., Ruckley, C. V., Fowkes, F. G. R. (1999). "Does Lifestyle Really Affect Venous Disease?" in Ruckley, C. V., Fowkes, F. G. R., Bradbury, A. W. (eds) *Venous Disease Epidemiology, Management and Delivery of Care.* Great Britain. Springer-Verlag London.

Lee, A. Y. Y., Levine, M. N. (2003). "Venous Thromboembolism and Cancer: Risks and Outcomes". *Circulation* 107: I-17 – I-21.

Lennon, E. (2004) Why fear of flying has just got even worse, DVT is no longer the scourge of just the economy class. *The Irish Independent.* Tuesday May 25 2004. p. 29.

Lewis, G., Drife, J (2001) "Why Mothers Die 1997-1999. The Confidential Enquiries into Maternal Deaths in the United Kingdom". London. RCOG Press. [Online]. Available: www.cemd.org.uk (at 16/12/03)

Liebman, H. A. (2005). "Current Perspectives on Primary Prophylaxis and Patient Risk Factors for Venous Thromboembolism in the Cancer Patient". *Cancer Control*. 12 (1), 11-16.

Lingamanaicker, J., Mukherjee, J. J., Fock, K. M., Khoo, T. K. (2001). "The Role of Spiral Computed Tomogram in the Diagnosis of Acute Pulmonary Embolism". *Singapore Med J*. 42(10), 455-59.

Loud, P. A., Katz, D. S., Bruce, D.A., Klippenstein, D. L., Grossman, Z.D. (2001). "Deep Venous Thrombosis with Suspected Pulmonary Embolism: Detection with Combined CT Venography and Pulmonary Angiography". *Radiology*, 219, 498-502.

Lowe, G. D. O., Rumley, A. (1999). "What Are the Risks of Thrombophilia?", in Ruckley, C. V., Fowkes, F. G. R., Bradbury, A. W. (eds). *Venous Disease Epidemiology, Management and Delivery of Care.* Great Britain. Springer-Verlag London Limited.

Lymgym (200 [Online]. Available: http://www.aviation-health.com-Lymgym (at 08/07/07)

Maganaris, C. N., Baltzopoulos V., Ball, D., Sargeant, A. J. (2001) "In vivo specific tension of human skeletal muscle" *J Appl Physiol*. 90, 865-72.

"Man develops blood clot 'on flight to SA'" (08/01/03). [Online]. Available: http://www.iol.co.za/index.php?set_id=1&click_id=13&art_id=qw1042025760249B216 (at 02/01/03).

Mantoni, M., Larsen, L., Lund, J. O., Henriksen, L., Karlsmark, T., Strandberg, C., Ogstrup, J., Ribel-Madsen, S., Gottrup, F., Danielsen, L. (2002). Evaluation of chronic venous disease in the lower limbs: comparison of five diagnostic methods. *Brit J Rad*, 75, 578-83.

Margaglione, M., Brancaccio, V., De Lucia, D., Martinelli, I., Ciampa, A., Grandone, E., Di Minno, G. (2000). "Inherited Thrombophilic Risk Factors and Venous Thromboembolism, Distinct Role in Peripheral Deep Venous Thrombosis and Pulmonary Embolism". *Chest* 118 (5) 1405-11.

Marik, P., Varon, J. (1998). "The Obese Patient in the ICU". *Chest*. 113 (2) 492-98.

Martinelli, I., Taioli, E., Battaglioli, T., Podda, G. M., Passamonti, S. M., Pedotti, P., Mannucci, M. (2003). "Risk of Venous Thromboemblism After Air Travel, Interaction

with Thrombophilia and Oral Contraceptives". *Arch Intern Med* 163: 2771-74. [Online]. Available: http://www.archinternmed.com (at 20/12/06).

Martini, F. H., Ober, W. C., Garrison, C. W., Welch, K., Hutchings., R. T. (4th ed). (1998). *Fundamentals of Anatomy and Physiology.* New Jersey. Prentice Hall Inc.

Mattson, M. (2002). *CNC Programming, Principles and Applications, Delmar – Thomson Learning*, Canada.

Mazzone, C., Chiodo, G. F., Sandercock, P., Miccio, M., Salvi, R. (2004). "Physical methods for preventing deep vein thrombosis in stroke (Review)". *Cochrane Database of Systematic Reviews*. 4, 1-12. [Online]. Available: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001922/frame.html (at 18/01/07).

McDonald, D. (2003). "Irish travel firms hit by DVT claims". *The Sunday Times*, Sunday February 9 2003.

"Medical Approval". (2007). [Online]. Available: http://www.veingaurd.co.uk/medicallyapproved.html (at 17/05/07).

Medical Devices Directive (93/42/EEC) [Online]. Available: http://eur-lex.europa.eu (at 17/05/07).

Medlineplus (2002). *DVT in the ileofemoral (groin) area*. [Online]. Available: http://www.nlm.nih.gov/medlineplus/ency/imagepages/2549.htm (at 25/11/02).

Medlineplus (2002). *Pulmonary Embolism*. [Online]. Available: http://www.nlm.nih.gov/medlineplus/ency/imagepages/9798.htm (25/11/02).

Medlineplus (2005). *Venous Blood Clot*. [Online]. Available: http://www.nlm.nih.gov/medlineplus/ency/imagepages/8984.htm. (at 02/03/05)

Meissner, M. H. (2002). "Thrombolytic Therapy for Acute Deep Vein Thrombosis and the Venous Registry". *Rev Cardiovasc Med*. 3 (2), S53-S60.

Menzoian, J. O., Arbid, E. J., Phillips, T. J., Bhawan, J., LaMorte, W. W. (1997). "Venous System of the Lower Extremities: Physiology and Pathophysiology" in Sidawy, A. N., Sumpio, B. E., DePalma, R. G. (eds). *The Basic Science of Vascular Disease*. New York. Futura Publishing Company, Inc.

Meyer, G., Emmerich, J., Helley, D., Arnaud, E., Nicaud, V., Alhenc-Gelas, M., Aiach, M., Fisher, A., Sors, H., Fiessinger, J. N. (2001). "Factors V Leiden and II 20210A in Patients with Symptomatic Pulmonary Embolism and Deep Vein Thrombosis". *Am J Med*. 110, 12-15.

Miller, J. D., Pegelow, D, F., Jacques, A. J., Dempsey, J. A. **(**2005). "Skeletal muscle pump *versus* respiratory muscle pump: modulation of venous return from the locomotor limb in humans". *J Physiol*. 56 (3), 925-43.

Miller-Keane, (1997) *Encylopedia of Medicine.* Saunders Philadelphia.

Mitchell, R. N., (7^{th} ed). (2005). "Hemodynamic Disorders, Thromboembolic Disease, and Shock" in Kumar, V., Abbas, A. K., Fausto, N. (eds). *Robbins and Contran Pathologic Basis of Disease*. Philadelphia. Elsevier Saunders.

Moffat, D. B., Mottram, R. F. (2^{nd} ed). (1987). *Anatomy and Physiology for Physiotherapists.* Oxford. Blackwell Scientific Publications.

Mohler, S. R. (1997). "Blood Clotting Presents Serious Medical Problems for Passengers and Crew, Especially on Long Flights". *Flight Safety Foundation Human Factors and Aviation Medicine* 44 (4), 1-4.

Moir, I., Seabridge, A. G (1992). *Aircraft Systems*. Longman, Essex.

Moir, I., Seabridge, A. G. (2003). *Civil Avionics Systems, Professional Engineering Publishing,* Suffolk: St Edmundsbury Press Limited.

Monkhouse, S. (2001). *Master Medicine Clinical Anatomy A core text with self-assessment.* Edinburgh. Churchill Livingstone.

Morris, R. J., Woodcock, J. P. (2004). "Evidence-Based Compression Prevention of Stasis and Deep Vein Thrombosis". *Ann Surg* 239 (2), 162-71.

Mozes, G., Gloviczki, P. (2004). "New Discoveries in Anatomy and New Terminology of Leg Veins: Clinical Implications". *Vasc Endovasc Surg*, 38 (4), 367-374.

Murciano, J. Harshaw, D., Neschis, D. G., Koniaris, L., Bdeir, K., Medinilla, S., Fisher, A. B., Golden, M. A., Cines, D. B., Nakada, M. T., Muzykantov, V. R. (2002). "Platelets inhibit the lysis of pulmonary microemboli". *Am J Physiol Lung Cell Mol Physiol*. 282, L529-39. [Online]. Available: http://www.ajplung.physiology.org (at 7/06/05).

Murphy, J. F. A. (2001). "The Folded Deckchair Position: The problem of long-haul flights". *Irish Medical Journal* 94 (9), 260.

Southwest Orthopaedic Surgery Specialists, PLC Muscles of the Foot (2007). [Online]. Available:http://www.eorthopod.com/images/ContentImages/foot/foot_anatomy/foot_anatomy_muscles01.jpg (at 3/04/07).

Nandi, P. L., Li, W. S., Leung, R., Chan, J., Chan, H. T. (1998). "Deep vein thrombosis and pulmonary embolism in the Chinese population". *HKMJ* 4 (3), 305-10.

Needham, T. (2005). "Assessment of Lower Extremity Venous Valvular Insufficiency Examinations". *JVU* 29 (3), 123-9.

Neglén, P. (2003). "Endovascular treatment of chronic iliofemoral venous obstruction – A review". *Phlebolymphology*. 43, 204-211.

Netterimages.com (2008). "Superficial posterior veins drain to the Popliteal Vein" http://www.netterimages.com/images/vtn/000/000/004/4669-150x150.jpg (at 02/01/2008).

Nicolaes, G. A. F., Dahlbäck, B. (2002). Factor V and Thrombotic Disease Description of a Janus-Faced Protein". *Arterioscler Thromb Vasc Biol.* 22:530-8. [Online]. Available: http://www.atvbaha.org (at 17/10/05).

Nicolaides, A. N., Summer, D. S. (1991). Investigations of Patients with Deep Vein Thrombosis and Chronic Venous Insufficiency. London, UK Med-Orion Publishing Company.

Nicolaides, A., Kalodiki, E. (1994). "The contribution of colour flow imaging in postoperative surveillance for DVT" in Bergqvist, D., Comerota, A. J., Nicolaides, A. N., Scurr, J. H. (eds). *Prevention of Venous Thromboembolism*. London. Med-Orion Publishing Company.

Nicolaides, A. (1999). "How Do We Select the Appropriate Tests of Venous Function?" in Ruckley, Fowkes and Bradbury (eds). *Venous Disease, Epidemiology, Management and Delivery of Care.* Great Britain. Springer – Verlag London Limited.

Nicolaides, A. N. (2000). "Investigation of Chronic Venous Insufficiency A Consensus Statement". *Circulation* 102e, 126-163. [Online]. Available: http://www.circulation.org (at 14/07/05).

Nicolaides, A. N., Breddin, H. K., Fareed, S., Goldhaber, S., Haas, R., Hull, E., Myers, M., Samama, A., Sasahara, A. (2002). "Guidelines, Prevention of venous thromboembolism, International Consensus Statement". *J Vasc Br.* 1 (2), 133-70.

Nicholson, A. N., Cummin, A. R. C., Giangrande, P. L. F. (2003). "The airline passenger: current medical issues". *Travel Medicine and Infectious Disease*. 1, 94-102.

Nordstrom M, Lindblad B, Bergqvist D, Kjellstrom T. (1992). "A prospective study of the incidence of deep-vein thrombosis within a defined urban population". *J Intern Med.* 232, 155-160.

Novamedix Inflation pad foot care (1998). [Online]. Available**:** http://www.novamedix.com/product.htm. (at 08/12/04).

Novamedix A-V Impulse System (1998). [Online]. Available**:** http://www.novamedix.com/product.htm. (at 08/12/04).

O'Donovan, K. J., O'Keeffe, D. T., Grace, P. A., Lyons, G. M. (2005). "Accelerometer based calf muscle pump activity monitoring". *Medical Engineering & Physics* 27:717-722.

O'Sullivan, G. J., Semba, C. P., Bittner, C. A., Kee, S. T., Razavi, M. K., Sze, D. Y., Dake, M. D. (2000). "Endovascular Management of Iliac Vein Compression (May-Thurner) Syndrome". *JVIR* 11:823-36.

Osman, T., McCorry, V., Cooper, C., Innes, B. (1973). *All about Science, Volume 2, Bo to Di*. London. Orbis Publishing Limited.

Ögren, M., Bergqvist, D., Eriksson, H., Lindblad, B., Sternby, N. H. (2005). "Prevalence and risk of pulmonary embolism in patients with intracardiac thrombosis: a population – based study of 23796 consecutive autopsies". *European Heart Journal*, 26, 1108-14.

Padberg, F., Cerveira, J. J., Lal, B. K., Pappas, P. J., Varma, S., Hobson, R. W. (2003). "Does severe venous insufficiency have a different etiology in the morbidly obese? Is it venous?". *J Vasc Surg*. 37, 79-85.

Padberg, F. T., Johnston, M. V., Sisto, S. A. (2004). "Structured exercise improves calf muscle pump function in chronic venous insufficiency: A randomised trial" *J Vasc Surg* 39:79-87.

Paganin, F., Laurent, Y., Gaüzere, B. A., Blanc, Ph., Roblin, X. (1996). "Pulmonary embolism on non-stop flights between France and Reunion Island". *The Lancet*, 347, 1196-6.

Palastanga, N., Field, D., Soames, R. (2nd ed.). (1994). *Anatomy and Human Movement, Structure and Function*. Oxford: Butterworth – Heinmann Ltd.

Partsch, H. (1999). "Compression Therapy: Is it Worthwhile?" in in Ruckley, C. V., Fowkes, F. G. R., Bradbury, A. W. (eds) *Venous Disease Epidemiology, Management and Delivery of Care.* Great Britain. Springer-Verlag London.

Partsch, H., Winiger, J., Lun, B. (2004). "Compression Stockings Reduce Occupational Leg Swelling". *Dermatol Surg*. 30, 737-43.

Peacock, A. J. (1998). "ABC of oxygen: Oxygen at high altitudes". *BMJ*. 317, 1063-66. [Online]. Available: http://www.bmj.com (at 22/02/05).

Pérez-Rodríguez, E., Jiménez, D., Díaz, G., Perez-Walton, I., Luque, M., Guillén, C., Mańas, E., Yusen, R. D. (2003). "Incidence of Air Travel-Related Pulmonary Embolism at the Madrid-Barajas Airport". *Arch Intern Med*, 163, 2766-70.

Perrier, A. (2000). Editorials. "Deep Vein Thrombosis and Pulmonary Embolism A Single Disease Entity With Different Risk Factors?". *Chest*. 118 (5), 1234-6.

Pickering, T., Howden, R. (eds) (1977). *Gray's Anatomy The Classic Collector's Edition*. New York. Bounty Books.

Philbrick, J. T., Shumate, R., Siadaty, M. S., Becker, D. (2007). "Air Travel and Venous Thromboembolism: A Systematic Review". *JGIM*, 22:107-114.

Pookarnjanamorakot, C., Sirisriro, R., Eurvilaichit, C., Jaovisidha, S., Koysombatolan, I. (2004). "The Incidence of Deep Vein Thrombosis and Pulmonary Embolism after Total Knee Arthroplasty: The Screening Study by Radionuclide Venography". *J Med Assoc Thai*. 87 (8) 869-76.

Porter, J. M., Moneta, G. L. (1995). An International Consensus Committee on Chronic Venous Disease. "Reporting standards in venous disease: An Update". *J Vasc Surg*, 21, 635-45.

Possick, S. E., Barry, M. (2004). "Air Travel and Cardiovascular Disease". *J Travel Med.* 11, 243-250.

Prandoni, P., Lensing, A. W.A., Prins, M. H., Bernardi, E., Marchiori, A., Bagatella, P., Frulla, M., Mosena, L., Tormene, D., Picciolli, A., Simioni, P., Girolami, A. (2002). "Residual Venous Thrombosis as a Predictive Factor of Recurrent Venous Thromboembolsim". *Ann Intern Med.* 137, 955-960.

Prandoni, P. (2003/2004). "Risk Factors of Recurrent Venous Thromboembolism:The Role of Residual Vein Thrombosis". *Pathophysiol Haemost Thromb.* 33, 351-53.

Quaresima, V., Homma, S., Azuma, K., Shimizu, S., Chiarotti, F., Ferrari, M., Kagaya, A. (2001). "Calf and shin muscle oxygenation patterns and femoral artery blood flow during dynamic plantar flexion exercise in humans". *Eur J Appl Physiol* 84, 387-394.

Quigley, C., Southall, D., Freer, M., Moody, A., Porter, M. (2001). "Anthropometric Study to Update Minimum Aircraft Seating Standards". *ICE Ergonomics* [Online]. Available: http://www.iboro.ac.uk/research/esri/ttec/pdf_files/Passenger%20seat%20space.pdf (at 16/01/04).

Radomski, M. W., Radomski, A. S. (2000). "Regulation of Blood Cell Function by Endothelil Cells" in Vallance P. J. T., Webb, D. J (eds). *Vascular Endothelium in Human Physiology and Pathophysiology.* The Netherlands. Harwood Academic Publishers.

Ramaswami, G., Nicolaides, A. N, (1994). "Natural history of deep vein thrombosis" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds) *Prevention of Venous Thromboembolism*. London: Med-Orion. Publishing Company.

Rautio, T. (2002). Primary Saphenous Vein Insufficiency. 2002. Oulo University Press, University of Oulo. [Online]. Available: http://herkules.oul.fi/isbn95147230/ (at 05/05/05).

Reilly, J. (2000). *Understanding Statistics*, Dublin, Folans.

Reuters. (2006). Oxygen clue to air travel clotting dangers. *The Irish Times*. Saturday, March 11 2006.

Ricci, M. A., Fisk, P., Knights, S., Case, T. (1997). "Hemodynamic evaluation of foot venous compression devices". *J Vasc Surg* 26:803-8.

Riddle, D. L., Wells, P. S. (2004). "Diagnosis of Lower-Extremity Deep Vein Thrombosis in Outpatients". *Physical Therapy* 84 (8), 729-35.

Ridker, P. M., Samuel, Z., Goldhaber, S. Z., Danielson, E., Rosenberg, Y., Eby, C. S., Deitcher, S. R., Cushman, M., Moll, S., Kessler, C. M., Elliot, C. G., Paulson, R., Wong, T., Bauer, K. A., Schwartz, B. A., Miletich, J. P., Bounameaux, H., Glynn, R. J. (2003). 'Long-term, Low-intensity Warfarin Therapy for the Prevention of Recurrnet Venous Thromboembolism'. *N Engl J Med.* 348 (15), 1-10.

Romanes, G. J. (15th ed). (1986). *Cunningham's Manual of Practical Anatomy, Volume One, Upper and Lower Limbs*. Oxford. Oxford Universtiy Press.

Rosendaal, F. R. (1999). "Venous thrombosis: a multicausal disease". *The Lancet.* 353, 1167-173.

Roy, P., K. (2002). "Physiological Adaptation and Anaesthesia at high altitude". *Indian J. Anaesth.* 46, 3, 175-81.

Samama, M. M., Conard, J., Horellou, M. H., Toulemonde, F. (1994). "Coagulation Abnormalities Predisposing to the Development of Deep Vein Thrombosis" in Bergqvist, D., Comerde, A.J., Nicolaides, A. N., Scurr, J. H. (eds). *Prevention of Venous Thromboembolism.* Cyprus. Med-Orion Publishing Company.

Schmitz, C. H., Graber, H. L., Barbour, R. L. (2006). "Peripheral Vascular Noninvasive Measurements". Encyclopedia of Medical Devices and Instrumentation. 234-252.

Schobersberger, W., Fries, D., Mittermayr, M., Innerhofer, P., Sumann, G., Schobersberger, B., Klingler, A., Stöllnberger, V., Fischbach, U., Gunga, H. C. (2002). "Changes of biochemical markers and functional tests for clot formation during long-haul flights". *Thrombosis Research,* 108, 19-24.

Schoene, R. B. (2001). "Limits of human lung function at high altitude". *The Journal of Experimental Biology.* 204, 3121-3127.

Scholten, P., Bever, A., Turner, K., Warburton, L. (2000). "Graduated elastic compression stockings on a stroke unit: a feasibility study" Age and Ageing; 29:357-9.

Schreijer, A. J. M., Cannegieter, S. C., Meijers, J. C. M., Middeldorp, S., Büller, H. R., Rosendaal, F. R. (2006). "Activation of coagulation system during air travel: a crossover study". *The Lancet*, 367, 832-8.

Scottish Intercollegiate Guidelines Network (SIGN). (2002). Prophylaxis of Venous Thromboembolism A Natural Clinical Guideline [62]. Edinburgh. Scottish Intercollegiate Guidelines Network. Royal College of Physicians, Queen St., Edinburgh, England. [Online]. Available: http://www.sign.ac.uk/pdf/sign62.pdf (at 14/07/05)

Scurr, J. H. (1994). "Graduated compression stockings for the prevention of venous thromboembolism" in Bergqvist, D., Comerota, A. J., Nicolaides, A. N., Scurr, J. H. (eds), *Prevention of Venous Thromboembolism.* London: Med-Orion. Publishing Company.

Scurr, J. H., Machin, S. J., Bailey-King, S., Mackie, I. J., McDonald, S., Coleridge Smith, P. (2001). "Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial". *The Lancet* 357, 1485-89.

Scurr, J. H. (2005). "Zinopen – its use as a food supplement in traveller's thrombosis, oedema and motion sickness". *European Bulletin of Drug Research.*13, 77-81. [Online]. Available: http://www.blood-clot.info/sites/documments/res2.pdf (at 14/02/2009).

Seeley, R, R., Stephens, T, D., Tate, P. (8th ed). (2006). *Anatomy & physiology*. New York, McGraw Hill.

Sharafuddin, M. J., Sun, S., Hoballah, J. J., Youness, F. M., Sharp, W. J., Roh, B-S. (2003). Endovascular Management of Venous Thrombotic and Occlusive Diseases of the Lower Extremities. *J Vasc Interv Radiol.* 14 (4), 405-423.

Sho, E., Nanjo, H., Sho, M., Kobayashi, M., Komatsu, M., Kawamura, K., Xu, C., Zarins, C. K., Masuda, H. (2004). "Arterial enlargement, tortuosity, and intimal thickening in response to sequential exposure to high and low wall shear stress". *J Vasc Surg* 39, 601-12.

Shrivastava, J. K. (2003). "Deep vein thrombosis in commercial pilot: A case Report". *Ind J Aerospace Med* 47 (2), 17-20.

Silverthorn, D. U. (1998). *Human Physiology An Integrated Approach*. New Jersey. Prentice-Hall Inc.

Simioni, P., Tormene, D., Prandoni, P., Zerbinati, P., Gavasso, S., Cefalo, P., Girolami, A. (2002). "Incidence of venous thromboembolism in asymptomatic family members who are carriers of factor V Leiden: a prospective cohort study". *Blood.* 99 (6), 1938-42.

Simons, R., Krol, J. (1996). "Jet leg, pulmonary embolism, and hypoxia". *The Lancet*, 348, 416.

Sims, N. (ed). (2000). *THE HEART & CIRCULATORY SYSTEM*. London. The Reader's Digest Association Limited.

Sky Walker (2006). [Online]. Available: http://www.aviation-health.com/shop/product_info.php?products_id=55 (at 4/4/ 06).

Sochart, D. H., Hardinge, K (1999). "The relationship of foot and ankle movements to venous return in the lower limbs" *J Bone Joint Surg* [Br] 81-B, (4), 700-4.

Society of Automotive Engineers, SAE, (2nd ed). (1996). *Spring Design Manual*. United States of America. Society of Automotive Engineers, Inc.

Solomon, E. P., Schmidt, R. R., Adragna, P. J. (2nd ed) (1990). *Human Anatomy & Physiology*. Orlando Florida, Saunders College Publishing.

Spiliotopoulou, I., Grouzi, E. (2003). "Hormone replacement therapy and thrombotic risk: effects on haemostasis, and the risk of venous thromboembolism". *Haema*. 6 (2), 166-75.

SpringMasters®. (2006). *Spring Directory*. United Kingdom, Springmasters Ltd.

Statutory Instrument SI 252 of 1994 [Online]. Available: http://www.irishstatutebook.ie (at 10/05/2006).

Stranden, E. (2000). "Dynamic leg volume changes when sitting in a locked and free floating tilt office chair". *Ergonomics* 43 (3), 421-33.

Strandness, D. E., Sumner, D. S. (1975). *Hemodynamics for Surgeons*. New York Grune and Stratton, Inc..

Strandness, E., van Breda, A. (1994). Vascular *Diseases: Surgical and Interventional Therapy. Volume 1*. United Stat es of America. Churchill Livingstone Inc.

Strandring, S. (39th ed). (2005). *Gray's Anatomy The Anatomical Basis of Clinical Practice*. Edinburgh. Elsevier Churchill Livingstone.

Sumner, D. S. (5th ed). (2000). "Essential Hemodynamic Principles" in Cronenwett, J. L., Gbviczki, P., Johnston, K. W., Kempczinski, R. F., Krupski. W. C. (eds) *Vascular Surgery, Volume 1*. USA. W. B. Saunders Company.

Tapson, V. F. (10th ed). (2001). "Pulmonary Embolism" in Fuster, V., Alexander, R. W., O'Rourke, R. A. (eds). *Hurst's The Heart, Volume 2.* United States of America. The McGraw Hill Companies.

Templeton, S. (2005) Flights triple blood clot risk. *The Sunday Times*. Sunday January 10 2005. p. 19.

Thaler, E., Huch, R., Huch, A., Zimmermann, R. (2001). "Compression stockings prophylaxis of emergent varicose veins in pregnancy: a prospective randomised controlled study" *Swiss Med Wkly*, 131:659-62.

The Human Skeleton (2007). [Online]. Available: http://www.contmediausa.com/.../Images/BS000A.jpg (at 3/03/07)

Tibbs, D. J. (1992). *Varicose Veins and Related Disorders*. Oxford: Butterworth-Heinemann Ltd.

Bagshaw, M., The Air Transport Medicine Committee, Aerospace Medical Association. (2001) "Travellers Thrombosis Review of Deep Vein Thrombosis associated with Travel". *Aviat Space Environ Med.* 72, 848-54. [Online]. Available: http://www.reiseklinikken.no/thrombosis-article1.pdf (at 19/05/2009).

Tyldesley, B., Grieve, J. I. (1989). *Muscles, Nerves and Movement, Kinesiology in Daily Living.* Oxford: Blackwell Scientific Publications.

Turpie, A. G. G. (1994). "Oral anticoagulants and antiplatelet drugs" in Bergqvist, D., Comerota, A. J., Nicolaides, A. N., Scurr, J. H. (eds). *Prevention of Venous Thromboembolism*. London. Med Orion Publishing Company.

Underwood, J. C. E. (4th ed). (2004). *General and Systematic Pathology.* Edinburgh. Churchill Livingstone.

Ulutin, O. H. (2002). "The Relationship of Haemostatic System to the Vessel Wall, Thromboemoblism, Atherosclerosis from Pathogenesis and Laboratory Standpoints". *Turk J Haematol.* 19 (1), 7-29.

Vander, A., Sherman, J., Luciano, D. (7th ed). (1998). *Human physiology The Mechanisms of Body Function.* United States of America. The McGraw – Hill Companies, Inc.

Varma, M. R., Moaveni, D. M., Dewyer, N. A., Varga, A. J., Deatrick, K. B., Kunkel, S. L., Upchurch, G. R., Wakefield, T. W., Henke, P. K. (2004). "Deep vein thrombosis resolution is not accelerated with increased neovascularization" *J Vasc Surg* 40, 536-42.

"Veingaurd Anti-DVT Cushion". (2007). [Online]. Available: http://www.veingaurd.co.uk/veingaurdcushion.html (at 17/05/07).

Watson, H. G. (2005). "Travel and Thrombosis". *Blood Reviews*. 19, 235-241.

Weitz, J. I. (2000). "New Anticoagulant Drugs" in Ansell, J. E., Weitz, J. I., Comerota (eds). *Advances in Therapy and the Management of Antithrombotic Drugs for Venous Thromboembolism*. American Society of Hematology, 266-284.

White, J. V., Katz, M. L., Cisek, P., Kreithen, J. (1996). "Venous outflow of the leg: Anatomy and physiologic mechanism of the plantar venous plexus". *J Vasc Surg*, 24, (5) 819-24.

White, J. V., Jones, D. N., Rutherford, R. B. (5th ed). (2000). "Integrated Assessment of Results: Standardised Reporting of Outcomes and the Computerized Vascular Registry" in Rutherford, R. B., Cronenwett, J. L., Gloviczki, P., Johnston, K. W., Kempczinski, R. F., Krupski, W. C. (eds).*Vascular Surgery*, Volume 1. USA. W. B. Saunders Company.

Wilson, K. J. W., Waugh, A. (8th ed). (1998). *Ross and Wilson, Anatomy and Physiology in Health and Illness*. United States of America. Churchill Livingstone.

Winwood, R. S., Smith, J. L. (6th ed). (1985). *Sear's Anatomy and Physiology for Nurses*. London. Edward Arnold Ltd.

Wood, A. J. J. (ed) (1996). "Drug Therapy, Management of Venous Thromboembolism" *N Engl J Med* 335 (24), 1816-28.

Woolf, N., Wotherspoon, A., Young, M. (2002). *Essentials of Pathology*. Edinburgh. Saunders.

World Health Organisation (WHO). (2002). *The World Health Report 2002, Reducing Risks, Promoting Healthy Life.* [Online]. Available: http://www.who.int/whr/2002/en/whr02_en.pdf (at 07/12/05).

Wright, O. (2003) 4 Passengers on every jumbo suffer DVT. *The English Times* Friday December 19 2003 p.1.

Zotz, R. B., Gerhardt, A., Kluft, C., Scharf, R. E. (2005). "Venous thromboembolism during pregnancy is not associated with persistent elevated activated protein C (APC) sensitivity ratio based on the endogenous thrombin potential". *Thromb Haemost*. 93, 306-10.

APPENDIX A
APPROVAL FROM BEAUMONT HOSPITAL ETHICS COMMITTEE

Beaumont Hospital
Ethics (Medical Research) Committee

Copy

Chairperson: Professor Gerry McElvaney
Convenor: Professor Kieran Murphy

Administrator: Gillian Vale

5th December 2006

REC reference: 06/56 **EudraCT No: nil** **Protocol No: nil**

Dr. Patricia Fitzgerald
Director of Non-Invasive Vascular Unit
Department of Surgery
Beaumont Hospital

Dear Dr. Fitzgerald

06/56 – Dr. Patricia Fitzgerald – The Tromped and Mediven ® Travel Compression Stocking Experiment

The Recognised Ethics Committee reviewed the above application at its meeting held on the 1st September 2006. A Quorum was present at this meeting.

The Committee has given a favourable ethical opinion for the above clinical investigation of a medical device based on the application, protocol and supporting documentation (as listed in the attached document)

This study was given a favourable opinion on the 5th December 2006. This favourable opinion is extended to the site listed below only.

Chief Investigator & Principal Investigator	Site
Dr. Patricia Fitzgerald	Beaumont Hospital

The following condition is attached to this favourable opinion:

- A Site Specific Assessment Form signed by Dr. Fitzgerald and the Beaumont Hospital CEC must be submitted for review. (marked as pending in the attached document.)

Yours sincerely

Prof. Kieran Murphy
Convenor
Ethics (Medical Research) Committee

Ethics (Medical Research) Committee Beaumont Hospital Dublin 9
Tel: 353-1-809 2680 Email: gillianvale@beaumont.ie

Ethics (Medical Research) Committee - Beaumont Hospital
Notification of ERC/IRB Approval

Investigator: Dr. Patricia Fitzgerald

Protocol No.: 06/56

Protocol Title: The Tromped and Mediven ® Travel Compression Stocking Experiment

Ethics Committee Meeting Date: 1st September 2006

Final Approval Date: 5th December 2006

From: Ethics (Medical Research) Committee - Beaumont Hospital, Beaumont, Dublin 9

Documents Reviewed

Document and Date	Date Reviewed	Approved
Application Form 06/56 V2, 10/06	5/12/06	Yes
Protocol, 06/56, undated	5/12/06	Yes
Letter to Participants V2, 10/06	5/12/06	Yes
Patient Information Leaflet & Consent Form, V2, 10/06	5/12/06	Yes
Poster, V2, 10/06	5/12/06	Yes
Questionnaire July, 2006, Footnoted V1, 1/1/06	5/12/06	Yes
Allianz Insurance Letter For DIT, 31/5/06	5/12/06	Yes
Irish Medicine's Board Letter, 28/9/06	5/12/06	Yes
Site Specific Assessment Form, (Beaumont Hospital) Signed P.I. & CEO	Pending	Pending
Study Agreement	N/A	N/A
Form of Indemnity	N/A	N/A

Professor Kieran Murphy
ERC/IRB – Convenor's Signature
Approval # 1, dated 5/12/06

Beaumont Hospital
Ethics (Medical Research) Committee

Chairperson: Professor Gerry McElvaney
Convenor: Professor Kieran Murphy
Administrator: Gillian Vale

To: The Principal Investigator

From: The Beaumont Hospital Ethics (Medical Research) Committee

Re: Terms of Approval

- The trial is conducted in compliance with the approved protocol and any deviation from the original protocol is not implemented without prior approval from the Ethics (Medical Research) Committee.

- All serious unexpected adverse events related to the drug medication are promptly reported to the Ethics Committee.

- Updates in the form of an Annual reports (one year after the month in which the approval was granted) and Final reports on completion, termination, or suspension of trial are submitted to the Committee.

- Arrangements are in place to ensure that Indemnity and/or compensation is available to cover all possible claims from participants.

- Full compliance with all regulatory and legal requirements currently in existence. In particular Irish Medicines Board approval for all clinical trials and their amendments.

- Trial conducted in accordance with the ethical principles that have been outlined in the Declaration of Helsinki and consistent with ICH GCP.

- All clinical trial drugs or medical devices supplied free of charge by a sponsoring company are not charged to patients participating in such trials either during the period of the trial or for any extended follow-up period.

Ethics (Medical Research) Committee Beaumont Hospital Dublin 9
Tel: 353-1-809 2680 Email: gillianvale@beaumont.ie

APPENDIX B
APPROVAL FROM DUBLIN INSTITUTE OF TECHNOLOGY ETHICS COMMITTEE

OFFICE OF GRADUATE STUDIES

Head: Bob Kavanagh, *B.Sc, M.Sc. M.A. (Hon).*

DUBLIN INSTITUTE *of* TECHNOLOGY
Institiúid Teicneolaíochta Bhaile Átha Cliath

Office of Graduate Studies
Dublin Institute of Technology
Fitzwilliam House
30 Upper Pembroke Street
Dublin 2, Ireland

Tel: +353 1 402 3434
Fax: +353 1 402 3431
Email: postgraduate@dit.ie

27th September 2006

Carolyn Collins
Department of Transport Engineering
DIT Bolton Street
Dublin 1

Re: Research ethics submission ref. 11/06

Dear Carolyn,

Thank you for submitting further documentation in relation to your research ethics submission for the project "*The Development of an In-Flight Exercise Machine 'The Tromped' to Prevent Stasis and the Onset of Flight-Related Deep Vein Thrombosis*" (ref. 11/06).

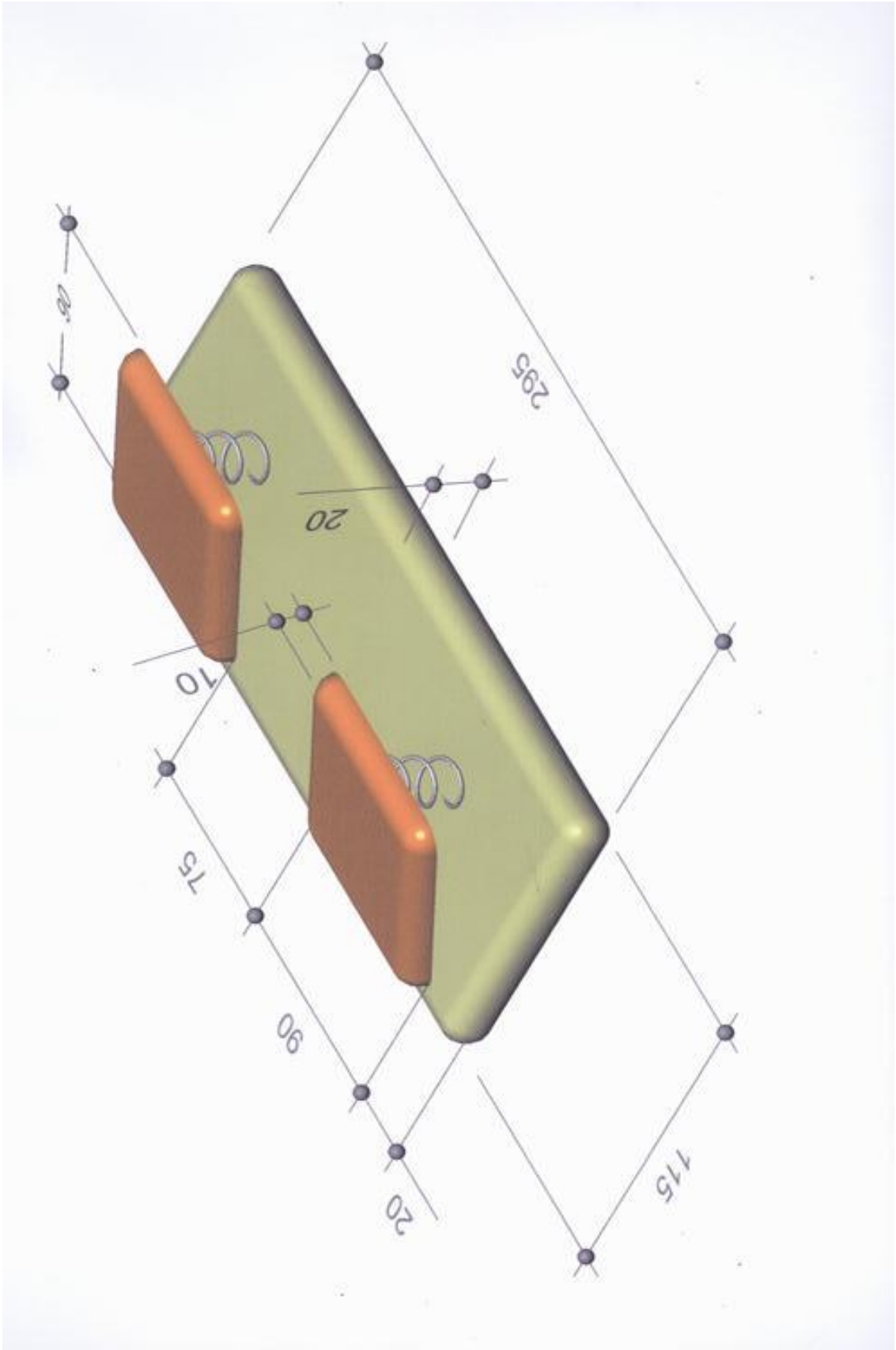
In light of these documents, the Research Ethics Committee agrees to grant ethical approval to your research project.

Kind regards,

Raffaella Salvante
Office of Graduate Studies

APPENDIX C
CHATILLION FORCE GAUGE

APPENDIX D
AUTOCAD DIAGRAM OF THE TROMPED FOOTREST


295
20
10
75
90
20
115

APPENDIX E
LETTER OF RECOMMENDATIONS FROM THE MEDICAL ETHICS BOARD IN BEAUMONT HOSPITAL

1 Beaumont Hospital
Ethics (Medical Research) Committee

Chairperson: Professor Gerry McElvaney
Convenor: Professor Kieran Murphy
Administrator: Gillian Vale

6th July 2006

2 Our reference: 06/56

Dr. Patricia Fitzgerald
Director of Non-Invasive Vascular Unit
Department of Surgery
Beaumont Hospital

Dear Dr. Fitzgerald

06/56 – Dr. Patricia Fitzgerald – The Tromped and Mediven ® Travel Compression Stocking Experiment

The above protocol was reviewed at a recent meeting of the Ethics (Medical Research) Committee, held on the 1st September 2006. The following points need to be addressed:

1. The Committee asks if the 'Tromped and Mediven ® Travel Compression Stocking' is classed as a 'medical device' and requests that the Principal Investigator confirm this with Dr. Niall MacAleenan, Medical Devices Section of the Irish Medicines Board. If this proves to be the case and if this study proves to be a 'clinical trial of a medical device', it may be necessary to complete Box B on page 3 of the application form.

2. The Committee states that the sections entitled **'Part 1 of the study'** and **'Part 2 of the study'** in the **Patient Information Leaflet** are too long and detailed. The description of the exercises is long and confusing, and would be better explained verbally to the patients during the assessment. Of note, the description of the exercises in the Patient Information Leaflet also differs from the description in the application form and in the protocol.

3. The Committee ask if it is possible to reach a statistically-significant conclusion **(Question 8)** with only 10 participants.

4. The Committee requests that the reply to **Question 14** be amended to state there is no direct benefit to participants in taking part in this study.

5. The Committee states that the reply to **Question 10** be amended to state there is a risk to participants and to outline what this risk is. (If there was no risk, the exclusion criteria in this study would not be so detailed.) The committee seeks clarification on what the risk of participation is for a participant who unknowingly fulfils one of the exclusion criteria (e.g. an undiagnosed bleeding disorder), and proceeds to participate in this study.

6. The Committee states that the **Recruitment Poster** does not need to include all the exclusion criteria. Participants will not understand the term 'exclusion criteria' and one needs medical knowledge to understand some of the exclusion criteria as currently listed in the poster. It is also possible for the participants to fulfill some of the exclusion criteria and to be unaware of this.

7. The Committee states that **Question 7 (a), page 1 of the Questionnaire** refers to "a journey of greater than four hours in length." However other parts of the application refer to 8 hours. Please clarify.

8. The Committee seeds confirmation that none of the ten participants will be in a supervisory or dependent relationship with any of the investigators.

9. The Committee states that it is not appropriate to send the 'research experiment protocol' to participants. Please amend the **'Letter to Participants'** accordingly.

10. Given the exclusion criteria, the Committee requests that written informed consent is obtained from all ten participants by Dr. Patricia Fitzgerald. **(Question 26).** It is not appropriate for Ms. Collins to obtain consent.

11. The committee requests that the sentence: *"You are obliged to COMPLY with the instructions and give honest true information,"* be deleted from **page 5 of the Patient Information Leaflet.**

12. The committee requests that all reference to contraception be removed from the **Patient Information Leaflet**, as this does not appear to be relevant to the study. Please amend and comment.

13. The committee requests that the paragraph **entitled "Confidentiality Issues" on page 6 of the Patient Information Leaflet** be amended. It is inaccurate to inform patients that only anonymous (rather than coded) data will be collected**. (See Question 38, Application Form).**

14. The committee requests that the Patient Information Leaflet inform participants that their data will be stored for 10 years and then shredded, **as per Question 37 of the Application Form**.

15. Please respond with a cover letter addressing each of these points, cover letter to be signed by Principal Investigator. This cover letter should address each of the above numbered points. (One copy of the cover letter is sufficient)

16. Please note that all revised documents must be clearly marked VERSION 2 and dated. In addition all changes made to version 2 documents as compared to originally submitted documents should be clearly underlined or highlighted. (One copy of all revised documents, VERSION 2, is sufficient)

With best regards

Yours sincerely

Professor Kieran Murphy
Convenor
Ethics (Medical Research) Committee

c.c. Ms. Carolyn Collins, 26 Croydon Green, Marino, Dublin 3

APPENDIX F
LETTER OF RECOMMENDATION FROM DR. MacALEENAN

IRISH MEDICINES BOARD

28th September 2006

Dr. P. FitzGerald,
Director,
Non-invasive vascular laboratory,
Beaumont Hospital,
Dublin 9.

Re: PhD thesis investigation – Tromped Test Jig Foot Pedal

Dear Dr. FitzGerald,

Thank you for your recent query relating to the investigation of the Tromped Test Jig Foot Pedal to be conducted as part of the PhD thesis of Carolyn Collins. It appears from the information provided and our telephone discussions that the Tromped Foot Pedal would be classified as a medical device as its intended use includes medical claims. You have confirmed that this device investigation represents pure clinical research and we understand that there is no commercial intent. In our opinion this represents non-commercial clinical research of a non-CE marked device that does not require notification to or review by the IMB prior to commencing. We assume that any other devices being used during the course of this research e.g. the APG device, are being used within their normal and intended use entirely within the terms of their CE marks.

As we discussed it is worth referring to the Medical Devices Directive (93/42/EEC) and the corresponding Statutory Instrument SI 252 of 1994. Annex I defines the Essential Requirements for Medical Devices and these can be used as a useful template to conduct the research and ensure that the data gathered will address the Essential Requirements relevant to your device.

Please feel free to contact me with any queries.

Yours sincerely,

Niall MacAleenan,
Medical Assessor,
Medical Devices Department.
☎01 6764971 🖷 01 6344033
✉ niall.macaleenan@imb.ie

Bord Leighseora na hEireann
Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2. Tel: [illegible] Fax: [illegible]
Website: www.imb.ie

APPENDIX G
ASSESSMENT I ABSOLUTE AND DERIVED VALUES

Patient	1	2	3	4	5	6	7	8	9	10
Age	4 /01 /39	6 /02 /77	5 /12 /56	1 /08 /64	6 /02 /81	22 /09/ 72	7 /12 /48	14 /12 /84	25 /04 /58	04 /01 /79
Control										
VV (mls)	110	100	150	100	75	130	135	166	70	150
90%VV	99	90	135	90	67.5	117	121.5	149.4	63	135
VFT (sec)	140	137	151	143	163	255	181	290	112.5	215
VFI (ml/sec)	0.78 5	0.729	0.99	0.699	0.46	0.5	0.745	0.572	0.622	0.697
EV mls)	100	58	101	60	70	80	60	92	51	57
EVF (%)	90.9	58	67.3	60	93.3	61.5	44.4	55.4	72.85	38
RV(mls)	10	47	26	10	7	15	10	34	3	49
RVF (%)	9.09	47	17.33	10	9.3	11.5	7.4	20.48	4.28	32.6
Av W EV	25	45	70	30	15	70	75	43	30	65
Av W RV	10	40	40	21	30	45	22	0	5	15
Sitting										
VV mls)	55	150	125	100	75	150	95	80	105	142
DA, EV (mls)	43	77	90	42	45	90	60	62	64	93
DA, EVF (%)	78.2	51.3	72	42	60	60	63.15	77.5	60.95	65.49
DA, RV (mls)	7	65	36	32	5	70	20	14	30	16
DA, RVF (%)	12.7	43.3	28.8	32	6.6	46.6	21.05	17.5	28.57	11.26
DB, EV (mls)	35	50	92	44	60	80	45	48	68	86
DB, EVF (%)	63.6 3	33.33	73.6	44	80	53.33	47.36	60	64.76	60.56
DB, RV (mls)	7	60	20	22	5	65	20	54	14	27
DB, RVF (%)	12.7 2	40	16	22	6.6	43.33	21.05	67.5	13.33	19.01

APPENDIX H
ASSESSMENT II RECRUITMENT POSTER

STOP THE CLOTS!

ARE YOU AWARE OF THE DANGERS OF FLYING LONG HAUL FLIGHTS?

WOULD YOU BE WILLING TO AID TESTING OF AN IN-FLIGHT EXERCISE DEVICE?

(ARE YOU BETWEEN 20 AND 35?)

10 HEALTHY VOLUNTEERS ARE REQUIRED.

THIS RESEARCH IS NON-INVASIVE.

An Air Chamber will be placed on the participants right calf (from knee to ankle). You will be required to conduct foot movements in a standing and seated position while wearing a Mediven®, knee length, compression stocking for the second half of the experiment.

NO DISCOMFORT OR PAIN WILL BE FELT!!

YOU MAY BE SUITABLE IF YOU HAVE NOT HAD:

1) VARICOSE VEINS OR PREVIOUS SURGERY FOR VARICOSE VEINS.
2) PREVIOUS EPISODE OF VENOUS THROMBOEMBOLISM (DVT).
3) TRAVELLED BY AIR FOR GREATER THAN 4 HOURS DURATION, DURING THE LAST 6 WEEKS
4) HAVE NOT HAD SURGERY IN THE LAST 12 WEEKS.

IF INTERESTED PLEASE CONTACT: CAROLYN
PHONE: 01-402 3605
EMAIL: Carolyn.Collins@dit.ie

Poster, Version 2, September 2006

APPENDIX I
ASSESSMENT II INFORMATION LETTER

DUBLIN INSTITUTE OF TECHNOLOGY

February 16th 2008.

Dear Sir or Madam,

Firstly many thanks for considering volunteering in this research study. As you may know the dangers of flight related deep vein thrombosis are real, so you will be aiding the attempt to provide a solution for long haul passengers, possibly yourself and family members.

This research is non-invasive. A chamber filled with air will be placed around your lower right limb (from ankle to knee). It is not as tight as a blood pressure cuff and you will experience no discomfort or pain.

You will be instructed when and how to conduct different exercise manoeuvres in the standing and seated position, with the air chamber surrounding your calf for the duration of the assessment.

I look forward to meeting with you in the near future. If you have any questions or queries, please do not hesitate to contact me, either by telephone or email.

Sincerely,

_____

Carolyn Collins

Postgraduate research student,
Department of Transport Engineering,
Faculty of Engineering,
Bolton Street,
Dublin 1.

Email: Carolyn.collins@dit.ie
Telephone: xxx xxxxxxx

APPENDIX J
ASSESSMENT II QUESTIONNAIRE

The Mediven® Travel Compression Stocking Experiment

(January, 2007)

Questionnaire for participants

Principal Investigator: Doctor Patricia Fitzgerald.

Please fill in the following questions, by ticking the appropriate boxes and filling in any relative additional information required.

Surname: _____

Forename: _____

Date of Birth: _____

1. Have you ever been diagnosed with a thrombus (clot)? Yes ☐ No ☐

2. Do you have varicose veins? Yes ☐ No ☐

3. Do you have arterial disease? Yes ☐ No ☐

4. Have you had any surgery within the last 12 weeks? Yes ☐ No ☐

5. Have you ever been diagnosed with cancer? Yes ☐ No ☐

6. Are you taking the oral contraceptive at the moment? Yes ☐ No ☐

7 (a) Are you pregnant or have you been pregnant within the last six months?

Yes ☐ No ☐

7 (a). Have you travelled a journey of greater than four hours in length, in the seated position, within the last six weeks?

Yes ☐ No ☐

7 (b). If so what was the duration of travel _____

7 (c) Which form(s) of transport did you travel by?

Car ☐ Bus ☐ Train ☐ Airplane ☐ Boat ☐

If you answered yes to ONE of questions numbered 1- 7, we regret that you will be unable to participate in this research experiment.

8 (a). Are you taking any medication at the moment? Yes ☐ No ☐

8 (b). If so, what is the purpose of the medication?_____

_____

8 (c). What is the name of your medication?_____

_____

11. Are you on Hormone Replacement Therapy at the moment? Yes ☐ No ☐

Signed (Participant) _____

Date: _____

I agree that the identity of this participant will remain anonymous.

Signed (Investigator) _____

APPENDIX K
ASSESSMENT II (PART I & II) ABSOLUTE AND DERIVED VALUES

Mediven assessment Results, (Without Stocking)

Patient	1	2	3	4	5	6	7	8	9	10
Date of Birth	12 /01 /80	13 /12 /76	18 /8/ 83	07 /02 /84	22 /09 /72	14 /12 /84	04 /01/ 79	13 /12 /81	11 /09 /77	08 /04 /77
Control										
VV (mls)	154	160	89	104	106	139	106	160	140	86
90%VV (ml)	138. 6	144	80.1	93.6	95.4	125.1	95.4	144	126	77.4
VFT (sec)	226	158	126	200	206. 5	201	144	152	206	167
VFI (ml/sec)	0.68	1.01	0.71	0.52	0.51	0.69	0.74	1.05	0.67	0.51 4
EV (mls)	94	76	65	65	54	66	52	106	77	75
EVF (%)	61.0 3	47.5	73.0 3	62.5	50.9 4	55.93	49.0 5	66.25	55	87.2
RV (mls)	18	13	13	40	18	27	8	44	25	10
RVF (%)	11.7	8.125	14.6	40	16.9	22.88	7.54	27.5	17.9	11.6 2
Av (W) EV	30	72	25	25	35	25	20	22	55	35
Av (W) RV	40	35	5	30	0.5	15	40	18	17	10
Sitting										
VV (mls)	123	118	72	76	62	107	110	109	116	92
Demonstrator A										
EV (mls)	74	81	45	43	38	52	70	65	95	56
EVF (%)	60.2	68.64	62.5	56.5	61.3	48.59	63.6	59.6	81.9	60.8 6
RV (mls)	24	11	16	41	30	38	22	53	28	18
RVF (%)	19.51	9.3	22.2	53.9	48.38	35.5	20	48.62	24.13	19.5 6

Patient	1	2	3	4	5	6	7	8	9	10
Date of Birth	12 /01 /80	13 /12 /76	18 /8/ 83	07 /02 /84	22 /09 /72	14 /12 /84	04 /01/ 79	13 /12 /81	11 /09 /77	08 /04 /77
PLANTARFLEXION										
EV (mls)	45	63	34	35	28	38	49	23	90	51.08
EVF (%)	36.58	53.3	47.22	46.05	45.16	35.51	44.54	21.1	77.58	51.08
RV (mls)	29	33	12	46	28	45	22	69	35	17
RVF (%)	23.57	27.96	16.6	60.5	45.16	42	20	63.3	30.17	18.47
DORSIFLEXION										
EV (mls)	47	65	50	35	30	43	55	13	63	52
EVF (%)	38.2	55.08	69.44	46.05	48.38	40.18	50	11.92	54.31	56.52
RV (mls)	15	16	19	20	19	23	17	74	13	33
RVF (%)	12.1	13.5	26.38	26.3	30.64	21.49	15.45	67.88	11.2	35.86
CIRCLE										
EV (mls)	34	53	24	21	14	25	32	17.5	36	17
EVF (mls)	27.6	44.9	33.33	27.63	22.58	23.36	29.09	160.5	31.03	18.47
RV (mls)	11	75	26	37	21	47	15	68	6	31
RVF (mls)	8.94	63.5	36.11	48.68	33.87	43.92	13.63	62.38	5.17	33.69

Mediven® Assessment II Results, (With stockings)

Patient	1	2	3	4	5	6	7	8	9	10
Date of Birth	12 /01 /80	13 /12 /76	18 /8/ 83	07 /02 /84	22 /09 /72	14 /12 /84	04 /01/ 79	13 /12 /81	11 /09 /77	08 /04 /77
Control										
VV (mls)	125	105	42	76	99	87	44	106	106	70
90%VV	112.5	94.5	37.8	68.4	89.1	78.3	39.6	108	95.4	63
VFT (sec)	190	106	145	178	302	161	164.5	130	134	158
VFI	0.657	0.99	0.28	0.42	0.32	0.54	0.26	0.92	0.79	0.44
EV(mls)	80	67	25	52	67	60	30	38	50	72
EVF (%)	64	63.8	66.66	68.42	67.67	68.96	68.18	31.66	47.16	102.82
RV mls)	36	14	14	35	12	48	7	38	44	10
RVF(%)	28.8	13.3	33.33	46.05	12.12	55.17	15.9	35.84	41.5	14.28
Average (W) EV	30	35	15	20	25	50	12	16	20	25
Average (W) RV	45	40	16	35	10	7	14	45	27	5
Sitting										
VV(mls)	95	89	37	66	64	75	35	115	84	54
Demonstrator A										
EV (mls)	42	55	24	42	41	54	15	88	55	50
EVF (%)	44.2	61.79	64.86	63.63	64.06	72	42.85	76.52	65.47	92.59
RV mls	14	18	23	17	25	63	12	21	9	15
RVF(%)	14.7	20.2	62.16	25.75	39.06	84	34.28	18.26	10.71	27.7

Patient	1	2	3	4	5	6	7	8	9	10
Date of Birth	12 /01 /80	13 /12 /76	18 /8/ 83	07 /02 /84	22 /09 /72	14 /12 /84	04 /01/ 79	13 /12 /81	11 /09 /77	08 /04 /77
Heel up, EV (mls)	43	50	21	34	44	57	31	16	50	54
Heel up, EVF (%)	45.26	56.17	56.75	51.51	68.75	76	88.57	13.91	59.52	100
Heel up, RV (mls)	29	33	3	19	25	11	6	42	12	28
Heel up, RVF %)	30.5	37.07	8.1	28.78	39.06	14.66	17.14	36.52	14.28	51.85
Toes up, EV (mls)	38	48	24	32	42	15	16	16	38	5
Toes up, EVF (%)	40	53.93	64.86	48.48	65.62	20	45.71	13.91	45.23	9.25
Toes up, RV (mls)	25	16	4	7	16	20	7	60	10	10
Toes up, RVF (%)	26.3	17.9	10.8	10.6	25	26.66	20	52.17	11.9	18.5
Circle, EV (mls)	34	24	25	9	15	17	18	39	45	14
Circle, EVF (mls)	35.78	26.96	67.56	13.63	23.43	22.66	51.42	33.9	53.57	25.92
Circle, RV (mls)	22.5	30	11	22	46	14	4	39	8	15
Circle, RVF (mls)	23.68	33.7	29.72	33.33	71.87	18.66	11.4	33.9	9.52	27.77

APPENDIX L
ASSESSMENT III
RECRUITMENT POSTER

STOP THE CLOTS!

ARE YOU AWARE OF THE DANGERS OF FLYING LONG HAUL FLIGHTS?

WOULD YOU BE WILLING TO AID TESTING OF AN IN-FLIGHT EXERCISE DEVICE?

(ARE YOU BETWEEN 25 AND 50?)

6 healthy, 6 obese (male/female) and 6 women taking the oral contraceptive pill are required.

THIS RESEARCH IS NON-INVASIVE.

Volunteers will wear an air chamber on their calf
(from knee to ankle),
& conduct foot movements in a standing and sitting position.

NO DISCOMFORT OR PAIN WILL BE FELT!!

IF INTERESTED PLEASE CONTACT CAROLYN:

PHONE: 402 3605

EMAIL: Carolyn.collins@dit.ie

APPENDIX M
ASSESSMENT III
QUESTIONAIRE

The Tromped Footrest Experiment

(March, 2007)

Questionnaire for participants

Principal Investigator: Carolyn Collins

Please fill in the following questions, by ticking the appropriate boxes and filling in any relative additional information required.

Surname: _____

Forename: _____

Date of Birth: _____

1. Have you ever been diagnosed with a thrombus (clot)? Yes ☐ No ☐

2. Do you have varicose veins? Yes ☐ No ☐

3. Do you have arterial disease? Yes ☐ No ☐

4. Have you had any surgery within the last 12 weeks? Yes ☐ No ☐

5. Have you ever been diagnosed with cancer? Yes ☐ No ☐

6 (a) Are you pregnant or have you been pregnant within the last six months?

Yes ☐ No ☐

7 (a). Have you travelled a journey of greater than four hours in length, in the seated position, within the last six weeks?

Yes ☐ No ☐

7 (b). If so what was the duration of travel _____

7 (c) Which form(s) of transport did you travel by?

Car ☐ Bus ☐ Train ☐ Airplane ☐ Boat ☐

If you answered yes to ONE of questions numbered 1- 7, we regret that you will be unable to participate in this research experiment.

8 (a). Are you taking any medication at the moment? Yes ☐ No ☐

8 (b). If so, what is the purpose of the medication?_____

_____

8 (c). What is the name of your medication?_____

_____

11. Are you on Hormone Replacement Therapy at the moment? Yes ☐ No ☐

12. Are you taking the oral contraceptive at the moment? Yes ☐ No ☐

12 (b) If yes, what is the name of this oral contraceptive pill?

_____

Signed (Participant) _____

Date: _____

I agree that the identity of this participant will remain anonymous.

Signed (Investigator) _____

APPENDIX N
ASSESSMENT III
CONSENT FORM

Section 3 CONSENT FORM

Researcher's Name: CAROLYN COLLINS (use block capitals)	Title:
Faculty/School/Department: FACULTY OF ENGINEERING, DEPARTMENT OF TRANPSORT ENGINEERING	
Title of Study: THE DEVELOPMENT OF AN IN-FLIGHT MEDICAL DEVICE THE TROMPED TO PREVENT FLIGHT RELATED DEEP VEIN THROMBOSIS.	
To be completed by the: subject/patient/volunteer/informant/interviewee/parent/guardian (delete as necessary)	

3.1 Have you been fully informed/read the information sheet about this study? YES/NO

3.2 Have you had an opportunity to ask questions and discuss this study? YES/NO

3.3. Have you received satisfactory answers to all your questions? YES/NO

3.4 Have you received enough information about this study and any associated health and safety implications if applicable? YES/NO

3.5 Do you understand that you are free to withdraw from this study?

- at any time
- without giving a reason for withdrawing
- without affecting your future relationship with the Institute YES/NO

3.6 Do you agree to take part in this study the results of which are likely to be published? YES/NO

3.7 Have you been informed that this consent form shall be kept in the confidence of the researcher? YES/NO

Signed_____ Date _____

Name in Block Letters _____

Signature of Researcher _____ Date _____

Please note:

- For persons under 18 years of age the consent of the parents or guardians must be obtained or an explanation given to the Research Ethics Committee and the assent of the child/young person should be obtained to the degree possible dependent on the age of the child/young person. Please complete the Consent Form (section 4) for Research Involving 'Less Powerful' Subjects or Those Under 18 Yrs.

- In some studies, witnessed consent may be appropriate.

- The researcher concerned must sign the consent form after having explained the project to the subject and after having answered his/her questions about the project.

APPENDIX O
ASSESSMENT III ABSOLUTE & DERIVED VALUES FOR ALL 18 PARTICIPANTS

Assessement III Results obtained when volunteers were standing

Patient	VV (mls)	90% VV	VFT (secs)	VFI (ml/s)	TT EV (mls)	TT EVF (%)	TT RV (mls)	TT RVF (%)
1	109	98.1	129	0.844	53	48.62	28	25.68
2	110	99	97	1.134	41	37.27	30	27.27
3	98	88.2	172	0.569	96	97.95	5	5.10
4	90	81	194	0.463	74	82.22	4	4.44
5	160	144	177	0.903	95	59.37	50	31.25
6	87	73.3	110	0.74	45	51.72	46	52.87
7	89	80.1	106	0.839	53	59.55	24	26.96
8	170	153	115	1.478	103	60.58	27	15.88
9	81	72.9	185	0.437	60	74.07	10	12.34
10	165	148.5	151	1.09	105	63.63	55	33.33
11	166	149.4	179	0.927	134	80.72	39	23.49
12	95	85.5	149	0.637	76	80	83	87.36
13	193	173.7	136	1.419	180	93.26	25	12.95
14	175	157.5	94	1.86	95	54.28	55	31.42
15	90	81	111	0.81	48	53.33	27	30
16	73	65.7	154	0.474	50	68.49	30	41.09
17	40	36	152	0.263	20	50	13	32.5
18	100	90	88	1.136	95	95	9	31.42

Assessement III Results (Volunteers 1-9) obtained when seated

Patient	1	2	3	4	5	6	7	8	9
Sitting									
VV (mls)	54	65	95	110	110	94	64	123	80
Footrest I, EV (mls)	35	17	36	67	84	26	46	39	45
Footrest I, EVF (%)	64.81	26.15	37.89	60.9	76.36	27.65	71.87	31.7	56.25
Footrest I, RV (mls)	32	59	65	35	45	74	44	54	32
Footrest I, RVF (%)	59.25	90.76	68.42	31.81	40.9	78.72	68.75	43.9	40
Footrest II, EV (mls)	19	22	20	40	76	22	43	38	36
Footrest II, EVF (%)	35.18	33.84	21.05	36.36	69.09	23.4	67.18	30.89	45
Footrest II, RV (mls)	24	33	79	55	45	61	60	50	17
Footrest II, RVF (%)	44.44	50.76	83.15	50	40.9	64.89	93.75	40.65	21.25
Footrest III EV (mls)	31	26	14	78	74	16	45	43	38
Footrest III EVF (%)	57.4	40	14.73	70.9	67.27	17.02	70.31	34.95	47.5
Footrest III RV (mls)	32	27	75	46	23	63	39	51	20
Footrest III RVF (%)	59.25	41.53	78.94	41.81	20.9	67.02	60.93	41.46	25
Footrest IV EV (mls)	30	15	4	56	98	23	43	38	33
Footrest IV EVF (%)	55.55	23.07	4.21	50.9	89.09	24.46	67.18	30.89	41.25
Footrest IV RV (mls)	36	5	86	55	36	47	25	24	12
Footrest IV RVF (%)	66.66	7.69	90.52	50	32.72	50	39.06	19.51	15
DA EV (mls)	33	18	56	104	91	25	28	66	31
DA EVF (%)	61.11	27.69	58.94	94.54	82.72	26.59	43.75	53.65	38.75
DA RV (mls)	48	28	54	16	38	69	30	25	21
DA RVF (%)	88.88	43.07	56.84	14.54	34.54	73.4	46.87	20.32	26.25

Experiment III Results (Volunteers 10-18) obtained when seated in aircraft seats.

Patient	10	11	12	13	14	15	16	17	18
Sitting									
VV (mls)	140	132	67	105	134	93	80	50	106
Footrest I, EV (mls)	88	124	16	69	73	25	21	8	74
Footrest I, EVF (%)	62.85	93.93	23.88	65.71	54.47	26.88	26.25	16	50
Footrest I, RV (mls)	56	36	26	50	65	77	53	38	20
Footrest I, RVF (%)	40	27.27	38.8	47.6	48.5	82.79	66.25	76	40.75
Footrest II, EV (mls)	78	93	30	55	96	23	14	33	63
Footrest II, EVF (%)	55.71	70.45	44.77	52.38	71.64	24.73	17.5	66	59.43
Footrest II, RV (mls)	43	36	30	43	64	69	53	35	14
Footrest II, RVF (%)	30.7	27.27	44.77	40.95	47.76	74.19	66.25	70	13.2
Footrest III EV (mls)	85	85	14	46	66	23	18	6	40
Footrest III EVF (%)	60.71	64.39	20.89	43.8	49.25	24.73	22.5	12	37.73
Footrest III RV (mls)	45	45	42	37	60	53	50	19	5
Footrest III RVF (%)	32.14	34.09	62.68	35.23	44.77	56.98	62.5	38	4.716
Footrest IV EV (mls)	100	76	15	60	90	23	29	18	35
Footrest IV EVF (%)	71.42	57.57	22.38	57.14	67.16	24.73	36.25	36	33.01
Footrest IV RV (mls)	36	40	12	10	60	62	48	34	5
Footrest IV RVF (%)	25.71	30.3	17.9	9.52	44.77	66.66	60	70	4.716
DA EV (mls)	80	63	25	96	75	45	65	23	53
DA EVF (%)	57.14	47.72	37.31	90.56	55.97	48.38	81.25	46	50
DA RV (mls)	53	55	33	46	80	75	54	30	15
DA RVF (%)	37.85	41.66	49.25	43.8	59.7	80.64	67.5	60	14.15

APPENDIX P
ASSESSMENT III
ABSOLUTE & DERIVED VALUES FOR NORMAL GROUP

Participant	1	6	7	8	11	13
STANDING						
VV (mls)	109	87	89	170	166	193
90VV	98.1	73.3	80.1	153	149	173.7
VFT	129	110	106	115	179	136
VFI	0.844	0.74	0.839	1.478	0.927	1.419
TT EV	53	45	53	103	134	180
TT EVF	48.62	51.72	59.55	60.58	80.72	93.26
TT RV	28	46	24	27	39	25
TT RVF	25.68	52.87	26.96	15.88	23.49	12.95
SITTING						
Sitting VV	54	94	64	123	132	105
Footrest I EV	35	26	46	39	124	69
Footrest I EVF	64.81	27.65	71.87	31.7	93.93	65.71
Footrest I RV	32	74	44	54	36	50
Footrest I RVF	59.25	78.72	68.75	43.9	27.27	47.6
Footrest II EV	19	22	43	38	93	55
Footrest II EVF	35.18	23.4	67.18	30.89	70.45	52.38
Footrest II RV	24	61	60	50	36	43
Footrest II RVF	44.44	64.89	93.75	40.65	27.27	40.95
Footrest III EV	31	16	45	43	85	46
Footrest III EVF	57.4	17.02	70.31	34.95	64.39	43.8
Footrest III RV	32	63	39	51	45	37
Footrest III RVF	59.25	67.02	60.93	41.46	34.09	35.23
Footrest IV EV	30	23	43	38	76	60
Footrest IV EVF	55.55	24.46	67.18	30.89	57.57	57.14
Footrest IV RV	36	47	25	24	40	10
Footrest IV RVF	66.66	50	39.06	19.51	30.3	9.52
DA EV	33	25	28	66	63	96
DA EVF	61.11	26.59	43.75	53.65	47.72	90.56
DA RV	48	69	30	25	55	46
DA RVF	88.88	73.4	46.87	20.32	41.66	43.8

APPENDIX Q
ASSESSMENT III ABSOLUTE & DERIVED VALUES FOR OBESE GROUP

Participant	3	4	5	9	14	18
STANDING						
VV (mls)	98	90	160	81	175	100
90VV	88.2	81	144	72.9	157.5	90
VFT	172	194	177	185	94	88
VFI	0.569	0.463	0.903	0.437	1.86	1.136
TT EV	96	74	95	60	95	95
TT EVF	97.95	82.22	59.37	74.07	54.28	95
TT RV	5	4	50	10	55	9
TT RVF	5.1	4.44	31.25	12.34	31.42	31.42
SITTING						
Sitting VV	95	110	110	80	134	106
Footrest I EV	36	67	84	45	73	74
Footrest I EVF	37.89	60.9	76.36	56.25	54.47	50
Footrest I RV	65	35	45	32	65	20
Footrest I RVF	68.42	31.81	40.9	40	48.5	40.75
Footrest II EV	20	40	76	36	96	63
Footrest II EVF	21.05	36.36	69.09	45	71.64	59.43
Footrest II RV	79	55	45	17	64	14
Footrest II RVF	83.15	50	40.9	21.25	47.76	13.2
Footrest III EV	14	78	74	38	66	40
Footrest III EVF	14.73	70.9	67.27	47.5	49.25	37.73
Footrest III RV	75	46	23	20	60	5
Footrest III RVF	78.94	41.81	20.9	25	44.77	4.716
Footrest IV EV	4	56	98	33	90	35
Footrest IV EVF	4.21	50.9	89.09	41.25	67.16	33.01
Footrest IV RV	86	55	36	12	60	5
Footrest IV RVF	90.52	50	32.72	15	44.77	4.716
DA EV	56	104	91	31	75	53
DA EVF	58.94	94.54	82.72	38.75	55.97	50
DA RV	54	16	38	21	80	15
DA RVF	56.84	14.54	34.54	26.25	59.7	14.15

APPENDIX R
ASSESSMENT III ABSOLUTE & DERIVED VALUES FOR ORAL CONTRACEPTIVE GROUP

Participant	2	10	12	15	16	17
STANDING						
VV (mls)	110	165	95	90	73	40
90VV	99	148.5	85.5	81	65.7	36
VFT	97	151	149	111	154	152
VFI	1.134	1.09	0.637	0.81	0.474	0.263
TT EV	41	105	76	48	50	20
TT EVF	37.27	63.63	80	53.33	68.49	50
TT RV	30	55	83	27	30	13
TT RVF	27.27	33.33	87.36	30	41.09	32.5
SITTING						
Sitting VV	65	140	67	93	80	50
Footrest I EV	17	88	16	25	21	8
Footrest I EVF	26.15	62.85	23.88	26.88	26.25	16
Footrest I RV	59	56	26	77	53	38
Footrest I RVF	90.76	40	38.8	82.79	66.25	76
Footrest II EV	22	78	30	23	14	33
Footrest II EVF	33.84	55.71	44.77	24.73	17.5	66
Footrest II RV	33	43	30	69	53	35
Footrest II RVF	50.76	30.7	44.77	74.19	66.25	70
Footrest III EV	26	85	14	23	18	6
Footrest III EVF	40	60.71	20.89	24.73	22.5	12
Footrest III RV	27	45	42	53	50	19
Footrest III RVF	41.53	32.14	62.68	56.98	62.5	38
Footrest IV EV	15	100	15	23	29	18
Footrest IV EVF	23.07	71.42	22.38	24.73	36.25	36
Footrest IV RV	5	36	12	62	48	34
Footrest IV RVF	7.69	25.71	17.9	66.66	60	70
DA EV	18	80	25	45	65	23
DA EVF	27.69	57.14	37.31	48.38	81.25	46
DA RV	28	53	33	75	54	30
DA RVF	43.07	37.85	49.25	80.64	67.5	60