MASTER THESIS

Investigating external compression as prevention of fainting incidences during upright weight-bearing MRI scans by measuring the deep veins of the legs

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Abstract

Objective This research focusses on the prevention of fainting incident during upright magnetic resonance imaging (MRI) scans. With the 0.25T MRI of Esaote and US, patients can be positioned in the upright position, which can have advantages to image gravity-dependent problems. A drawback that is seen, is that fainting incidences can occur due to inactivity of the lower leg muscles. The use of a compression pump for the legs decreases the fainting incidences by influencing the veins in the legs. Nevertheless, an alternative method to replace the pump is desired. Compression stockings are considered to have the same effect as the fluctuating compression on these veins. To investigate the behaviour of the veins, US is used as the cross-sectional area and the blood velocity of the deep veins can be measured.

Methods Two measuring methods were performed to measure the deep veins in the calf and the groin to investigate why fainting occurs, what the effect is on the veins due to fluctuating and constant compression, and if the constant compression can achieve the same effect as the fluctuating compression.

Results The first method focuses on the change in the cross-sectional area of the posterior tibial vein (PTV). There is no increase in the cross-sectional area seen in the upright position. For 2 of the 4 subjects, the compression of the fluctuating compression decreases the cross-sectional area. In all subjects, the cross-sectional area of the constant compression stays constant.

The second method focuses on the change in blood displacement to link this to the change in blood velocity in the common femoral vein (CFV). In 2 of the 4 subjects, a decrease in blood displacement is seen. For the fluctuating compression it was seen that when compression is increased, the blood displacement also increases. This was not seen when the constant compression is applied.

Conclusion The effect of the upright position, which causes a fainting incident, on the deep veins is still unclear. The effect of external compression on the deep veins is that when compression increases, the cross-sectional area decreases, and the blood velocity increases. When a constant compression is applied, the cross-sectional area decreases but the blood velocity stays constant. Therefore, constant compression cannot achieve the same effect as fluctuating compression.

Keywords weight-bearing MRI – fainting incident – deep veins – US - cross-sectional area – blood velocity

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Samenvatting

Objectief Dit onderzoek focust op het voorkomen van een flauwval incident tijdens rechtopstaande scan in een gewicht-dragende MRI. Met de 0.25T MRI scanner van Esaote en US kunnen patiënten in rechtopstaande positie geplaatst worden, wat voordeel kan hebben tijden de beeldvorming van zwaartekracht afhankelijke problemen. Een nadeel is dat flauwval incidenten kunnen voorkomen doordat de onderbeenspieren inactief zijn. Het gebruik van een compressie pomp voor de benen verlaagd de kans op flauwval incidenten, doordat het de venen in het onderbeen beïnvloed. Desondanks is een alternatieve methode voor deze pomp gewenst. Compressie sokken worden beschouwd hetzelfde effect te hebben op de venen als de fluctuerende compressie. Om het gedrag van de venen te onderzoeken, wordt de US gebruikt om de dwarsdoorsnede en de bloedsnelheid van de diepe venen te meten.
Methode Twee meetmethodes zijn uitgevoerd om te diepe venen in de kuit en de lies om te onderzoeken waarom flauwval incidenten voorvallen, wat het effect van de fluctuerende en constante compressie is op de venen, en of de constante compressie hetzelfde effect kan bereiken als de fluctuerende compressie.
Resultaten De eerst methode focust op de verandering in de dwarsdoorsnede van de achterste scheenbeenader. Er is geen toename in de dwarsdoorsnede te zien in de rechtopstaande positie. Voor twee van de vier proefpersonen neemt de dwarsdoorsnede af door de fluctuerende compressie. In alle proefpersonen blijft de dwarsdoorsnede constant wanneer constante compressie gebruikt wordt. De tweede methode focust op de verandering in de bloed verplaatsing, om te koppelen aan de bloedsnelheid, in de gemeenschappelijke dijbeenader. In twee van de vier proefpersonen is er een afname in de bloedsnelheid te zien. Voor de fluctuerende compressie was te zien dat wanner de compressie toeneemt, de bloedsnelheid ook toeneemt. Dit effect was niet te zien wanneer de constante compressie toegepast werd.
Conclusie Het effect op de diepe venen in rechtopstaande positie, waarbij flauwval incidenten voorkomen, is nog steeds onduidelijk. Het effect van externe compressie op de diepe venen is dat wanneer de compressie toeneemt, de dwarsdoorsnede afneemt en de bloedsnelheid toeneemt. Wanneer een constant compressie toegepast wordt, neemt de dwarsdoorsnede wel af, maar blijft de bloedsnelheid constant. Hierdoor kan de constante compressie niet hetzelfde effect behalen als de fluctuerende compressie.

Zoekwoorden gewicht-dragende MRI – rechtopstaande positie – flauwvalincident – diepe venen – US – dwarsdoorsnede

Contents

1. Introduction

1.1 Motivation

1.1.1 Imaging methods

There are many imaging techniques available to examine the human body of which most are performed while the patient is lying down, in either the supine or prone position. For example, the most used imaging techniques in the clinic are Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Ultrasound (US). Some situations are better visualized and understood in an upright position instead of lying down.

The main difference between these positions is the effect of gravity on the body.[1] In the lying down position, the effect of gravity is perpendicular to the body while in the upright position, the effect of gravity is parallel. Changing the body position from lying down to upright position can be beneficial for problems that are gravity dependent.

Two frequently used imaging devices to investigate the advantages of scanning patients in the upright position, is the 0.25T Esaote MRI scanner and US. Because the MRI has a low magnetic field, it has a permanent magnet. A disadvantage of this permanent magnet is that the field strength is limited. But because this magnet does not need to be cooled by helium, it gives the system the possibility to rotate. This makes it possible to change the position of the patient from a lying down to an upright position and also some different angles in between. For this reason, the MRI is referred to as weight-bearing MRI in this research. Some researchers who found the benefits of scanning in an upright position are discussed next.

1.1.1.1 Lumbar spine

The study by Hansen et al.[2][3] shows that investigating patients with back pain in a supine and upright position is an excellent method to image the anatomical regions of the lumbar spine. A proper diagnosis is essential to be able to understand the cause of lower back pain and provide the necessary treatment. With the addition of the upright position, a proper diagnosis can be achieved.

1.1.1.2 Pelvic organ prolapse

Both Abdulaziz et al.[4] and Grob et al.[5] investigated the advantages of scanning with weight-bearing MRI in an upright position when investigating pelvic organ prolapse (POP) in women. POP is the descent of the bladder, cervix, and/or rectum, which can occur in women after giving birth. The descent of the pelvic organs can lead to problems such as urinary and faecal incontinence. When imaging upright, the descent appears to be much larger, because of gravity in this position. This method can be used to improve the diagnosis, determine both the site and the extent of POP, and the choice of surgery type.

1.1.1.3 Behaviour of veins

Comparing the arterial and venous systems, the venous system turns out to be more prone to the force of gravity in an upright position than the arterial system.[1] This is because of the lower venous pressure and the relatively higher compliance of venous vessels. This makes it interesting to investigate the veins in an upright position in certain situations.

Partsch et al.[6] investigated the influence of compression stockings on the diameter of veins in the legs of patients with varicose veins in the upright position. The results of this research showed that the deep veins were more affected by the compression than the superficial veins. This research concluded that the best method to demonstrate diameter reduction in the veins of the legs is the use of the weight-bearing MRI in a lying down and upright position with and without compression.

Besides the weight-bearing MRI, US is also used to perform measurements to investigate the behaviour of veins in the leg.[7] In this research, Partsch and Partsch [7] investigated the compression needed in both upright and supine positions to narrow the veins and perform complete occlusion. Higher compression in an upright position is needed to deform the veins due to higher blood pressure in the veins.

1.1.2 Disadvantages of upright imaging

Although the upright scanning position with the weight-bearing MRI and US has shown its advantages, there is an important drawback seen mainly with the weight-bearing MRI. During scanning, the chance of a fainting incident increases in the upright position compared to the supine position.[8][9] Here, a fainting incident is defined as a full or partial collapse. A partial collapse occurs when dizziness, severe light-headedness, and nausea is seen. The lower leg muscles help the veins return blood to the heart. When standing completely still in an upright position, the lower leg muscles are inactive and so less blood flows back to the heart. This can lead to less blood flowing to the head, which can causes a fainting incident.[8]

In the research of Mauch et al.[9] 12% of the 41 patients fainted during weight-bearing MRI scans in an upright position, which had a total scan time of 20 minutes. In this research, it was suggested to look at using compression stockings to prevent fainting incidences from occurring, but this suggestion was not investigated.

Hansen et al.[8] investigated the fainting incidence with a total scan time of 14 – 17 minutes. He saw that 19% of a group of 86 fainted, of which 76% fainted between 7 and 13 minutes. When using a compression pump, shown in Figure 1, on another group of people, he saw only 2% of 63 people fainted. He concluded that a compression pump needs to be used during weight-bearing MRI scans in the upright position to prevent fainting incidences from occurring.

The compression pump was developed to treat deep vein thrombosis (DVT) by stimulating the blood circulation. This is performed by a pneumatic pump which activates the compression garments periodically. The compression pump is further described in Section 2.2.1.

The thought is that the compression pump imitates the function of the lower leg muscles. However, it remains unclear from the research of Hansen et al. how the compression pump influences the veins in the legs and prevents fainting incidence from occurring. This makes it interesting to investigate the changes in the legs before and after the compression pump is applied.

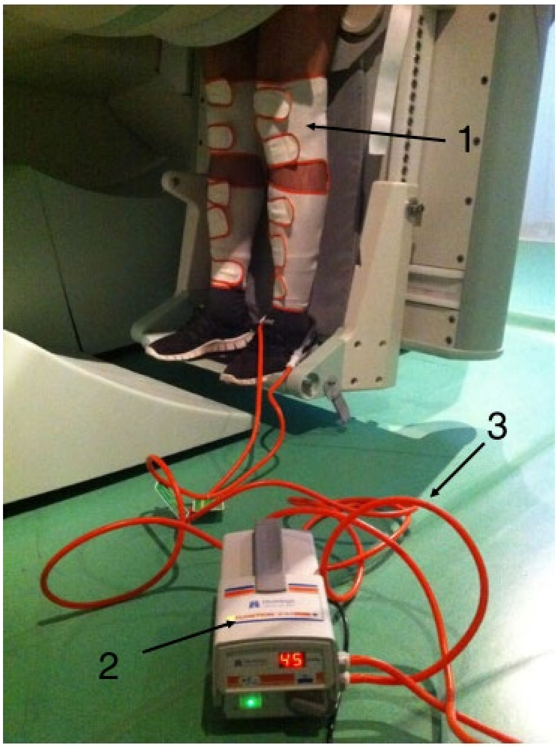

Figure 1 Used compression pump by Hansen et al. [8] Each garment (1) is connected to the compression pump (2) by a tube (3).

A disadvantage of the compression pump is that it is not designed to be used in or near an MRI scanner. It also takes extra time to apply the garments to the patient and to the pump, which is undesired. Therefore, an alternative would be preferable. As suggested by Mauch et al., compression stockings could be an alternative to prevent fainting.[9] Compression stockings are also used to prevent DVT as is the compression pump.[10] An advantage to the compression stockings is that they are MRI compatible as they do not have metal parts. It is debatable if the compression stockings are relatively easy to put on, as claimed by Lim et al.[11], because especially the stockings with high compression are tight. This makes it difficult for someone to put them on without help. Because the compression stockings have the same purpose of preventing DVT and are MRI compatible unlike the compression pump, the compression stockings are further investigated as a method to prevent fainting to replace the compression pump.

1.2 The goal and hypothesis of the research

1.2.1 The goal

As discussed in the previous section, it is seen that the compression pump, which has a fluctuating compression, decreases fainting incidences but does have its disadvantages. It is desirable to investigate if there is another method which can be used to prevent fainting, but which does not have the disadvantages of the compression pump. As suggested by Mauch et al., compression stockings, which have a constant compression, can be used to prevent fainting from occurring, but this has not yet been investigated.

US is used to image deep veins in the legs, which are mainly responsible for the return of blood to the heart.[12] Because the 0.25T Esaote MRI at the University of Twente was unavailable during this research, another imaging technique had to be used to perform this research. As with the weight-bearing MRI, the US is a non-invasive technique that can give information about the cross-sectional area of the deep veins. An advantage of using US over weight-bearing MRI is that it can image real-time without losing resolution and it can measure the blood velocity. The cross-sectional area and the blood velocity are two important parameters to investigate the behaviour of the veins in certain situations.

The main goal of this research is to find a method that prevents fainting incidence from occurring during weight-bearing MRI scans that do not cost a lot of extra time, works under any circumstances and does not influence the results of the MRI images. To find out if a constant compression can be this method, other situations need to be understood first. To begin with, the situation without compression in an upright position over a certain time needs to be investigated. This makes it is possible to explain why fainting incidences occur and how this can be prevented. Secondly, it is necessary to look into the effect of the compression pump to help understand why this decreases the fainting incidences. Thirdly, the effect of the compression stockings needs to be investigated so it can be compared to the effect of the compression pump, to evaluate if this method could also prevent fainting incidences.

1.2.2 Hypothesis research

The hypothesis for this research is that the cross-sectional area of the deep veins in the legs increases in the upright position compared to the cross-sectional area in the supine position. This is due to the increase of blood volume in the lower legs when standing in the upright position caused by the effect of gravity on the blood.

Also, when standing in the upright position for a longer period, it is expected that blood volume in the lower legs should increase over time. The blood volume increases due to gravity and inactivity of the lower leg muscles. As less blood is returned to the heart, more blood stays in the legs. For this reason, the cross-sectional area of the deep veins should also increase. As for the blood velocity, it should decrease over time within the deep veins.

It is known that the constant compression garments decrease the cross-sectional area in the deep veins when compression is applied. It is expected that for the fluctuating compression device the cross-sectional area of the deep veins will decrease the same. It is known that for the fluctuating compression, the blood velocity increases and if the cross-sectional area of a vein decreases, the blood velocity increases to keep the blood flow constant. Therefore, it is expected that the decrease in the cross-sectional area causes the blood velocity to increase to keep the blood flow constant. The compression prevents the cross-sectional area from increasing and the blood velocity from decreasing over time. It is expected that when the garments of the fluctuating compression device deflate, the cross-sectional area and blood velocity will go back to the same value as before the inflation of the fluctuating compression garments.

Because of this, it is expected that the effect of the fluctuating compression device and constant compression garments will be similar leading to the conclusion that the constant compression garments could also be used as a method to prevent fainting incidence from occurring.

1.3 Research questions

To be able to find a method that will prevent fainting incidences and satisfy the set requirements, both the effect of gravity and external compression on the deep veins in the upright position needs to be understood. This leads to the main research question, "What are the effects of gravity and external compression on the deep veins in the legs in the upright position?"
To answer this main research question, it has been divided into five sub-questions:

1. What are the differences in cross-sectional area and blood velocity in the deep veins in the legs between supine and upright position?
2. How do the cross-sectional area and the blood velocity in the deep veins in the legs change over time, standing in the upright position?
3. How does the fluctuating compression device influence the effect of gravity on the cross-sectional area and the blood velocity in the deep veins in the legs, standing in the upright position?
4. How does the constant compression garments influence the effect of gravity on the cross-sectional area and the blood velocity in the deep veins in the legs, standing in the upright position?
5. Can the constant compression garments achieve the same effect as the fluctuating compression device when comparing the effect on the cross-sectional area and the blood velocity in the deep veins in the legs?

Chapter 2 explains more in-depth about the theory to understand the deep veins, the use of compression, and US. In Chapter 3 the measurements of the deep veins within the calf are explained. With these results, a second experiment, which is discussed in Chapter 4, was designed where a deep vein in the groin is measured. Finally, an overall discussion followed by recommendations and conclusions are given in Chapter 5 and Chapter 6 respectively.

2 Theory

Before the measurements on the deep veins can be performed using US, some theory needs to be understood to know how to perform the measurements. In this chapter, the theory for this research is introduced.

First, the anatomy and physiology of the deep veins in the legs will be discussed, as it is important to understand the purpose of the veins within the body and how they return blood the heart. However, in case of venous diseases, it can influence this functionality, which is discussed later. Next, the different kinds of external compressions are explained and how these affect the cross-sectional area and the blood velocity of the veins. The last section discusses the use of US to image the veins. Also, the US techniques used to perform measurements on the veins and how veins can be recognised when using US is explained.

2.1 Veins in the legs

The veins are responsible for the return of blood to the heart. There are two main differences in the anatomy between the arteries and the veins. The first difference is that the wall of veins are more flexible compared to the arteries, as the veins have thinner walls.[12] The second difference is that the veins have valves, which prevent blood from flowing backwards due to gravity. The blood flows through the valves upwards and when the blood flows back, the valves close.

The body consists of several types of veins: superficial veins, deep veins, and perforator veins. In the legs, the deep veins are mainly responsible for transporting blood back to the heart as the flow is directed from superficial to deep veins.[12] The superficial veins are responsible for the regulation of body temperature and transport blood from body tissues to the deep veins. The veins that connect the superficial and deep veins are the perforator veins. The valves in these veins make sure that the blood can only flow from the superficial to the deep veins and not the other way around. For this research, the focus is set on the behaviour of the deep veins because of their function. Also, research shows that when measuring the difference in blood velocity or cross-sectional area of the veins with and without external compression, the deep veins show to be the most affected.[6][13]

As this research is focusing on the deep veins, the anatomy of these veins in the legs is described next.

2.1.1 Deep veins

A schematic overview of the deep venous system of the calf can be seen in Figure 2. This includes the anterior tibial veins (ATV), posterior tibial veins (PTV), and peroneal veins (PEV).[12] These veins all come together to form the popliteal vein (PV), which is referred to as the femoral vein (FV) when it is in the upper leg. The deep femoral vein (DFV) from the outer thigh, joins the femoral vein and forms the common femoral vein (CFV). The inguinal ligament is the landmark that divides the CFV from the external iliac vein (EIV). The more proximal the vein is, the larger the diameter is, which is also indicated in Figure 2.[14] Apart from the location, the size of the vessels in the body is also dependent on the type of vessel, which is visualised in Figure 3.

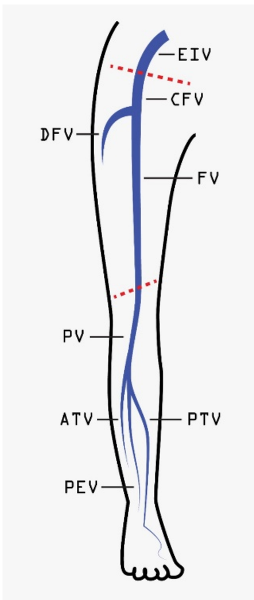

Figure 2 Schematic representation of the deep veins within the legs containing the common femoral vein (CFV), deep femoral vein (DFV), femoral deep vein (DFV), femoral vein (FV), popliteal vein (PV), anterior tibial vein (ATV), posterior tibial vein (PTV), and the peroneal vein (PEV)

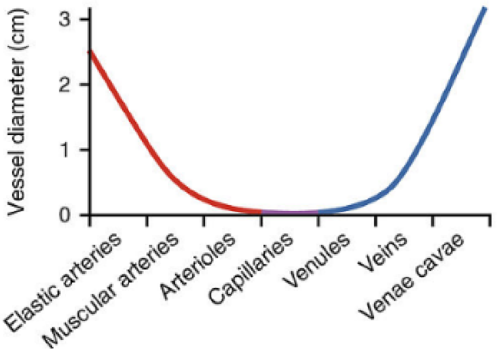

Figure 3 Schematic overview of the vessel diameter of the blood circulation. Arterioles is the term for are small arteries and venules for small veins. [14]

2.1.2 Blood return to the heart

Now that the deep vein network in the legs is known, it is important to understand how the blood flows through these veins back to the heart. The blood flow (Q) is the volume of blood that moves per time unit, expressed in [mL/s]. The blood flow depends on the blood velocity (v), which is the distance the blood moves per time unit, expressed in [cm/s], and the cross-sectional area (A) of the blood vessel, expressed in [cm^2]. The equation for the blood flow is given in Formula 1.

$$Q = v \cdot A \tag{1}$$

When the body is at rest, Q stays constant. However, the cross-sectional area of the vessels differs per position in the body, so the blood velocity also differs.[14] This can be seen in Figure 4.

There are four mechanisms which influence the venous return, which is another term used for the flow of blood back to the heart. These four mechanisms are the pressure gradient, the lower leg muscles, gravity, and the respiratory pump, each respectively discussed next.

2.1.2.1 Pressure gradient

When the heart pumps the blood into the aorta, the pressure to do so is applied to the blood. As a fluid, the blood applies this pressure on the blood vessel walls. This pressure is known as the blood pressure and forms a pressure gradient. As blood flows from high to low pressure, it can move through the vessels due to this pressure difference.[15] When the blood leaves the left atrium of the heart into the arterial system, the average pressure is 100 mmHg. The blood pressure in the right atrium, where blood returns to the heart via the veins, is 0 mmHg.[14] In between these two atriums, the curve of the blood pressure can be seen in Figure 5. The pressure mainly drops within the arteries, before it enters the capillaries. After this point, the pressure drops slowly, which is due to the elastic walls of the veins.[14]

When in a lying down position, this process can be executed without any influence from gravity. In an upright position, the blood pressure in the veins is in the opposite direction of gravity, unlike the arteries. The blood needs to return to the heart from the toes against gravity.

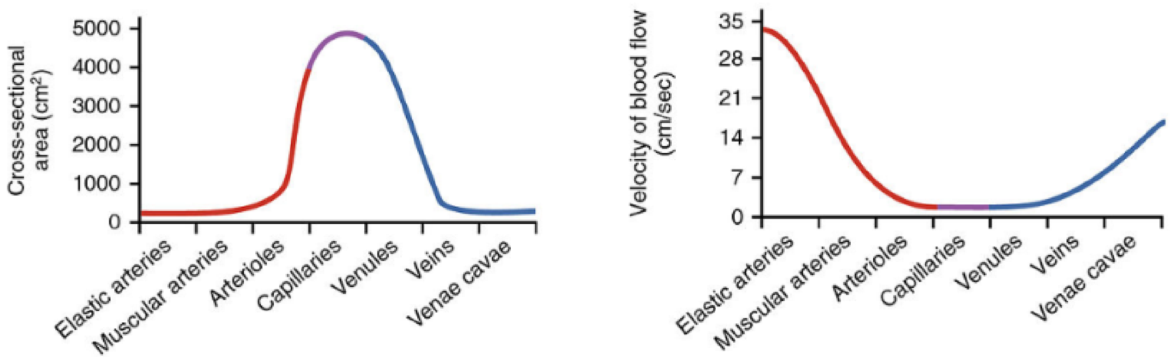

Figure 4 Schematic overview of the total cross-sectional area of vessels (left) and the velocity of the blood flow (right) within the different vessels of the body. Arterioles is the term used for small arteries and venules for small veins. [14]

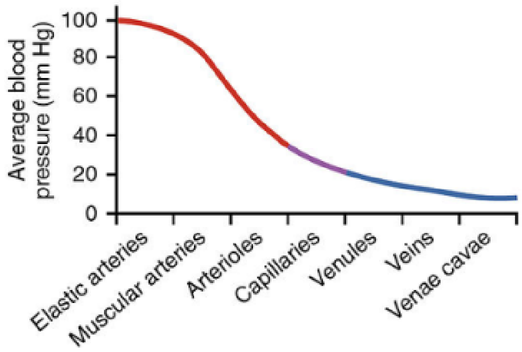

Figure 5 Schematic overview of the blood pressure of the blood circulation. Arterioles is the term for are small arteries and venules for small veins. [14]

2.1.2.2 Lower leg muscle pump

When standing still, the muscles contract and relax rhythmically, causing a swaying motion of the body.[16] During muscular contraction, blood is squeezed in the proximal direction and the veins are refilled during the relaxation phase. As discussed in the previous section, the return of blood also depends on cardiac activity and so does not entirely depend on the functioning of the lower leg pump. This pump consists of three different mechanisms: the muscle pump, the distal calf pump, and the foot pump as can be seen in Figure 6.[17]

As shown in Figure 6, the position of the deep veins (DV), superficial veins (SV) and perforator veins (PV) are illustrated as being around and within the muscle (M). All three lower leg mechanisms are shown during active and relaxed position. As illustrated, when contracting the calf muscle due to plantar flexion of the foot at the ankle joint, the muscle presses the vein to increase the blood velocity upwards. When contracting the calf muscle due to dorsiflexion of the foot at the ankle joint, the bulk of the calf muscle descends and presses the vein just above the level of the ankle. During weight-bearing, the joints between the foot bones are extended and the arch of the foot is flattened. This causes the veins to stretch which in turn causes them to eject their blood content. During the relaxation phase of all three lower leg pumps, the vein refills itself with blood. These three individual movements all take place during walking.

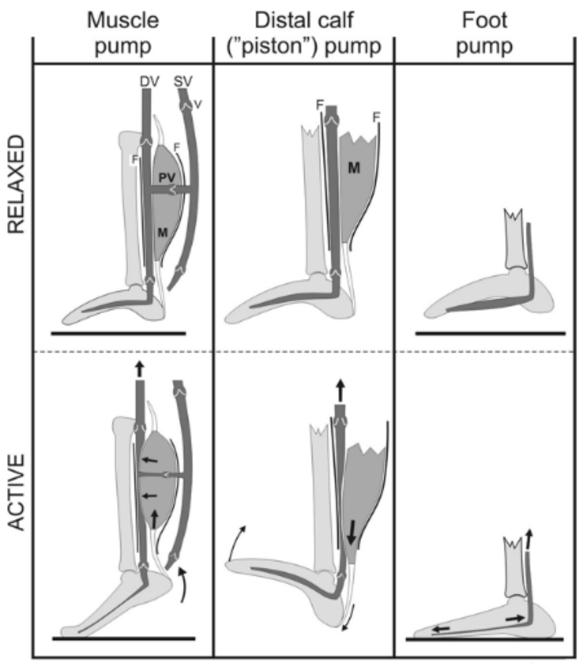

Figure 6 Schematic illustration of the venous pump system of the foot and the calf during both relaxation and active state.[16]

During exercise, the amount of blood pumped out of the heart per time unit, also known as the cardiac output (CO), increases.[15] This means that the venous return should also increase, as the heart cannot pump out more blood than it receives. In this situation, the lower leg muscles support the venous return by increasing the blood velocity.

Although it is well established that muscle contraction in the lower legs increases venous velocities, reduces venous volume, and drops the venous pressure, the actual changes in pressure, flow, volume, resistance, and compliance in the intramuscular veins is poorly understood.[4]

2.1.2.3 Gravity

As mentioned in Section 1.1.2, gravity influences the venous return to the heart. When looking at the veins below the heart level, gravity works against the pressure gradient of the veins. For this reason, the blood flow needs to overcome gravity to be able to return blood to the heart. When in a standing or sitting position for a long period, pooling in the legs can occur causing DVT.[18][19] The blood volume in the legs increases and the venous return decreases. This leads to a decrease in CO.[15] This can cause people to faint as the brain does not receive enough blood and so it does not receive enough oxygen. When there is not enough oxygen in the brain, the brain forces the body to go in lying down position by fainting. This way, the effect of gravity in the upright position is gone and the oxygen level in the brain restores to normal. To prevent fainting in this situation can, for instance, be performed by moving the lower leg muscles.

2.1.2.4 Respiratory system

Blood flow also depends on the changes in volumes and pressures of the abdominal and thoracic compartments.[16] For instance, the respiration influences the pattern of blood flow of the veins in the legs due to movements of the diaphragm. During inhalation, the diaphragm descends, increasing intra-abdominal pressure and decreasing the flow in the femoral veins.

2.1.3 Venous diseases

When veins fail to return the blood to the heart, it is mainly caused by venous diseases. In general, venous diseases fall into two categories: venous thrombosis and venous insufficiency. For both categories, external compression can be used as a treatment. Because the effect of the external compression is of interest in this research, venous diseases need to be understood first and how the external compression is used as treatment. Venous thrombosis and venous insufficiency are discussed in the following two sections.

2.1.3.1 Venous thrombosis

Thrombosis occurs when the blood velocity is low, and a blood clot, or thrombus, arises which sticks to the wall of the veins.[7] This can occur in the superficial veins, called superficial thrombophlebitis, or in the deep veins, called deep vein thrombosis (DVT). DVT can be very dangerous as it can be difficult to detect due to a low (50%) occurrence of symptoms in patients and it carries a high risk of pulmonary embolism.[7] This is when a piece of the thrombus breaks away and travels in the blood to the arteries in the lungs causing a blockage of the arteries. Due to this blockage, there is no exchange of oxygen, which can lead to shortness of breath, a heart attack, or even death. DVT can also block the blood flow through the deep veins in the legs, causing a decrease in efficiency of the venous return. Reduced blood flow increases pressure within the vein segments between two valves and may cause fluid to leak thought the valves, leading to swelling of the legs. As blood clots form at a low blood velocity, DVT can be prevented by keeping the blood flowing.

2.1.3.2 Venous insufficiency

The most common disease involving venous insufficiency is varicose veins, which affects the superficial veins.[20] Varicose veins are veins which are enlarged and tortuous which decreases the venous return. When the valves within the veins become incompetent, which results in backflow of blood and blood pooling, it causes the enlargement and tortuous. The venous pressure increases which can cause symptoms of painful swelling in the legs. The risk of varicose veins increases with age as the valves can become incompetent more easily. Varicose veins can also cause delayed healing and significant bleeding of wounds. This damaged tissues or wounds can develop into nonhealing ulcers, which can then lead to soft tissue infection. Varicose veins can be treated using ablation techniques, which increase the temperature of the vessel wall causing contraction of the vessel. Recurrence of the disease is possible, so it is not a permanent solution.

Backflow of blood within the deep veins is another type of pathology that is caused by chronic venous insufficiency.[21] This can be caused by obstruction of blood flow from the limbs or by leaky venous valves leading to swelling and pain in the legs and dark, rough skin.

2.2 External compression as venous diseases treatment

To treat or prevent venous insufficiency, external compression can be used. There are different kinds of external compression methods. For this research, these methods are divided into fluctuating and constant compression. In this section, the use of these two different compression methods is discussed.

2.2.1 Fluctuating compression devices

Fluctuating compression devices have different designs, but all have a period in which the compression increases until a certain maximum pressure after which it decreases again for a certain amount of time.[2] This cycle is repeated for a desired amount of time. This method can be compared to the compression the lower leg muscles can apply to the veins, as discussed in Section 2.1.2.2.

These devices have found their main function in preventing DVT during bed rest in the hospital, an example of this can be seen in Figure 7. When the compression increases, the velocity of the blood flow also increases. Because patients at bed rest cannot walk around, the fluctuating compression devices can help to keep the velocity of the blood flow high enough to prevent DVT. These devices can be applied for hours during bed rest.

As the fluctuating compression method is closer to the physiological function of the lower leg muscles than the constant compression method, Hansen et al.[8] choose a fluctuating compression device to prevent fainting. A few disadvantages to using the fluctuating compression device is that it is not designed to use near an MRI scanner, it is more expensive than constant compression garments, and it takes extra time to apply the garments to the patient and the device.

2.2.2 Constant compression garments

The pressure applied by the constant compression garments to the legs is constant while wearing them. The mechanism of the constant compression can be explained as follows: the constant compression reduces the diameter of the veins. The greatest degree of compression is applied at the ankle and the lowest degree of compression at the knee or thigh, depending on which kind of garments are worn.[9] A pressure gradient forms from the ankle up to below the knee or the thigh. This gradient supports the venous return to overcome gravity to let the blood flow against the gravity gradient.

Constant compression garments are mainly used to prevent DVT and treat varicose veins, an example of a thigh-high constant compression garment can be seen in Figure 7. As the diameter decreases, the constant compression garments support the varicose veins to apply pressure against the blood. This ensures the cross-sectional area of the veins from expanding, which has negative consequences for the veins and the venous return, as discussed in Section 2.1.3.2. The constant compression garment can always be worn to treat varicose veins and prevent DVT.

Constant compression garments are easier to move around in for the patient than the garments of the fluctuating compression devices, as these also need to be connected to the pump for it to apply compression. This way the patient remains mobile while preparing for the weight-bearing MRI scan. Because of this mobility, the patient can come to the weight-bearing MRI scan with the constant compression garments already on as it can be worn underneath their clothes. This way, it does not cost extra time to apply them during the preparation of the scan. Another advantage is that constant compression garments are cheaper and simpler than

Figure 7 Treatment examples of the use of the fluctuating compression device (left) [22] and the constant compression garments (right).[11]

fluctuating compression devices. For this reason, they remain the most popular physical method to prevent DVT.[23] However, how they exactly work remains unclear. As the blood velocity within a vessel is dependent on its cross-sectional area, it is expected that the garments would increase the velocity of the blood flow. Some later studies using US have found no increase in blood velocity when stockings are worn.[23] However, it is found that the diameter under the stockings does decrease. A major drawback is the fitting of the garments. In particular, thigh-length stockings appear to be difficult to apply. For this reason, the calf-length garments are preferred over thigh-length stockings.

2.3 Operating US on veins

For this research, US is used to image the veins. The theory for this imaging method is first described to understand how images are acquired with US. Next Doppler techniques are explained to understand how the blood velocity is measured in the veins and finally, how the veins are recognised with US.

2.3.1 US in general

US is an imaging method that uses high-frequency sound waves to make an image.[24] US used for medical purposes uses frequencies in the range of 2 to 10 MHz, with specialized ultrasound applications up to 50 MHz. The sound wave is sent into the body by a probe as a pulse.

The US probe produces soundwaves using piezoelectric elements. When a voltage is applied over these elements, they vibrate to generate a sound wave. The piezoelectric elements also work the other way around. When a sound wave causes the elements to vibrate, it generates a voltage. This voltage is used by US systems to create an image.

The sound wave generated by the piezoelectric elements is sent into the body where it interacts with the different tissues. Because the different tissues within the body have different characteristics and densities, known as acoustic impedance, the sound wave interacts differently with each type of tissue. A fraction of the pulse is reflected at tissue boundaries, where there is a difference of acoustic impedance, as an echo. This echo returns to the probe. This makes it possible to see the difference between tissues on the image. The pulse can only reach a certain depth as when the penetration depth is too large, all the sound waves have interacted with the tissue.

2.3.2 Doppler US

Doppler Ultrasound is based on the shift of frequency in the received signal which is caused by a moving reflector, such as blood cells.[24] It is possible to determine the blood velocity by looking at the Doppler shift. The Doppler shift (f_d) is the difference between the incident frequency (f_i) and reflected frequency (f_r). When blood moves away from the probe it produces lower frequency echoes. Blood moving towards the probe produces higher frequency echoes. This can be compared to the siren of an ambulance. When it moves towards someone, the sound this person hears is higher than when the ambulance has passed this person. The formula for the Doppler shift is shown by Formula 2, where v is the velocity of the blood in [cm/s], c is the speed of sound in [cm/s], and θ is the Doppler angle.

$$f_d = f_r - f_i = \frac{2f_i\ v\ \cos(\theta)}{c} \tag{2}$$

When rearranging the Doppler equation, the blood velocity can be calculated as seen in Formula 3.

$$v\ = \frac{f_d c}{2f_i\ v\ cos(\theta)} \tag{3}$$

The Doppler angle is used to determine the blood velocity. This angle is the angle between the direction of the blood flow and the direction of the sound waves. The component of the velocity vector directed towards the probe is less than the velocity vector along the vessel axis by the cosine of the angle, cos(θ). The Doppler angle compared to the probe can be seen in Figure 8.

To achieve an accurate velocity value, the measured Doppler shift at Doppler angle θ is adjusted by 1/cos(θ). When the Doppler angle is 60°, the given Doppler frequency is ½ of the actual Doppler frequency. The Doppler angle at 90° gives a measured frequency of 0. Therefore, the preferred Doppler angle ranges from 30 to 60 degrees.

When using the Colour Doppler function, the direction and speed of the blood

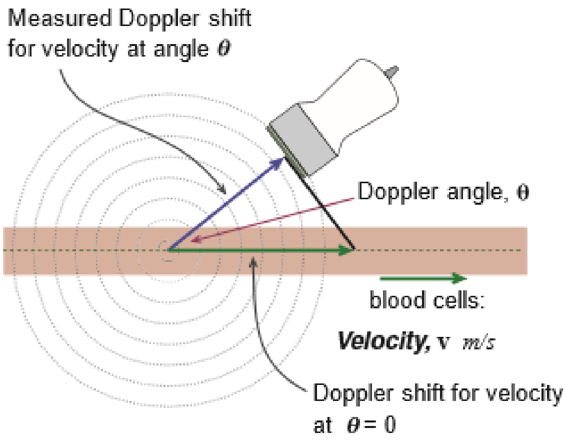

Figure 8 Schematic overview of the Doppler method used in US. The Doppler shift is a function of the Doppler angle (ϑ) of the incident US pulse and the blood velocity (v).[24]

are indicated with colours. In the clinic, the probe is held in such a position that the red colour represents the blood flowing away from the transducer, which normally is the blood inside the arteries, and the blue colour represents the blood flowing towards the transducer, which normally is the blood inside the veins.

To measure the blood velocity over a certain time frame, the Pulsed Wave Doppler function of US can be used. It shows a real-time measurement of the blood velocity. In this case, ultrasound is emitted in pulses, which is paired with a corresponding return signal. This makes it possible to determine where the reflection has occurred and determine its location.

A drawback to Doppler is that aliasing can occur. Aliasing is related to the pulse repetition frequency (PRF), which is the number of pulses of a repeating signal. PRF is limited by depth, the greater the distance to the vessel of interest, the longer it takes to transmit and receive echoes. For instance, when the sampling frequency is ½ the frequency of the received signal, the signal will be analysed as if it is the lower frequency, as can be seen in Figure 9. Due to the lower frequency, the blood velocity is lower than it is. This causes to produce a wrap-around effect on the other side of the baseline, where the velocity is zero, of the velocity graph. This signal is from the higher blood velocity values which fall outside the analysed blood velocity. This way, an incorrect blood velocity is shown. This can be eliminated by increasing the velocity of the Colour Doppler or the velocity scale.

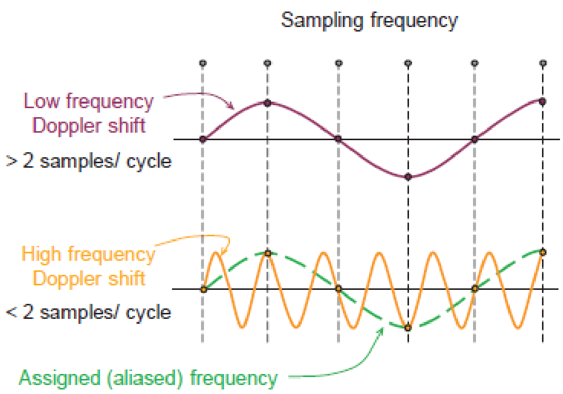

Figure 9 Aliasing during Pulsed Wave Doppler US.[24]

2.3.3 Recognising veins with US

As previously discussed, the main difference between the veins and the arteries is the thickness of the walls and the direction of the blood flow.[12] These differences can be used to distinguish the veins from the arteries when using US. Because the veins have thinner vessel walls, they can be compressed by the transducer. Another difference that can be seen is the pulsating blood that flows within the arteries. When using the Colour Doppler, it can be seen if the blood flow is pulsating or not. Also, the flow direction will indicate if it is an arterial or venous blood vessel.

The more proximal the vein is located, the larger the diameter will be, as can be seen in Figure 2. This makes it easy to detect these veins and their blood velocity. When the velocity is too slow, it cannot be measured with US. Also, when the legs have too much tissue between the surface and the deep veins, the sound waves of the US cannot reach this vein due to the high penetration depth. To find the deep veins in the calf for the measurement, the cortical shadow of the tibia and fibula can be used as a reference.

3 Calf measurements

3.1 Introduction

When wearing external compression, the veins within the calf are affected. As the change of the cross-sectional area can give insight into the change of the blood velocity at that point, the veins in the calf are investigated.

It was chosen to investigate the change in cross-sectional area of the posterior tibial vein (A_{PTV}) in the left leg. This deep vein was mainly chosen because of its location. The PTV is located posterior to the tibia, as the name suggests. It is located more medial than the other deep veins and can be imaged on the medial side along the tibia, which shows up black in the US image and thus is easily recognised. As there are two PTV, the lateral PTV is measured as this vein is closer to the surface. When the penetration depth is deeper, the pulse interacts more with the different tissues it must pass through and therefore a weaker signal will return as an echo to the probe.

Within the literature, no results of the change in an upright position over time can be found. On the contrary, there is literature found that look at the effect of compression on the deep veins e.g. the PTV.[10][25][26] Because the garments of both fluctuating and constant compression methods go around the calf, as seen in Figure 7, the calf is compressed. The effect of this compression on the cross-sectional area of the deep veins is, therefore, best measured in the calf.

To investigate A_{PTV}, four measurements are performed. These are a measurement without compression (no compression, upright position), a measurement with the use of a compression pump (fluctuating compression, upright position), a measurement with the use of a handpump (constant compression, upright position), and a measurement in the supine position without compression (no compression, supine position).

3.1.1 Goal calf measurements

The main goal of this measurement is to investigate the difference in A_{PTV} in four different situations: in upright position versus supine position, upright position over time without compression, and fluctuating compression versus constant compression in the upright position. With these measurements, the cross-sectional area of the PTV in each situation is compared to determine the effect of each situation.

3.1.2 Hypothesis calf measurement

The hypothesis for the calf measurement is first that A_{PVT} will increase over time when standing in the upright position. As more blood will stay in the lower legs due to inactivity of the lower leg muscles, more volume is present and so, A_{PVT} will increase.

When the fluctuating compression is applied and the compression is at its maximum, A_{PVT} will decrease. A_{PVT} will be smaller at maximal compression than without compression.

When the constant compression is applied, A_{PVT} will be decreased compared to when there is no compression. Over time, A_{PVT} will stay constant.

The decrease of A_{PVT} at compression during fluctuating compression is similar to the A_{PVT} at constant compression.

To confirm these expectations, the research questions formulated in Section 1.3 are used for this research, looking at A_{PVT}.

3.2 Materials and methods

3.2.1 Materials

The used materials for the calf measurements are US, the compression pump, and the hand pump setup. These materials are explained next, respectively.

3.2.1.1 Ultrasound

To perform the measurements, a Siemens Acuson s3000 US is used with the linear probe, type 14L5. When using the other available US probes, it was seen that the resolution was not as good as when using the linear probe. Therefore, the linear probe was used to examine the deep veins. The linear probe has a linear array and is designed to image vascular properties. The frequency range is 5 to 14 MHz, this provides better resolution but less penetration. For this research, the frequency of 11 MHz was used. To examine the veins, the setting of PV-Ven is selected on the US system.

3.2.1.2 Compression pump

To perform the fluctuating compression on the legs, the Huntleigh Flowtron ACS900 is used, which can be seen in Figure 10. This contains a compression device which is connected to the two garments which can be applied around the legs, one garment per leg. These garments consist of bags which can be inflated to perform compression on the legs.

In contrast to the compression device used by Hansen et al. [8] of which the maximal compression is not fixed and can be set by the user, the Flowtron ACS900 has a fixed maximal compression of 40 mmHg.

This pump works as follows, which is also visualised in Figure 11, the garments inflate over a period of 12 seconds to increase the compression to 40 mmHg. Next, it deflates decreasing the compression to 0 mmHg. 48 seconds after deflation the cycle of inflation starts again. At the halfway point of this 60-second cycle, the pump will start to inflate garment of the other leg. So, during inflation and deflation of the left leg, the right leg is in rest. When the pump is finished with deflation of the garment of the left leg, it will start inflating the garment of the right leg.

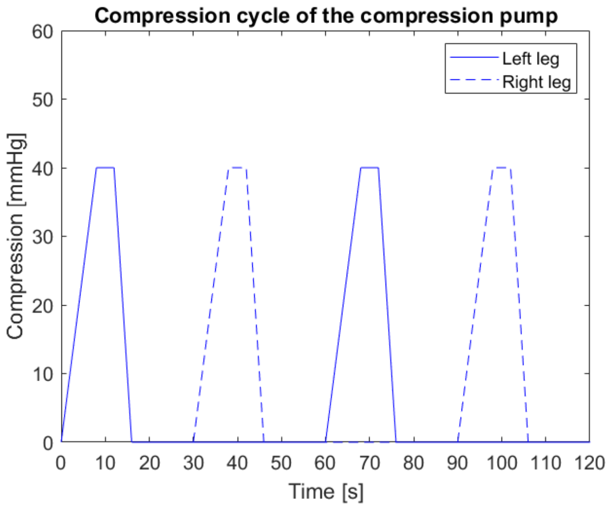

Figure 11 A visualisation of the compression cycle of the compression pump where the left and right leg are alternately inflated

3.2.1.3 Hand pump

For the constant compression method, the garments of the compression pump are used. A hand pump is used to inflate the left garment to a constant compression. A manometer is added between the hand pump and the garment to measure the compression within the garments more accurate. This set up can be seen in Figure 10. The compression of the garment is held between 38 and 42 mmHg as the compression does not stay constant within the garments due to their design. There is a drop seen of roughly 4 mmHg/min. This means that when keeping the compression between 38 and 42 mmHg, the compression can be increased by 4 mmHg using the hand pump by squeezing it once a minute.

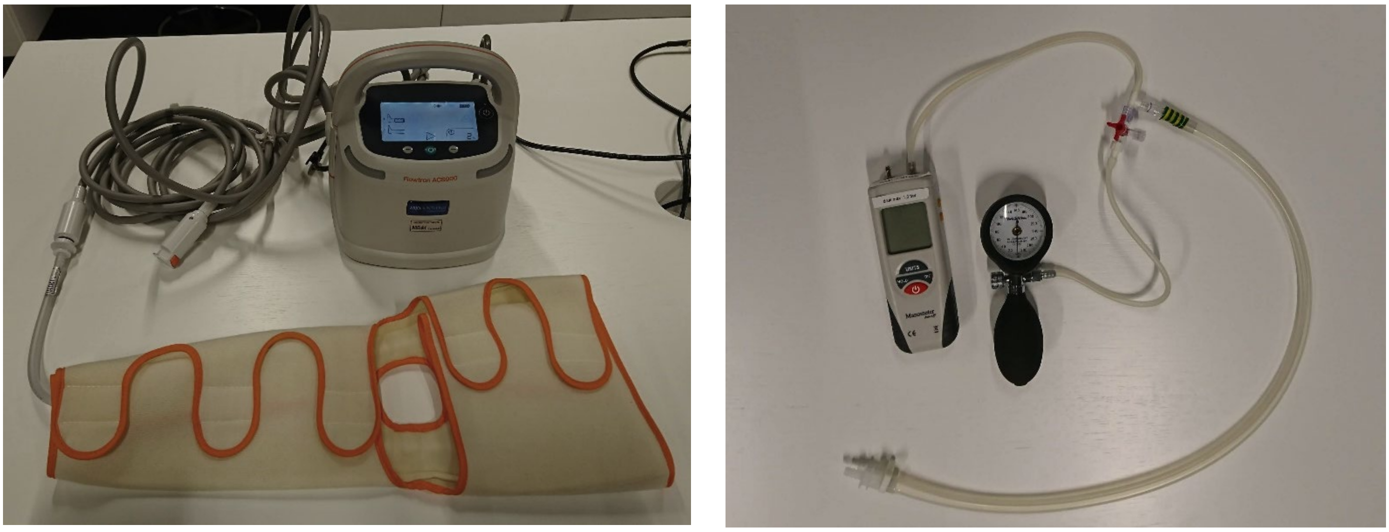

Figure 10 The compression pump Flowtron ACS900 (left) and the self-made setup for the constant compression with a hand pump (right).

3.2.1.4 Measurement set up

To make sure that the error between the measurements due to probe positioning is as small as possible, a stand with a clamp is used to keep the ultrasound probe on the same place and at the same angle. This step is placed against the wall to let the subject lean against it to mimic the situation in the weight-bearing MRI. This step also helps to make it easier to access the calf for the person executing the measurements. Another step is used to help the subject to sit on the end of the examination bed for sitting breaks of 5 minutes in between the measurements to reset the blood flow within the legs.[27][28] This setup can be seen in Figure 12.

The duration of the measurement is set to be 7 minutes, because in the research of Hansen et al. it was seen that most of the people fainted between 7 and 12 minutes.[8] For this reason, the measurement cannot last longer than 7 minutes without taking the risk of people fainting. As it is not the intention of this research to have people fainting, this risk needs to be reduced by setting the maximum measuring time to 7 minutes.

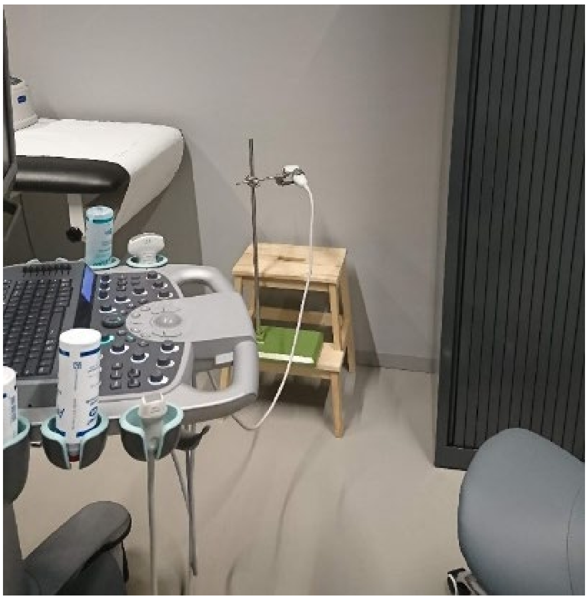

Figure 13 Measurement setup for the calf measurements with a step for the subject to stand on and a stand with clamp to keep the probe stable during measurements.

3.2.2 Methods

3.2.2.1 Measured vein

The transversal plane in which the PTV can be seen near the tibia can be seen in Figure 13.

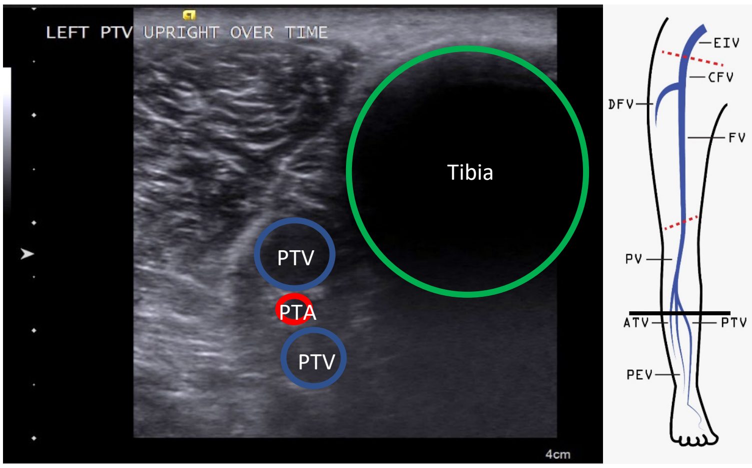

Figure 12 The transversal plane of the two Posterior Tibial Veins (PTV) around the Posterior Tibial Artery (PTA) near the tibia imaged with the US. In the schematic overview of the deep veins in the legs right shows at which height the US image is taken.

When using Colour Doppler in the transversal plane, the posterior tibial artery can be located by looking at its pulsating signal. Around this artery, two veins are located. One is located laterally from the artery and the other one is located medially. This can be checked by looking in the sagittal plane if the transverse plane does not give enough information to confirm the posterior tibial veins and artery. Another way to recognise if the imaged vessel is a vein or artery is by performing compression using the probe. The two veins should be easy to compress and the artery not. When this is confirmed, the measurements can then be performed.

3.2.2.2 Protocol

The protocol consists of four different measured situations. The first three are measured standing up and the last one is measured in the supine position. Between the standing measurements, there is a sitting break to reset the blood flow. Before both the fluctuating compression and constant compression, baseline measurements are performed to compare these baseline results with each other. For all the upright

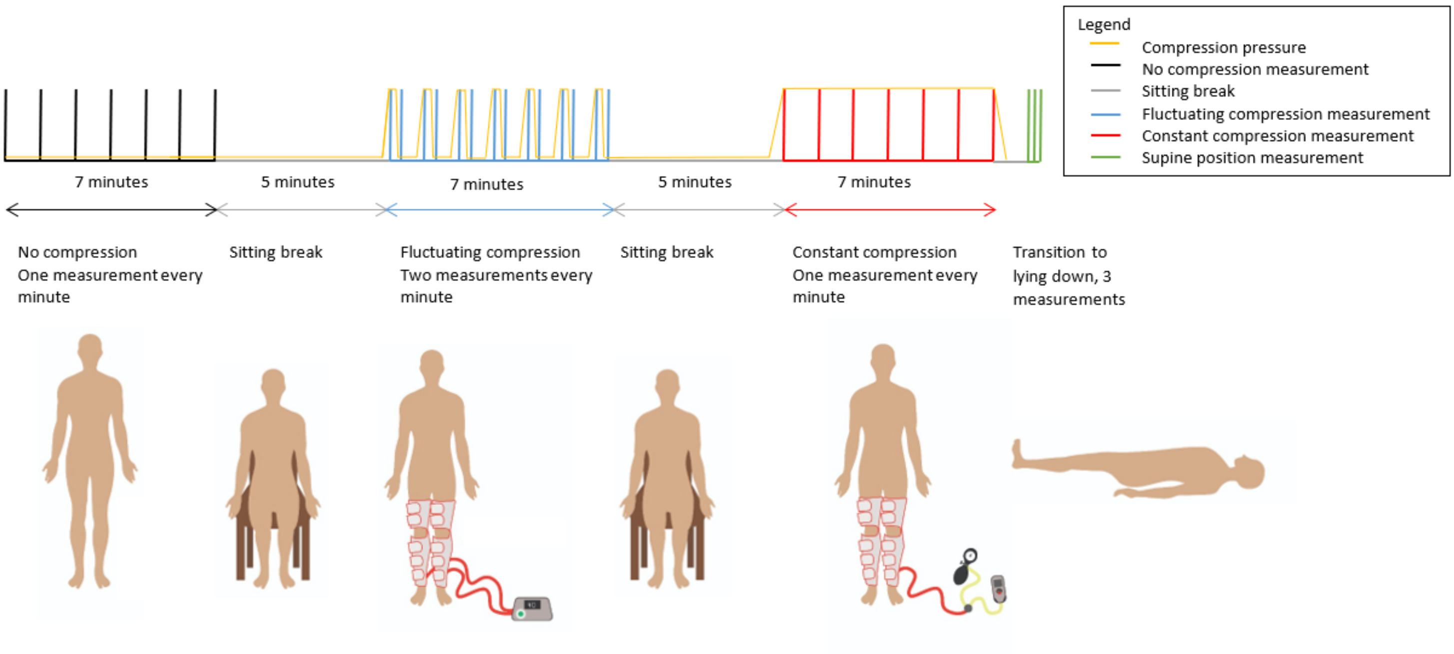

Figure 14 Method of the performed calf measurement using the US to measure the Posterior Tibial Vein (PTV) with illustration of the position of the subject

measurements, a measurement is performed every minute. The first measurement is t_0, the measurement after 1 minute is t_1 and so on until t_7. The protocol is visually described in. The different colours used in the figure indicate the four different situations. These colours also correspond to the colours of the results. The complete protocol can be found in Appendix I: Protocol calf measurements.

3.2.2.3 US settings

Before starting the measurements with US, some settings are set. The depth was set to 4 cm to image the PTV and the gain was set to the maximal value to achieve high contrast. Next, the gain per depth and focus was adjusted to get the best contrast at the depth of the PTV.

3.2.2.4 Data analysis

After the US measurements are performed, the images are analysed. To determine A_{PTV}, an image processing program called ImageJ (NIH, Bethesda, USA) is used to manually draw an ellipse that matches the wall of the posterior tibial vein to calculate the number of pixels that are within the ellipse. The use of the tools can be seen in Figure 15. This analysis is performed three times for each image. One set of images, obtained from one measured situation, is always analysed after another set of images. This is to prevent the observer from being biased too easily when drawing the same ellipse multiple times after each other.

The standard deviation, which is obtained from the three analyses performed on the same image, gives the intra-observer variation. This is the amount of variation between the observations performed by one person when the images are analysed more than once. This gives the precision of the

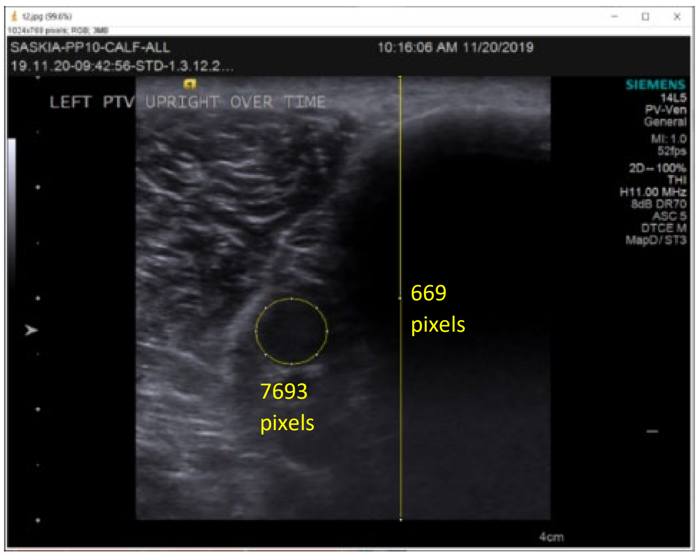

Figure 15 The use of ImageJ to determine the cross-sectional area and the length of the field of view in pixels.

drawn ellipses, but it does not say anything about the accuracy of these ellipses.

For the data of the fluctuating compression measurement, the Wilcoxon signed-rank test is used to determine if the differences between A_{PTV} without compression and A_{PTV} with compression, noted as $\Delta A_{PTV\ FC}$, are statistically significant. The Wilcoxon signed-rank test also shows which $\Delta A_{PTV\ FC}$ data points are positive, referred to as positive ranks, or negative, referred to as negative ranks. The p-value is based on the number of positive ranks and the value of $\Delta A_{PTV\ FC}$. The more the positive ranks and the larger $\Delta A_{PTV\ FC}$, the higher the rank and the lower the p-value.

3.3 Results calf measurements

The subjects used during this measurement, of which 2/5 were women, were aged between 21 to 32. Unfortunately, the posterior tibial vein in Subject 5 could not be found and so no measurements in the calf could be performed. The results of the other 4 subjects can be seen per executed measurement.

3.3.1 Baseline measurements

To verify the accuracy of the measurements, the difference between the measurements without compression and the two baseline measurements of both the compression measurements are compared. The overall absolute maximal difference expressed as a percentage of the mean value is between 3.5% and 49.6% of which Subject 3 has the lowest percental standard deviation and Subject 4 the largest. This can also be seen in Table 1.

Table 1 Mean of A_{PTV} measured at t_0 without compression and the two baseline measurements with the corresponding standard deviation

Subject number	A_{PTV} upright position, no compression [mm^2]
1	9.3 ± 0.5
2	26.9 ± 2.4
3	11.5 ± 0.2
4	10.1 ± 2.5

3.3.2 Measurement 1: no compression, upright position

Overall, there is no increase in the cross-sectional area seen over time in any of the 4 subjects. In Figure 16 the results of the measurement without compression in the upright position of Subject 3 and Subject 4 are shown. In Figure 16 it is seen that A_{PVT} of Subject 3 fluctuates and does not increase or decrease. This pattern corresponds to the patterns seen in both Subject 1 and 2. The cross-sectional area of Subject 4 first decreases but it does increase at the end of the measurement. This pattern is different from the other three subjects.

3.3.3 Measurement 2: fluctuating compression, upright position

Within all the subjects, 78% of the measured A_{PTV} values at 40 mmHg compression are smaller than the A_{PTV} without compression. In

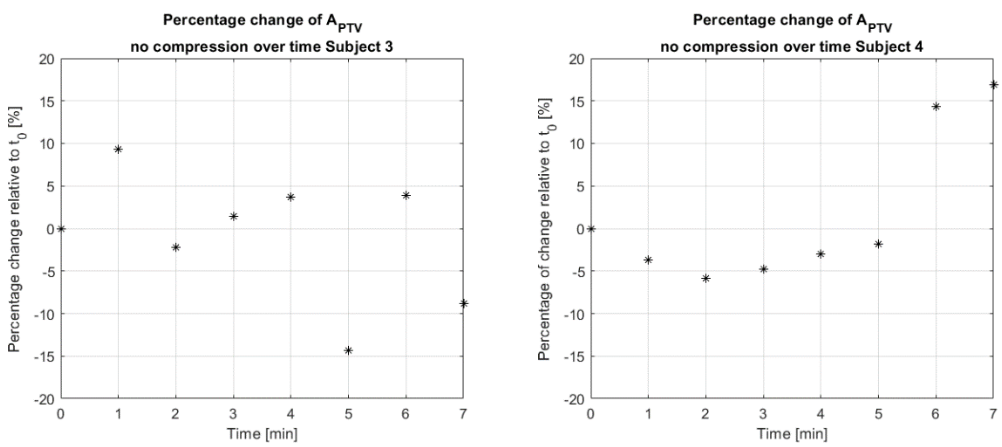

Figure 16 The difference in the no compression measurement between Subject 3 (left) and Subject 4 (right). For Subject 3 the difference in A_{PTV} fluctuates. For Subject 4 A_{PTV} first decreases but increases at the end of the measurement.

Table 2, the results of the Wilcoxon signed-rank test can be seen. For Subject 2 and Subject 4, the differences between A_{PTV} at 0 mmHg and A_{PTV} at 40 mmHg are statistically significant. For Subject 1 and Subject 3 this difference is not statistically significant.

Table 2 The results for the Wilcoxon signed-rank test with the results of the significant difference value between A_{PTV} at 0 mmHg and A_{PTV} at 40 mmHg. Negative ranks is when A_{PTV} at compression is larger than A_{PTV} without compression. Positive ranks is when A_{PTV} at compression is smaller than A_{PTV} without compression.

Subject number	Negative ranks	Positive ranks	p-value*
1	3	5	0.161
2	1	7	0.017
3	3	5	0.484
4	0	8	0.012

** significant when p-value < 0.05*

3.3.4 Measurement 3: constant compression, upright position

In Table 3 the mean and standard deviation of A_{PTV} of all the eight data points of the constant compression measurement per subject can be seen. The overall standard deviation expressed as a percentage of the mean value is between 1.4% and 16%.

Table 3 Results A_{PTV} of measurement with constant compression in the upright position with the corresponding p-value of all the subjects

Subject number	A_{PTV} constant compression [mm^2]
1	5.0 ± 0.8
2	27.8 ± 0.4
3	11.4 ± 0.2
4	10.3 ± 0.7

3.3.5 Measurement 4: no compression, supine position

As can be seen in Table 4, the ratio of change upright:supine is between 1.3 to 1.9. The value used for “Upright position cross-sectional area” is the first measurement of Measurement 1: no compression, upright position.

Table 4 Results cross-sectional area of measurement 4: supine position, compared to the first upright position measurement of measurement 1: no compression, upright position of all Subjects.

Subject number	A_{PTV} upright position [mm^2]	A_{PTV} supine position [mm^2]	Ratio (upright :supine)
1	7.6	5.9 ± 0.3	1.3
2	29.6	15.5 ± 0.9	1.9
3	11.3	7.8 ± 1.2	1.5
4	8.0	5.4 ± 0.3	1.6

3.4 Discussion measurements calf

3.4.1 Determining the accuracy with baseline measurements

A baseline measurement was performed before each measurement for the different compression methods. The compression measurements consist of multiple data points while the baseline measurements consist of only one data point. Because the baseline measurement does not have multiple data points and so no standard deviation, it does not give a true representation of the situation. This makes it hard to compare the baseline measurement to the compression measurements. Therefore, the baseline measurement is not shown in the results of the different compression methods.

The baseline measurements do give insight into the accuracy of the measurement because it can be compared to the other upright position measurement. As it is the same situation, it is expected that these values are the same. The absolute difference between these values can be used as an accuracy range. When the absolute difference of the mean of the measured values is within this range, the difference can be an inaccuracy of the measurement. In this case, the accuracy range is between 0.4 mm^2 and 5.0 mm^2, which is the maximal absolute difference from Table 1.

3.4.2 Measurement 1: no compression, upright position

For the measurement without compression, it is seen that A_{PTV} does not increase in all the subjects when measured in the upright position. From the results, it can be said that the A_{PTV} does not increase in every subject over time since the lower leg muscle is inactive and more blood stays in the legs.

The images obtained from the US system have a low resolution and for some, the PTV is not always clearly seen. Because the images are observed by the same person who has executed the US measurements, this person knows where the veins are. As it is a deep vein, the acoustic wave must penetrate through the leg muscles and fat tissue to image the posterior tibial vein. The attenuation of the acoustic wave increases when the penetration depth is deeper resulting in a weaker signal reaching the PTV as compared to the superficial veins.

A theoretical explanation can be given to why the cross-sectional area of the PTV does not increase. The deep veins do not expand more when less blood is returned to the heart. The blood may shift to other parts in the legs, for instance, the superficial veins. This would mean that the volume of the whole calf would increases.

3.4.3 Measurement 2: fluctuating compression, upright position

The fluctuating compression shows that from the performed measurements, 78% of $\Delta A_{PTV\ FC}$ data points are positive ranks. As Formula 1 suggests, the assumption can be made that a decrease in A_{PTV} increases the blood velocity where the compression is applied.

The results show that $\Delta A_{PTV\ FC}$ is not always positive, as 22% is negative ranked. This could be due to inaccuracy of the measurement of A_{PTV} or movement of the subject. The maximal measured increase is measured to be 3.8 mm^2, which is smaller than the accuracy range of 0.4 to 5.0 mm^2. The mean value of $\Delta A_{PTV\ FC}$ is 1.0 mm^2. The difference between the largest increase and the mean of $\Delta A_{PTV\ FC}$ is 2.7 mm^2 which is within the accuracy range and therefore the maximal increase could be a measurement error.

3.4.4 Measurement 3: constant compression, upright position

The constant compression shows a constant cross-sectional area value, but it is hard to compare the results with A_{PVT} at 40 mmHg of the fluctuating compression measurements due to the difference in probe position, which makes it hard to compare all the measured situations with each other. As the aim was to evaluate if the constant compression could achieve the same effect as the fluctuating compression by comparing A_{PVT} at the compression values of both measurements, the inaccuracy makes it difficult to do so.

The inaccuracy of the change in angle between the probe and the skin is caused due to differences in the performance of the measurement. It was hard to keep the probe at the same angle for every measurement, which makes it difficult to compare the results of the measurement of each situation with each other. This will have influenced the cross-sectional area of the measurements due to the difference in angle of the probe on the skin. For each measurement, the time measurements can be compared easily with each other as the probe was in the same position in the clamp. Due to the sitting breaks and repositioning of the subject, the cross-sectional area of the different measured situations can vary. An option is to mark the feet of the subject and mark the position of the probe on the leg such that the same position can be taken for each measurement. Also, the stand where the probe is in should not be moved during the transition between measurement and sitting break.

The compression of the constant compression was kept between 38 and 42 mmHg, but the compression was not always within these values. Because this was monitored by the US executer, the values sometimes dropped below 38 mmHg. Also, the values sometimes raised above 42 mmHg due to the inaccurate pumping of the hand pump.

3.4.5 Measurement 4: supine position

The cross-sectional area increases with a ratio of 1.3 to 1.9 in the upright position when comparing this to the supine position. With these results, it can be said that A_{PTV} increases when comparing the results of the upright position and the supine position with each other and so the corresponding research question can be answered.

3.4.6 Data analysis

Another aspect which can influence the accuracy of determining A_{PVT} is the method used for the data analysis. When using the ImageJ tool to determine the cross-sectional area, the data is also influenced by the way the ellipse is drawn. As this is only performed by one inexperienced person, it will influence the data. When having an expert evaluate these images, the intra-observer variation will be less. Another solution is to eliminate manual drawing of the ellipses by using an algorithm specialised in analysing US images. In some images it is hard to determine the difference between the veins and the surrounding tissue, one person can see the cross-sectional area of the vein differently compared to another person. The standard deviation of the intra-observer variation for all the measurements in this research varies between 0.1 mm^2 and 2.4 mm^2. The absolute difference of the intra-observer variation is between 0.2 mm^2 and 4.8 mm^2. This variation contributes to the accuracy range from 0.4 mm^2 to 5.0 mm^2 and is smaller than the maximal inaccuracy.

3.4.7 Protocol improvement

For the executed measurements performed in the calf, there are some suggestions for improvements. As can be seen in Table 1, Table 3, and Table 4 the A_{PTV} of Subject 2 in the upright position is around three times as high compared to the other subjects. It is thought that this is due to the fact the weight of Subject 2 was not distributed equally on both feet. The body weight was on the right leg and so less weight was on the left leg, which was the measured leg. The hypothesis is that because there is less weight on the left leg, the A_{PTV} is larger compared to when body weight is normally distributed. This theory was checked using US and it was seen that when more weight was on the left leg, the A_{PTV} decreases and could not be seen anymore. This is probably due to the muscles which contract more when the weight is applied on the leg.

To check if the weight is equally distributed, two weighing scales could be used. When standing with each foot on one weighing scale, the weight of each scale should be the same. To improve the position of the subjects in this setup, the position of the feet can be marked on the ground. This way the subject can take the same position for each measurement. A different method to improve the weight-bearing position and the ability for the subject to stand still is the use of a tilt table. Because in the bed of the weight-bearing MRI is rotated to an angle which is lower than 90°. When rotating to 90°, the patients might experience the feeling of falling forwards which makes the patient uncomfortable and so also unstable. When rotating the bed slightly lower than 90°, the weight of the patient is more to the back which makes standing still in the upright position more comfortable. As the angle of this tilt table can be changed similar, it mimics the bed that is used within the weight-bearing MRI scanner better than standing against the wall, where people are standing more unstable.

3.5 Conclusion measurements calf

From the calf measurement it can be concluded when compression is applied, A_{PTV} decreases and so in theory the blood velocity increases. When comparing the upright to a supine position, it is seen that in an upright position A_{PTV} is higher compared to the supine position.

Furthermore, it can be concluded that, apart from the fact that the blood velocity could not directly be measured, these results are not enough to answer all the researches sub-questions. It is still unknown how the cross-sectional area and the blood velocity in the deep veins of the legs change over time in the upright position. Because of this, it cannot be concluded if the constant compression garments achieve the same effect as the fluctuating compression device. Therefore, another method should be considered, where blood velocity can be measured.

4 Groin measurements

4.1 Introduction

As discussed in Section 3.5, the deep veins within the calf are too small to measure the blood velocity with US. Therefore, a larger vein is required to measure blood velocity. For this reason, a vein in a more proximal position in the legs can be investigated to measure the blood velocity. All the deep veins from the leg together form the common femoral vein (CFV), which together with the great saphenous vein (GSV) form the femoral vein (FV). This vein is not compressed by the garments as the garments stop halfway the thighs and this vein is measured at the groin. Therefore, the cross-sectional area would not change due to the compression of the garments.

The CFV has also been investigated by other researches. A research performed by Westrich et al.[13] investigated different compression devices and their effect on the velocity in the common femoral vein (v_{CFV}) and the femoral vein (FV), which is above and below the junction of the CFV with the GSV. These two locations were chosen to study both the deep and superficial venous systems. Their results show that the greatest effect of the compression devices was mainly observed in the CFV, which represents the deep venous system. Due to the interest of this research in the effect on the deep veins, the CFV was selected to be investigated to exclude GSV, which is a superficial vein.

For the groin measurement, the same setup as for the calf measurements was used. Because the difference of supine position and the upright position was seen with the calf measurements, it was decided to only perform the groin measurements in the upright position. So, to measure the v_{CFV}, three measurements were performed including a measurement without compression (no compression), a measurement with the use of a compression pump (fluctuating compression), and a measurement with the use of a handpump (constant compression).

4.1.1 The goal of the groin measurements

The main goals of the groin measurements are to investigate v_{CFV} without compression, fluctuating compression and constant compression to measure the effects on v_{CFV} in these different situations in the upright position.

4.1.2 Hypothesis groin measurements

The hypothesis for the groin measurements is that when someone stands in an upright position for 7 minutes, the blood velocity in the legs drops due to lack of lower leg muscle activity. In this situation, the lower leg muscles do not contribute to the return of blood to the heart.

Furthermore, it is known that the fluctuating compression will increase the blood velocity during the change of compression in the CFV. It is also known that compression decreases the cross-sectional area of the veins in the legs. When the cross-sectional area is decreased, it is expected that blood velocity will increase and so the blood volume that returns to the heart will be increased as well. Because this compression is performed every minute, the blood velocity will not decrease over time when measuring for 7 minutes.

For the constant compression, it is expected that the cross-sectional area stays constant during the 7 minutes. Therefore, it is expected that the blood velocity also stays constant. The cross-sectional area does not decrease due to the support of constant compression. Therefore, blood flow also does not decrease.

To confirm these expectations, the research questions formulated in Section 1.3 are used for this research, looking at v_{CFV}.

4.2 Materials and Methods

4.2.1 Materials

The materials for these measurements are similar to the calf measurements, which are explained in Section 3.2.1. The setup is a little different since no steps are used for the subjects to stand on. The groin is high enough for the US executor of this research to reach and so to perform the measurements. Also, the stand with clamp was not used as in this case the probe cannot reach the groin. Due to this, it was hard to position to probe correctly every time the subjects took their position for the measurement, as is discussed in Chapter 3. A chair with an armrest was used during the measurement to keep the arm of the US operator as steady as possible.

4.2.2 Methods

The blood velocity is measured using the Pulsed Wave Doppler measurement over 13 seconds. The time frame of 13 seconds is chosen because the cycle of the compression pump is 12 seconds and the 1 second gives some space to crop the blood velocity graph.

This research intends to compare the blood velocity within each subject for all the different situations. It is not the idea to compare the blood velocity of the subjects with each other.

4.2.2.1 Measured vein

The CFV is measured, at the point before the junction with the Great Saphenous Vein (GSV) but after the junction with Deep Femoral Vein (DFV). During the measurement, the vein is located first in the transverse plane, as shown in Figure 17, to see at what point the junction is located. Next, the CFV is located in the sagittal plane. In this plane, the valves can also be seen. It is not desirable to measure within the proximity of a valve due to the turbulent flow. This can make the measurement less reliable as blood also flows back to close the valves in the vein.

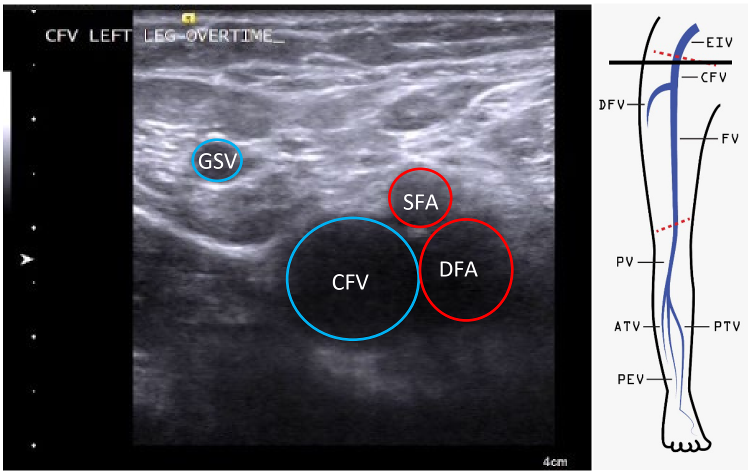

Figure 17 The Common Femoral Vein (CFV) with the Great Saphenous Vein (GSC), the Superficial Femoral Artery (SFA) and the Deep Femoral Artery (DFA) in transverse plane. In the schematic overview of the deep veins in the legs right show at which height the US image is taken.

In the sagittal plane, the Pulsed Wave Doppler measurement is performed, as is explained in Section 2.3.2, to determine the blood velocity over a time frame of 13 seconds for every minute. An example is shown in Figure 18. The protocol for the measurement will be explained in the next section.

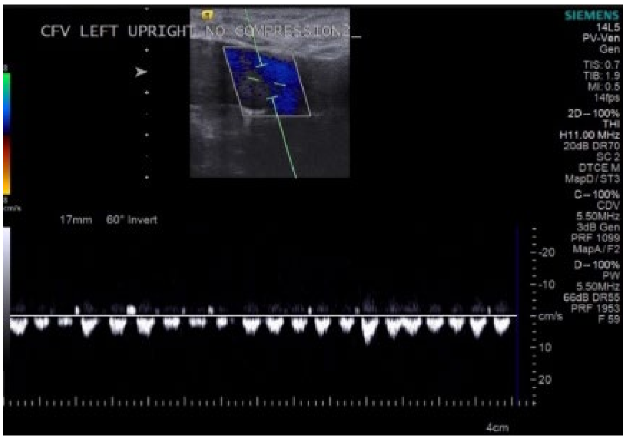

Figure 18 The sagittal plane of the CFV performing a Pulsed Wave Doppler measurement to gain the blood velocity

4.2.2.2 Protocol

The protocol consists of three different measurements, which are all performed in an upright position. Between these measurements, a sitting break is inserted. Before both the fluctuating compression and constant compression, baseline measurements are performed to compare these results with each other. For all the upright measurements, a measurement is performed every minute. The first measurement is t_0, the measurement after 1 minute is t_1 and so on until t_7. The protocol is visually described in Figure 19. The different

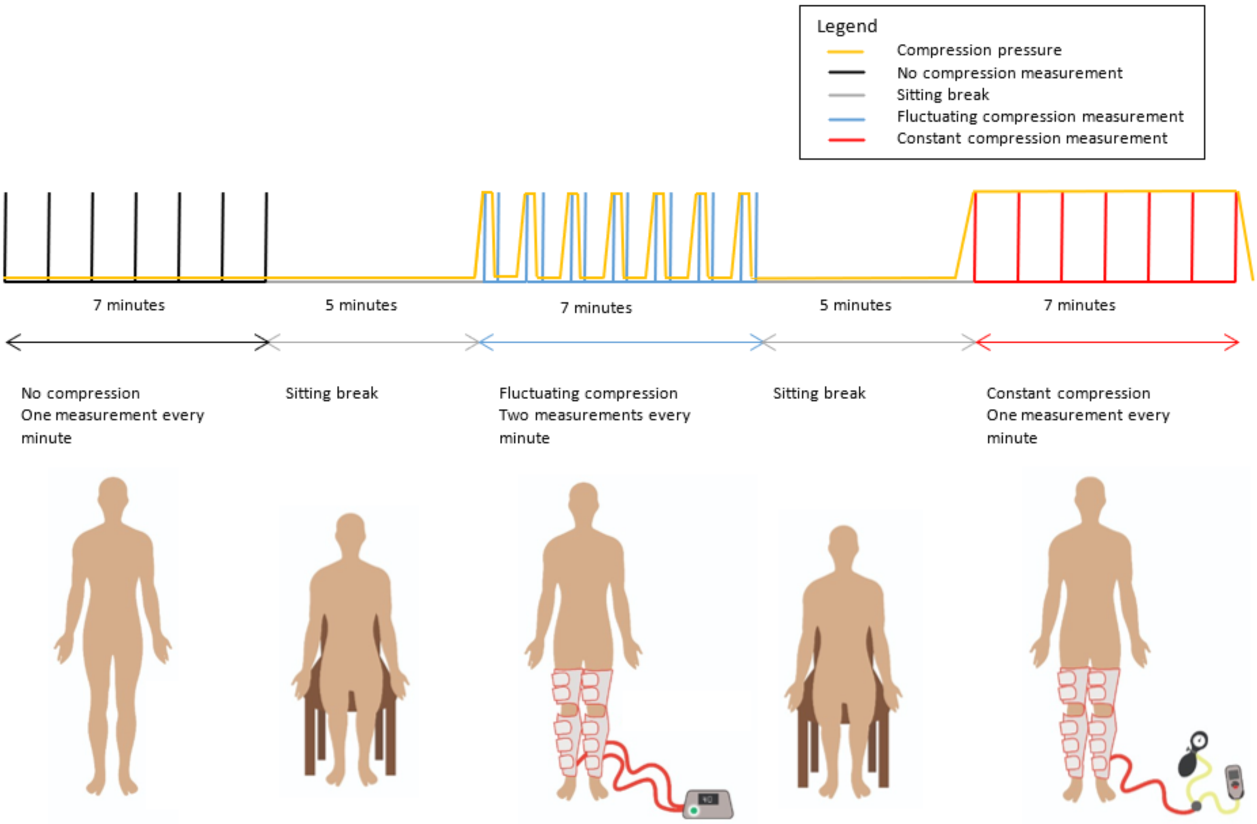

Figure 19 Method of the performed groin measurement using the US to measure the Common Femoral Vein (CFV) with illustration of the position of the subject

colours used in the figure indicate the three different situations. These colours also correspond to the colours of the results. The complete protocol can be found in Appendix II: Protocol groin measurements.

4.2.2.3 US settings

Before starting the measurements with US, some settings are configured. The depth was set to 4 cm to image the CFV and the gain was set to the maximal value to achieve high contrast. Next, the gain per depth and focus was adjusted to get the best contrast at the depth of the PTV.

4.2.2.4 Assumptions

Some test measurements were performed before the groin measurements and it was seen that the cross-sectional area of the CFV does not change when compression is applied on the calf and the lower half of the thigh. For this reason, it was assumed that the cross-sectional area stays constant and only the blood velocity in the CFV is measured to determine the blood flow.

4.2.2.5 Data analyses

The data is analysed in MATLAB 2019a (The MathWorks Inc, Natick, USA). An explanation of the used script made by Lennart van de Velde is given in Appendix III: MATLAB script groin measurements.

For this research, the numerical integral of the velocity profile from US is calculated to determine the area under the velocity profile for the measured 13 seconds. This method is chosen because the venous blood velocity does not have a repeated cycle as the arterial blood velocity profile has. For this reason, the average blood velocity or the peak velocity does not give a good representative of what happens within the measured 13 seconds. The numerical integral of the velocity graph can be seen in Formula 4.

$$s_{blood} = \int_{t_{begin}}^{t_{end}} v_{blood}(t)\, dt \qquad (4)$$

In this formula, s_{blood} is the displacement of blood in a vessel in [cm], the t_{begin} is the starting time of the measurement and t_{end} the ending time in [s], t is the time in [s] between t_{begin} and t_{end}, and $v_{blood}(t)$ is the velocity of blood at time point t in [cm/s].

When multiplying s_{blood} with the cross-sectional area of the blood vessel, this will give the blood flow using Formula 1. In this case, the cross-sectional area is not measured. As was seen in Chapter 3, measuring the cross-sectional area of the veins can be inaccurate. If this can be avoided, it will eliminate the possibilities of inaccuracies being included in the blood velocity. Following the assumption that the cross-sectional area of the CFV stays constant during the measurements within each subject, the value of the cross-sectional area does not need to be known.

4.3 Results of groin measurements

The same subjects for the calf measurement are used for the groin measurement. Only in this case, Subject 2 was not measured. This is because the measurement of four subjects gave enough information for this measurement.

First, the disturbances which are seen within the velocity profile during the measurements are discussed. Next, the baseline measurements are compared to determine the accuracy of the performed measurement. Because the results of Subject 3 and Subject 4 are similar, these will be discussed first for all the measured situations, followed by the results of Subject 1 and Subject 5.

4.3.1 Disturbances in the velocity profile

During analysing the results, some difficulties were seen due to disturbances in the velocity profile. First, when looking at the results of Subject 1, blood velocity graph measured by with the US, the signal intensity of Subject 1 for all three measurements was lower compared to the other subjects. An example of a blood velocity profile of Subject 1 compared to the blood velocity graphs of Subject 3 can be seen in Figure 20. Also, it was seen that these data points per measurement are fluctuating more compared to the other subjects. Because of this, the results of Subject 1 are overall less trustworthy than the results of the other three subjects.

Secondly, there are also some disturbances seen during laughing or coughing of the subjects. In Figure 21 an example is shown of v_{CFV} graph from the US from Subject 3 during the fluctuating compression. In the left image shows a v_{CFV} graph without disturbance during the increase of the compression and the v_{CFV}. A small backflow is seen on the left side of the blue line, however, this is due to the deflation of the compression pump. On the right image, it is seen that during the increase of the compression and v_{CFV} a sudden backflow occurs, indicated by the yellow circle. This influenced the results with a lower s_{CFV}.

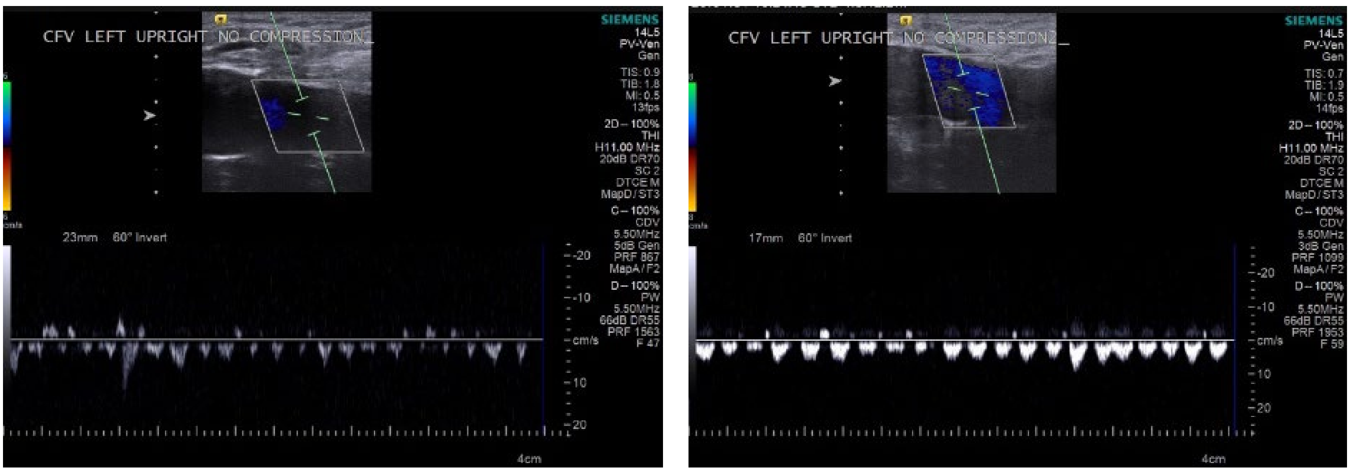

Figure 20 Velocity profile of Subject 1 (left) with a lower signal intensity compared to Subject 3 (right)

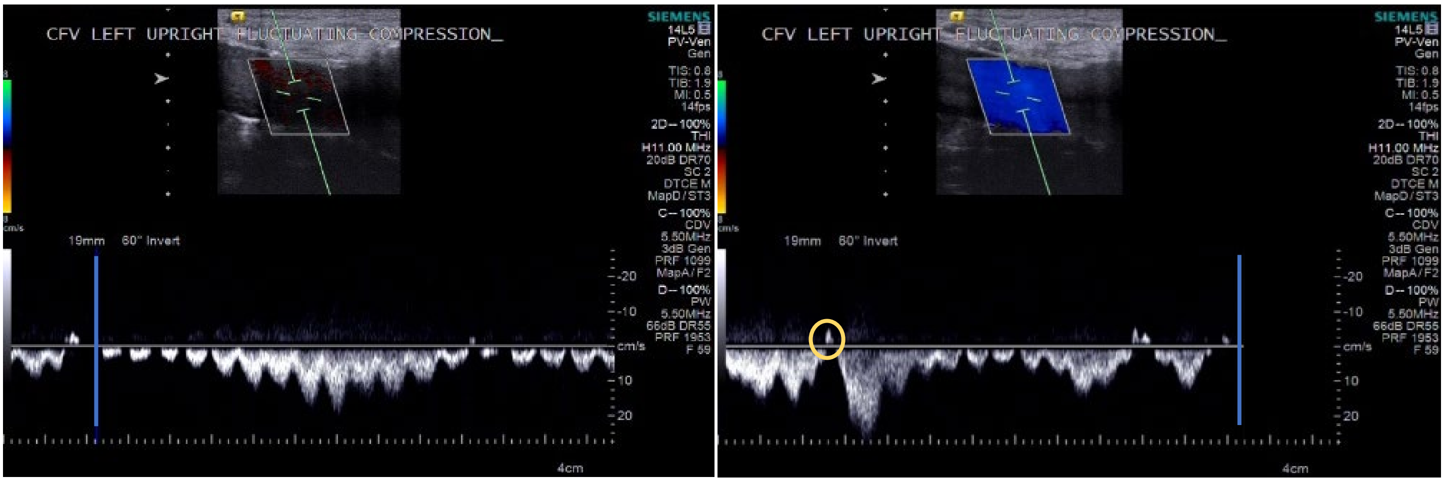

Figure 21 Blood velocity profile of Subject 3 without any disturbances (left) and with a backflow due to laughing or coughing (right) during the fluctuating compression measurement

Thirdly, movement of the leg also influences the blood velocity profile. In Figure 22, aliasing occurring in the velocity graph can be seen, indicated by the yellow circle. Because the velocity was higher than the scale of the graph, this results in wraparound of the curve with the peak displayed below the zero-line. This was due to the fluctuating compression device which stimulated the leg to move. During data analysis, this wrapped around peak is cropped from the graph to decrease the effect of the leg movement on the results.

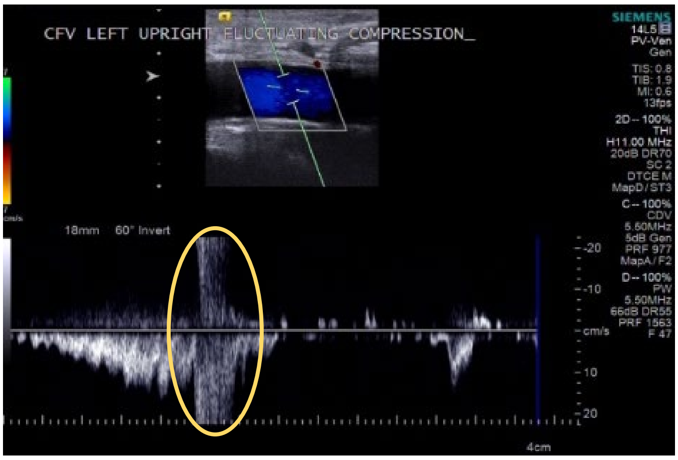

Figure 22 Blood velocity profile of Subject 4 with aliasing and wraparound of the curve due to leg movement

4.3.2 Baseline measurements

To verify the accuracy of the measurements, the difference between the no compression measurements and the baseline measurements of both the compression measurements are compared. The overall absolute maximal difference expressed as a percentage of the mean value is between 35.2% and 81.8% of which Subject 4 has the lowest percentage and Subject 1 the largest. This can also be seen in Table 5 for every subject.

Table 5 Mean value of s_{CFV} of the measurement without compression: the no compression measurement at t_0 and the baseline measurements of both fluctuating and constant compression, with the corresponding standard deviation.

Subject number	s_{CFV} upright position, no compression [cm]
1	11.5 ± 4.7
3	12.0 ± 3.9
4	10.1 ± 3.1
5	13.1 ± 2.3

In Error! Reference source not found. the increase of s_{CFV} due to compression can be seen. This is expressed in a percentage of the increase of the compression compared to its corresponding baseline measurement. For every subject, the s_{CFV} due to fluctuating compression increases more than s_{CFV} due to constant compression. That said, three of the four subjects show an increase in s_{CFV} due to constant compression. Subject 4 shows a decrease in s_{CFV}. The average increase of fluctuating compression and constant compression over all subjects, in percentage, is 176% and 29% respectively.

Table 6 Increase of s_{CFV} between the baseline measurement and the fluctuating compression (FC) and the constant compression (CC) measurements.

Subject number	Compression method	s_{CFV} compression [cm]	s_{CFV} baseline [cm]
1	FC	27.80 ± 12.68	16.49
	CC	13.24 ± 4.45	11.07
3	FC	32.45 ± 5.45	10.74
	CC	9.92 ± 3.52	8.70
4	FC	39.28 ± 5.89	12.07
	CC	6.99 ± 2.36	12.26
5	FC	41.13 ± 10.29	13.37
	CC	20.95 ± 10.29	10.70

4.3.3 Results Subject 3 and Subject 4

4.3.3.1 Measurement 1: no compression, upright

The results of the measurements for Subject 3 and Subject 4 show a decrease of s_{CFV} over time, as can be seen in Figure 23.
The first data point of Subject 4 is very low after which the second data point is higher, after that the blood displacement drops. When comparing the blood velocity profile from US with the other time measurements of the measurement without compression, shown in Figure 24, it is seen that this profile diverges from the others. Because of this, this point can be disregarded. In that case, a clear decrease over time can be seen.

4.3.3.2 Measurement 2: fluctuating compression, upright

For the fluctuating compression, the blood velocity increases when the compression increases as can be seen in Figure 21. When the compression is constant, the velocity first decreases and then remains constant at a certain value. This value is different per person. When the compression pump deflates, there is backflow or no flow measured within the CFV.

When looking at the results of s_{CFV}, there is some scattering in the values of the fluctuating compression measurement. When comparing it with no compression and constant compression, it can be seen that s_{CFV} of the fluctuating compression measurement is always higher, which can also be seen in Figure 23.

4.3.3.3 Measurement 3: constant compression, upright

When comparing the v_{CFV} graphs from the constant compression measurements with the no compression measurements obtained from US, the two graphs look similar. When increasing the compression during the velocity measurement, due to the slow decrease of the compression in the garments, the velocity increases. A higher peak is seen in the velocity graph as was also seen at the fluctuating compression.

When looking at the results, s_{CFV} of the constant compression measurement is overall lower than the s_{CFV} without compression measurement.

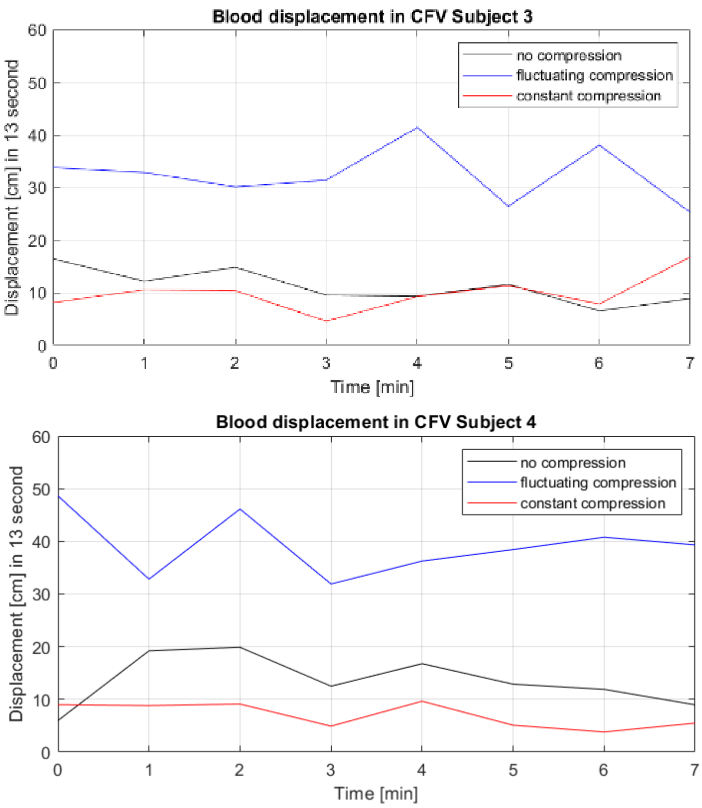

Figure 23 s_{CFV} Subject 3 (above) and Subject 4 (below) with no compression, fluctuating compression and constant compression measurements.

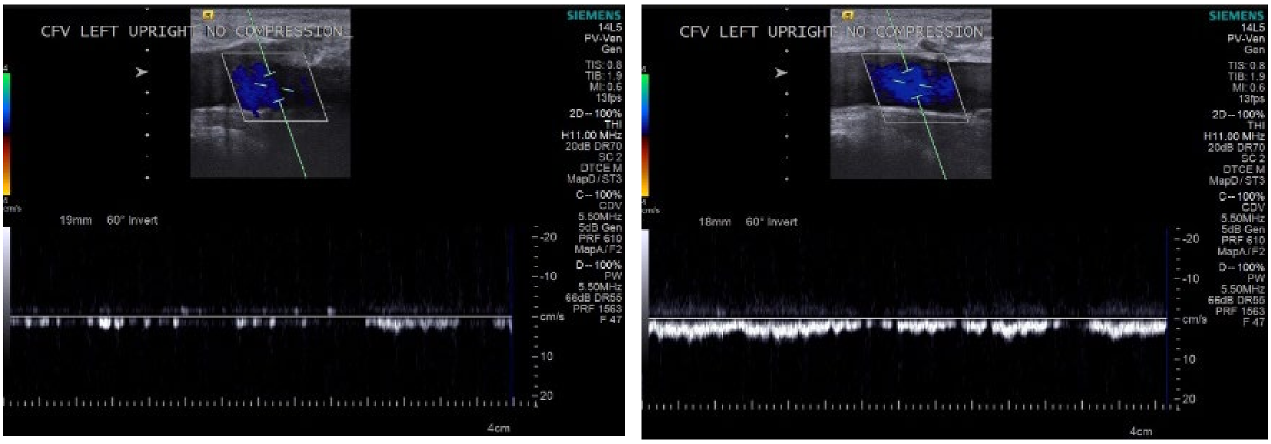

Figure 24 Blood velocity profiles of Subject 4 of no compression measurement of t_0 (left) and t_1 (right)

4.3.4 Results Subject 1 and Subject 5

4.3.4.1 Measurement 1: no compression, upright

As the results of Subject 1 and Subject 5 are similar, only the results for Subject 5 is shown in Figure 25. A decrease in the first half of the measured time frame is seen but for the second half of the measured time s_{CFV} increases.

4.3.4.2 Measurement 2: fluctuating compression, upright

For the results of Subject 1, four s_{CFV} values for the fluctuating compression measurement are lower than the highest s_{CFV} values for the constant compression measurement. For Subject 5, two s_{CFV} values for fluctuating compression measurement are lower than s_{CFV} values for the constant compression measurement, as can also be seen in Figure 25. The t_7 measurement for the constant compression is missing for this measurement.

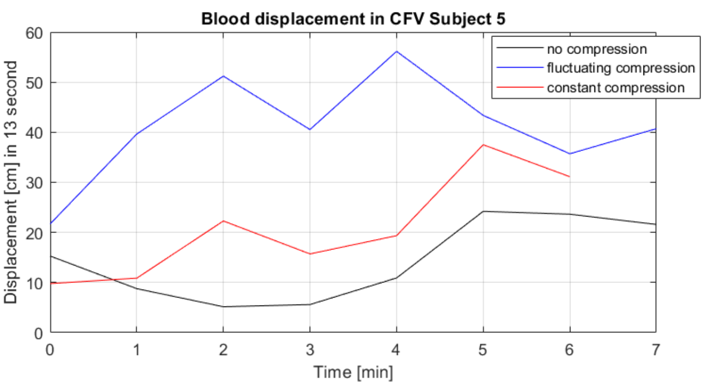

Figure 25 s_{CFV} of the measurement with Subject 5 without compression, fluctuating compression and constant compression.

4.3.4.3 Measurement 3: constant compression, upright

Subject 1 and Subject 5, when the constant compression is used, s_{CFV} is on average higher than s_{CFV} of the measurement without compression. The constant compression measurement of Subject 5 increases in the same way as the no compression measurement does, which can be seen in Figure 25.

4.4 Discussion

In this section, the results for the groin measurements are discussed. First, the measurement without compression is discussed, followed by the fluctuating compression, and then the constant compression. Next, the data analyses, method, and finally the improvement for the protocol are discussed.

4.4.1 No compression

The expectation for the measurement with no compression was that v_{CFV} would decrease over time due to inactivity of the lower leg muscles, as was discussed in section 4.2.1. In two of the four subjects, a decrease of s_{CFV} overtime was seen. For Subject 3, this decrease is 7.6 cm which is a decrease of 46% of t_0. For Subject 4, when discharging the first datapoint t_0, the decrease is 10.3 cm which is a decrease of 53% of t_1. It can be said that for these subjects s_{CFV} decreases as a result of a decrease of v_{CFV} in the upright position without compression.

For the other two subjects, s_{CFV} increases are seen after a few minutes, which is due to v_{CFV}. This is more clearly seen for Subject 5 than for Subject 1. There are a few factors that could influence v_{CFV}. The contraction of the muscles of the pelvic floor influences the pressure in the veins of the groin, as was learnt from an experienced US sonographer from the MST hospital in Enschede. When these muscles contract, v_{CFV} decreases because of the increase of pressure on the pelvic floor. Also breathing influences the pressure in the veins of the groin, as explained in Section 2.1.2.4.[16] Contraction of muscles also occurs during laughing or coughing, as was seen in Figure 21.

Due to the low accuracy of the measurements, it is uncertain if the decrease of s_{CFV} shows that v_{CFV} decreases due to no compression, or that it was the inaccuracy of the measurements. As was discussed in section 4.3.2 the average maximal absolute difference between the no compression measurements between 4.6 cm and 9.4 cm, which gives the accuracy range of the measurement. The decrease in blood displacement for Subject 3 is 7.58 cm, which is within the accuracy range. Although the graph of Subject 3 shows a decrease in blood displacement, it is still uncertain if this is a decrease in blood velocity or inaccuracy in the measurements performed.

For Subject 4, the decrease in blood displacement is 10.26 cm, which is just outside the accuracy rang. For both, it could be said that the values for the measurements are consistent. If the first datapoint of Subject 4 can be disregarded, as described at the beginning of this section, the absolute maximal difference of the measurements might be less and so the accuracy range is also less.

4.4.2 Fluctuating compression

The expectation for the measurement with the fluctuating compression was that the v_{CFV} would stay constant and thus would not drop over time. The results give some fluctuating values, which is unexpected. This could be because the v_{CFV} profile measurement did not always start at the beginning of the time axis during the Pulsed Wave Doppler measurement. The time axis of one graph in US is only 13 seconds, which makes it difficult to have the inflation exactly at the beginning of the graph and the deflation at the end of the graph. Any mistakes in timing can lead to an error in the estimation of s_{CFV}. An example of this can be seen in Figure 26. Also, the intensity of the signal of the velocity is not always the same, which makes it difficult to process the correct value. More noise can be seen in the blood velocity graphs created by the used MATLAB script.

The results of s_{CFV} for the fluctuating compression measurement is roughly 2 to 3 times as high as the results of the constant compression measurement within each subject. This is because the 13 seconds that are measured during the fluctuating compression is when compression is applied. For the remaining 47 seconds, the compression pump does not do anything. For this reason, it would be much more correct to measure v_{CFV} for the

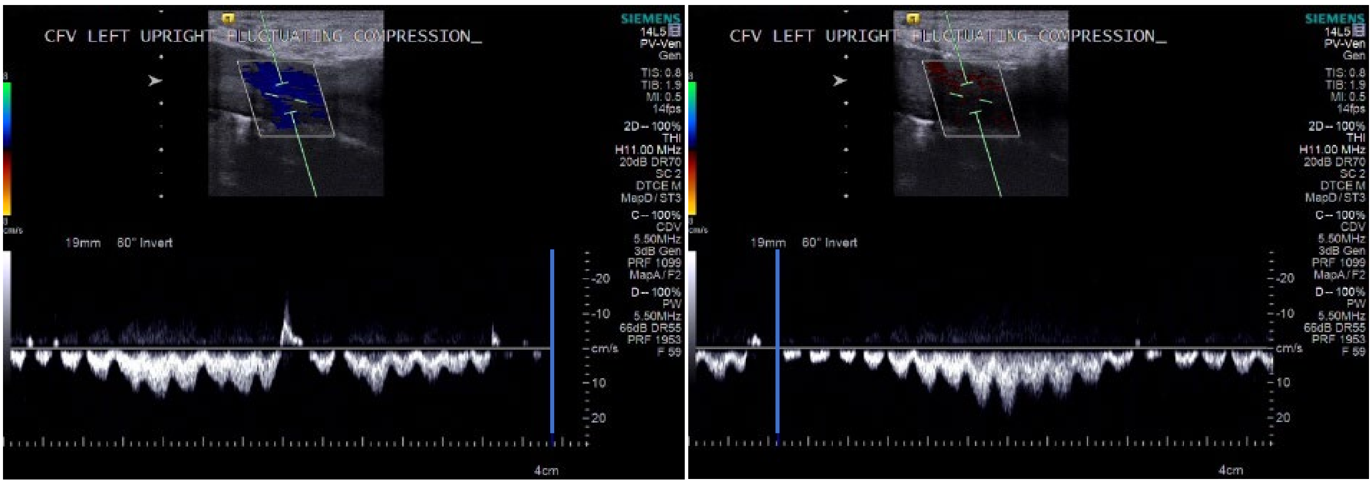

Figure 26 Blood velocity profile of the fluctuating compression of Subject 3 at t_0 (left) and at t_1 (right)

whole cycle of the pump, which is 1 minute. This should then also be done for the constant compression and no compression to evaluate what happens within this minute for all three situations. This would give a more realistic view of the situation.

4.4.3 Constant compression

As the constant compression applies compression for the full minute and the fluctuating compression does not, it makes sense that s_{CFV} during constant compression is lower than s_{CFV} of the fluctuating compression.

When comparing the increase in s_{CFV} of the baseline measurement with the constant compression measurement, s_{CFV} does increase in general with 29% so this means that the constant compression does increase v_{CFV} slightly.

During this measurement, it is clear that the drop in pressure within the hand pump setup does not influence v_{CFV} as much as was suggested in Section 3.4.4. Only when the pressure increases within seconds, does v_{CFV} changes. The drop of 4 mmHg/min is not fast enough to influence v_{CFV}.

4.4.4 Data analysis

When looking at the literature, the peak velocity is used to evaluate the effect on the blood velocity in certain situations.[13][27][28] The peak velocity gives the velocity of the maximal blood velocity recorded. However, for this research, the interest lies within the change of blood return due to the change of the blood velocity within the measured time frame. The peak velocity does not say anything about how many peaks there are present in the measured time frame and so does not give the full information which is necessary for this research. Taking the numerical integral of the blood velocity graph over the 13 seconds gives information about the entire measured time frame, which is desired for this research.

As is discussed previously, some blood velocity profiles have a low signal intensity which influenced the thresholding of during data analysis when the velocity graph is converted from a US image to data points. If the signal is constant and the same threshold value is used, it would give a better representation of how each time measurement relates to one another.

4.4.5 Improvements protocol

To improve the measurement performed in the groin, some improvements can be suggested. For example, something that could help to make it less hard to stand still is to have longer sitting breaks. It was noticed that the subjects had trouble standing still for 7 minutes. Subjects started to make small movements, which causes some inaccuracies and variables within the measurements which are discussed earlier. Lee et al.[29] used sitting breaks of 20 minutes. This makes the ratio of the time in an upright position to the time in sitting position smaller. As sitting down is more comfortable than standing, this will improve the comfort of the measurement. A downside is that the total time to perform the measurement will increase.

To check if 5 minutes sitting break is enough for the blood flow to reset or if this needs to be increased, a measurement can be performed to check the recovery time of the cross-sectional area in the calf and the blood velocity in the groin.

4.5 Conclusion

Although v_{CFV} decreases in two of the four subjects without compression, this difference in v_{CFV} is only slightly larger than the measured accuracy value. This makes it uncertain if this difference in v_{CFV} is because of gravity or the inaccuracy of the measurement.

The fluctuating compression has the highest value for s_{CFV} compared to the constant compression when looking at the inflation and deflation part of the cycle of the compression pump. However, it does remain unknown what the v_{CFV} is during one compression cycle of one minute.

The constant compression shows an increase in s_{CFV}, but it can be concluded that this effect is not similar to the effect of the fluctuating compression as a fluctuating compression is necessary to increase the blood velocity.

5 Overall discussion

The main goal of this research was to find a method that prevents fainting incidences from occurring during weight-bearing MRI scans in an upright position other than the fluctuating compression method. To understand why a fainting incident occurs, the cross-sectional area in the calf was investigated to see if it would increase and if the overall blood velocity in the groin would decrease when standing in the upright position over a period. It was also investigated to see if a compression stocking could be used to prevent people from fainting when standing in an upright position instead of fluctuating compression, such as delivered by a compression pump.

5.1 Learnt from this research

The main research question that was formulated at the beginning of this research was: "What is the effect of gravity and external compression on the deep veins in the legs in the upright position?". The following sections explain the findings of this research concerning this research question.

5.1.1 Upright position over time

As was discussed in Chapter 3 it cannot be concluded for the calf measurements that fainting occurs due to the increase of the cross-sectional area of the deep veins in the calves as this increase was not seen in the results. This is because only one deep vein was investigated and so does not show the effect on all the deep veins in the lower leg. Another reason is that subjects are not standing completely still is because they are standing upright against the wall. When standing in the weight-bearing MRI, the angle of the subject is slightly tilted backwards. When using a tilt table, the situation is better mimicked, and people would be able to standstill due to more support and stability.

Furthermore, the blood volume, which was expected to increase in the legs, was not directly measured. This can be investigated by measuring the difference in the volume of all the veins in the calf and the calf itself. Partsch et al.[6] uses the weight-bearing MRI to create a 3D reconstruction of a part of the calf with both the deep and superficial veins. This is used to investigate the diameter of the veins but can also be used to investigate the vein volume, which can be correlated to the blood volume. Apart from the veins, this can also be used to investigate if the volume of the calf increases in an upright position over time.

What was seen was that the cross-sectional area increases when comparing the results of the upright position to the supine position. This change in position increases the cross-sectional area.

As was discussed in Chapter 4 for the groin measurements, the decrease in blood velocity was not confirmed due to the inaccuracy of the measurement. It would help to let an experienced US sonographer perform the measurements to increase the inaccuracy of the angle of the probe and reduce the unnecessary movement of the hand.

To conclude, the expectations for the cause of fainting incidences cannot be confirmed by the two performed measurements.

5.1.2 Constant compression vs fluctuating compression

From this research, it cannot be concluded that a compression stocking can be used to prevent people from fainting during an upright weight-bearing MRI scan. The results of the constant compression measurement did not show a similar effect in the veins as the fluctuating compression. It showed that when constant compression was applied, the blood velocity stayed constant. To increase the blood velocity, a change in compression is needed as seen for the fluctuating compression. A constant compression does not increase the blood velocity as much as the fluctuating compression.

5.1.3 Sponge theory

To understand the increase in blood velocity in the veins, the veins can be compared with a sponge. When the veins are compressed, the cross-sectional area decreases which increase the blood velocity temporarily. To increase the blood velocity again, the veins need to be released from the compression to increase the blood volume. This way, the veins can be compressed to increase the blood velocity again. When keeping the compression constant, the blood velocity does not increase as the blood volume does not change. This is also seen when a sponge is kept compressed, no water is absorbed by the sponge. This theory helps to understand why the effect of a constant compression on the veins is different compared to the effect of a fluctuating compression.

5.2 Missing information

Using the information gained from this research, the main question cannot be fully answered, as there is still information missing. For instance, it is still unclear if blood remains in the leg due to inactivity of the lower leg muscles in an upright position. Also, this research aimed to find a method that has the same effect on the veins as the compression pump. Three categories that can be considered to change are to investigate another prevention method, change the imaging technique, and measure at a different location in the body. Two things that can be considered are first to change the imaging technique and second to change the measured location in the body.

5.2.1 Another prevention method: feet movement

A method that seems to have a similar effect as the fluctuating compression, is the movement of the feet. As discussed in Chapter 2, the lower leg muscles are the main mechanisms that support the venous return in an upright position.[17]

During the groin measurement, the effect of feet movement was measured to investigate the influence of these movements on the blood velocity. The feet movement was performed by only lifting the toes and not moving the heel to prevent movement of the rest of the body in the vertical direction, as this would cause motion artefacts in the measurement, influencing the accuracy of the blood velocity. The feet movement can be used to increase the blood velocity with a fluctuating compression effect, similar to the compression pump.

A research performed by Yamashita et al.[30] investigated the effect of feet movement compared to a foot compression device, of which the garment is only positioned around the foot, in a supine position. Yamashita et al. saw that the foot exercise, which was performed by a nurse, was equally or more effective compared to the foot compression device. The foot exercise was performed by the nurse for 5 minutes and the effect lasted for 2 hours in the supine position. For this research, it would be interesting to investigate if this effect also holds for the upright position. Also, it is important to investigate how the feet movement can be performed in an upright position.

Advantages of the feet movement are that it is easily available as nothing needs to be purchased or worn, which is cost and time efficient. The patient does need to have directions, but these should not be complicated. These advantages fit within the requirements that were set in Section 1.2.1, to which the fainting prevention method should suffice. It is required to investigate this method, which is elaborated on in Chapter 6.

5.2.2 Low-field MRI vs the US

As mentioned in Chapter 1, the Esaote 0.25T MRI present at the University of Twente was unavailable when this research was performed. At the beginning of this research, some test scans with different sequences were performed with the weight-bearing MRI which looked promising when imaging the veins in the calf in the transversal plane in the supine position. Also when looking at the literature [10][31], it was considered a promising imaging method when investigating the cross-sectional area of the veins in the legs. Both Partsch et al.[31] and Downie et al.[10] stated that MRI is the best method to demonstrate diameter reduction in a lying down and upright position with and without compression. It allows for a more accurate assessment of the anatomy of the whole leg compared to US. To investigate the difference between MRI and US in more detail, the advantages and disadvantages of the use of MRI are discussed next.

5.2.2.1 Advantages low-field MRI

The weight-bearing MRI can visualize the veins in the transversal plane to investigate the cross-sectional area of all the veins in the calf, while US cannot image all the veins of the calf at the same time. It could be useful to investigate the effect on superficial as deep veins, to see if the same effect is achieved as was seen by Partsch et al.[6] Also, the weight-bearing MRI images show high contrast between the veins and the surrounding tissues. When looking at the Fast Spin Echo T_2 (FSE T2) sequence, which looked the most promising, the resolution was high enough to see the boundaries between the veins and the surrounding tissue. An example can be seen in Figure 27. Veins with a minimum diameter of approximately 2 mm can be imaged. Due to this high image contrast and resolution, the boundaries between the veins and the surrounding tissues are better visible compared to the US images. This makes the measured cross-sectional area from the weight-bearing MRI image more accurate compared to that of US. Another advantage is that the quality of the MRI images is independent of how the protocol is executed by the operator.

Figure 27 Low-field MRI scan with the sequence Fast Spin Echo T_2 (FSE T2) of the calf in transversal plane in supine position. The white ellipse shapes in the calf are the veins.

5.2.2.2 Disadvantages of weight-bearing MRI

A disadvantage of the weight-bearing MRI scanner is that the scan time is longer than the compression cycle of the compression pump. US has a good temporal resolution compared to the weight-bearing MRI. The weight-bearing MRI can scan within several minutes when using the FSE sequence. An MRI technique which can be used to image real-time is the use of HYCE, which stands for hybrid contrast enhancement. The drawback of this is that what is gained in time is lost in resolution. This method could be investigated to see if this could be used for real-time cross-sectional area measurements during compression from the compression pump. With the weight-bearing MRI, it is not possible to visualize the blood velocity of the veins as it does not have the software, but it is theoretically possible. With US, the blood velocity can be measured. In practice, it is also not yet possible to visualize the blood flow with the weight-bearing MRI in an upright position.

From the literature, Downie et al.[10] indicates that the weight-bearing MRI is not as flexible as US when it comes to positioning options of the patient. However, another positioning besides supine and upright was not needed for this research.

5.2.3 Other measure locations

In this research, the veins in the legs were measured to investigate the fainting incidence during upright weight-bearing MRI scanning. These veins were chosen since Hansen et al.[8] applied a fluctuating compression to the legs. So, something changed within the legs that prevented people from fainting in an upright position.

5.2.3.1 Neck measurements

Fainting is caused when the supply of oxygen to the brain is insufficient, which can be for instance because less blood is transferred to the brain. To investigate the direct problem of fainting, it would be better to look at the blood supply to the brain by measuring the blood flow in the carotid arteries in the neck.

5.2.3.2 *Hemodynamic responses*

Another method to directly measure the cause of fainting in an upright position is to look at the hemodynamic responses of the human body. Lee et al.[29] included hemodynamic responses to his research when comparing different compressions pressures to one another in different positions. A parameter to add, which is not investigated by Lee et al., is the return of the blood to the heart by the inferior vena cava, which returns the blood from the lower and middle body. When also measuring the stroke volume and the heart rate, the cardiac output (CO) can be calculated, which gives the amount of blood pumped by the heart per unit time. When comparing the stroke volumes per heartbeat, it can be measured if the stroke volume decreases as less blood returns via the inferior vena cava. The heart cannot pump out more blood than returns. When comparing the difference in the stroke return of the inferior vena cava, it can be concluded if this stroke return also decreases which causes the stroke volume to decrease. This could give useful information about blood circulation in different positions and situations.

5.3 Clinical relevance

A meeting with Roland Beuk, a vascular surgeon at the MST hospital in Enschede, was held to learn if there were more clinical relevance to this research, apart from the fainting incidences of patients occurring during upright weight-bearing MRI scans. During this meeting, two different subjects were discussed which were clinically relevant: the general anatomy of the veins in the legs and the blood flow in the veins when compression is applied. These are discussed next respectively.

5.3.1 Anatomy of the veins within the legs

The anatomy of the veins in the calf was partly imaged by Partsch et al.[6] using the weight-bearing MRI as all the veins in the legs can be imaged at the same time. In this research, the weight-bearing MRI scans were used to make a 3D image of the veins in the measured part of the calf to visualize the anatomy. More scans can be made to expand the research by Partsch et al.[6] allowing the growth of the veins to be followed. This is, for instance, interesting when insufficient perforator veins are removed to follow the regrowth of these veins. Insufficient perforator veins are the most common cause of recurrent varicose veins after treatment, which is often unrecognized.[32] Misfunction of the valve in the perforator veins can result in pain, skin changes, and skin ulcers. When removing the insufficient perforator vein, a new vein can grow back in its place.

A theory by Roland Beuk is that when the lower leg pump does not work sufficiently, they can cause the perforator veins to become insufficient. If this theory is true, the problem is not solved by removing the insufficient perforator veins. To investigate this, the compression of the lower leg muscles can be investigated with patients who suffer from insufficient perforator veins. Because there is no solid treatment for these patients, their costs are high mainly due to the care of the open wounds, hospital visits, and diagnosis.

5.3.2 Blood flow with compression

The exact blood velocity when compression is applied is still unclear. Unfortunately, with the weight-bearing MRI, the flow cannot be imaged in practice. Phase-contrast MRI methods can be used to measure the flow by measuring the three velocity components in each gradient direction.[33] This should be further looked into to investigate the possibilities to measure flow with the weight-bearing MRI. In this case, US can be used, but the disadvantage of US is that only the blood velocity within one vein can be measured.

6 Recommendations and Conclusion

As was discussed in Chapter 5, there are some possibilities to extend this research. The recommendations are discussed first, followed by a conclusion drawn from this research.

6.1 Recommendations

6.1.1 Feet movement

For further research, the recommendation is to look further at feet movement as a prevention method for fainting incidence in upright weight-bearing MRI scans, as this seems promising and has not yet been investigated in this setting. Clarification is needed on how frequently the feet movement needs to be performed to make a comparison with the compression pump. For this, US measurements of the blood velocity during the inflation and deflation of the compression pump should be compared to the blood velocity during the feet movement. The measurements have already been performed, but not yet analysed. The same data analysis technique, by taking the numerical integral of the blood velocity graph, can be performed on the feet movement measurement.

When the frequency of the feet movement is known, it can be implemented into the protocol of the weight-bearing MRI scans. However, it needs to be known if the movement can be performed during the scan time, without causing motion artefacts on the images. If this is not possible, it needs to be known how many feet movements needs to be performed in between the scan time to last in an upright position without fainting incident occurring.

6.1.2 Hemodynamic responses

A better understanding of why fainting occurs is still necessary to be able to know how to prevent it. The question remains if this can be due to less blood returning to the heart because of the inactivity of the lower leg muscles. This theory has not yet been confirmed. This could be investigated by measuring stroke return in the inferior vena cava, stroke volume, heart rate, and CO as discussed in Section 5.2.3.2.

As was performed within the research of Lee et al.[29] the hemodynamic responses are measured in both the lying down position and the upright position, to investigate how the hemodynamic responses change for these two situations. However, what was not considered within the research of Lee et al., which is important to understand why fainting incidences occur, is how hemodynamic responses change over time without applying compression. This would be useful information for this research. The focus would be on how the stroke return of the inferior vena cava would change and what this effect would have on the stroke volume, the heart rate, and the CO. The expectation is if the stroke volume decreases as the stroke return decreases, and the heart cannot pump out more blood than is present, that the heart rate will increase to keep the CO around the same value. In the research of Lee et al.[29], it was seen that in the upright position, the stroke volume decreased and the heart rate increases, compared to the upright position. As a result, the CO in the upright position was still lower than in the supine position. When a difference in stroke return and stroke volume is seen, the carotid arteries in the neck can be measured to see if blood supply decreases when the stroke return decreases.

When applying the fluctuating compression while in the upright position, it would be interesting to see how this influences the hemodynamic responses. The expectation is that the hemodynamic responses to the fluctuating compression would be similar to the hemodynamic responses during the lying down position. To fully complete these measurements, the investigation of the feet movement and the hemodynamic responses should be added so that it is possible to compare this to the hemodynamic responses of the fluctuating compression.

6.2 Conclusion

In conclusion, this research gives insight into the influence of gravity on the venous return to the heart in an upright position and what the effect is of fluctuating and constant compression on the deep veins in the legs. When using US, it is seen that the cross-sectional area of the PTV can be investigated, which does not increase over time during an upright position. Also, the blood velocity of the CFV can be investigated, which does not decrease in all the measured subjects. However, the change in the volume of blood that returns to the heart during upright position overtime should be measured directly at the heart instead of in the legs.

It was seen that fluctuating compression decreases the cross-sectional area of the PTV and increases the blood velocity in the CFV during the increase of compression. This compression method seems to have more effect on the venous return than the constant compression. Another fluctuating method that seems promising to replace the compression pump, is feet movement. The exact effect of the feet movement needs to be compared to the compression pump to understand how the cycle of feet movement could replace the compression pump. This can then be implemented in the MRI protocols.

The constant compression does not seem to have enough potential, as the blood velocity does not increase as much as seen with the fluctuating compression. This research shows that fluctuating compression is necessary to increase blood velocity while it was seen that the constant compression does not increase the blood velocity as much as the fluctuating compression.

The main research question "What are the effects of gravity and external compression on the deep veins in the legs in an upright position?" cannot fully be answered yet. As was discussed in the recommendations, the next step is to investigate the feet movement as a method to prevent fainting during weight-bearing MRI scans and to implement this in the currently used protocols. To have a better understanding of why fainting incidences occur, the stroke return of the inferior vena cava should be measured in the upright position to investigate if this decreases over time. Next, the blood supply to the brain by measuring the amount of blood going through the carotid arteries should be measured. This would confirm the expectation that if more blood stays in the legs, resulting in less blood returning to the heart, which causes less blood to go to the brain due to which fainting incidences occur. The conclusion of such research could then be compared with the results of investigating the stroke return in the inferior vena cava in the upright position and the amount of blood going to the brain through the carotid arteries when the fluctuating compression and feet movement is performed.

7 Bibliography

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Appendix I: Protocol calf measurements

Inform subject:

- Bring shorts (above the knee)
- Eat and drink normal (don't skip)

Materials:

- Questionnaire subjects
- Blood pressure monitor (omron)
- Flexible measuring tape
- 2 steps, one for against the wall and one at the end of the examination bed (measure the height)
- Stand + clamp to fix the position of the ultrasound probe
- Stopwatch
- A room with a closet
- Examination bed
- Ultrasound (Acuson S3000)
- Left leg of the subject (posterior tibial vein)
- Set up for constant pressure (manometer, hand pump)

Method

1. Preparation
    a. Turn on the Ultrasound, select the correct probe (14L5) and the correct measuring method (PV-Ven). Add the patients' name in the system.
    b. Connect the compression pump to the electricity.

    c. Let the subject change in the shorts and take their shoes off.
    d. Mark with the garments on the measure window on the leg below the knee.
    e. To make sure the ultrasound is in the right position in the stand, let the subject stand in position on the steps. This way the ultrasound can be positioned correctly before measuring.
    f. Let subject fill in the questionnaire. (only necessary if it is the first measurement performed with the subject).
    g. Measure the blood pressure. (also, if it is not the first measurement)
    h. Let the subject sit at the end of the examination bed.
2. Upright over time
    a. Write "Left PTV upright overtime" on the image of the examination on the US screen.
    b. Let the subject stand on the top part of the step against the wall between the examination bed and a closet. Make sure the subject is in a stable position.
    c. Make an image as soon as possible and do so every minute for 7 minutes. The first set of images is t_0 and the last set of images is t_7. In total there will be 8 sets of images.
    d. Let the subject sit back down on the examination bed for 5 minutes, meanwhile prepare for the next measurement.
3. Compression pump fluctuating compression
    a. Apply both the compression garments to the legs of the subject, adjust the screen title on the US to "Left PTV fluctuating compression".
    b. Connect the compression garments to the pump. Make sure that the left leg garment is connected with the first connection and the right leg garment with the second connection. This way the left leg will inflate first.
    c. Make sure that the compression pump can be seen from the Ultrasound measuring position.

   d. Instruct the subject to look at the compression pump and to say when the pump is at 40 mmHg and back at 0 mmHg. This way the US executer can focus on the US images.
   e. Let the subject stand-up again and make an image before starting the compression pump.
   f. Start the compression pump: make two images every time the compression pump is at 40 mmHg for every leg (so one set of images will show 40 mmHg and the other set of images will show 0 mmHg).
   g. Make a video when the compression pump deflates and stop the video when the compression is at 0 mmHg.
   h. Do this 7 times of inflation and deflation of the left garment. This will take 7 minutes in total.
   i. After 7 minutes, let the subject sit down on the examination bed again for 5 min and meanwhile prepare for the next measurement.
4. Compression pump constant compression
   a. Disconnect the compression pomp from the cuffs and connect the hand pump set up. Change the screen title on the US to “Left PTV constant compression”.
   b. Let the subject stand up again, make an image before inflating the cuffs.
   c. Blow up the cuffs to 40 mmHg and make sure the pressure stays constant, look at the manometer instead of the hand pump. Blow up the cuffs to make sure the pressure is 40 mmHg if need to. Make sure the pressure stays between 42 mmHg and 38 mmHg.
   d. When the cuffs are inflated, immediately make and image. Make images every minute for 7 minutes.
5. Lying down
   a. Let the subject lie down in the examination bed on their left side.
   b. Make three images of the cross-sectional area.

Appendix II: Protocol groin measurements

Inform subject:
- Measurement in underwear
- Eat and drink normal (don't skip)

Materials:
- Questionnaire subjects
- Blood pressure monitor (Omron)
- Flexible measuring tape
- Examination bed
- Ultrasound (Acuson S3000)
- Left groin of the subject (common femoral vein)
- Set up constant pressure (manometer, hand pump)
- Cloth/small towel
- Tape

Method
1. Preparation
    a. Turn on the Ultrasound, create a patient, select the correct probe (14L5) and the correct measuring method (PV-Ven).
    b. Connect the compression pump to the electricity and place in the correct spot, somewhere the subject can see the pump.

    c. Let the subject fill in the questionnaire (only necessary if it is the first measurement performed with the subject).
    d. Measure the blood pressure (always do this before the measurement)
    e. Let the subject change into the underwear and let them place the cloth/small towel around the underwear to prevent it from getting dirty due to the gel.
    f. Let the subject stand against the examination bed/wall, see what is more stable. First test with the US if the vein can be found a set the settings for the PW measurement. See if there is a valve visible. Put the tape around the feet to make sure the subject can easily stand in the same position again. Make sure there is a chair close to the upright position place.
    g. Let the subject sit for 5 min
2. No compression, upright position, over time
    a. Meanwhile, type "Left CFV no compression" on the US screen.
    b. Let the subject stand up. Make sure the subject is within the marked position and in a stable position.
    c. Find the CFV and measure the blood velocity using PW, with the Doppler gate should measure 2/3 of the vessel, of the make an image from the velocity graph. Repeat this for 7 min, look at the US time on the screen. The first image is t_0 and the last measurement is t_7, in total this makes a set of 8 images.
    d. After the 7 min, let the subject sit down again for 5 minutes. Meanwhile, prepare for the next measurement. Explain the next measurement and the task of the subject: to see when the compression is 40 mmHg and when 0 mmHg.
3. Fluctuating compression, upright position, over time
    a. Meanwhile type "Left CFV fluctuating compression" on the US screen. Also, prepare the compression pump.

   b. Let the subject put on the cuffs after the 5 min break. Connect the cuffs to the compression pump. Make sure that the left leg is connected to the first connection. This way the left cuff will inflate first.
   c. Find the CFV and measure the blood velocity using PW, make an image from the velocity graph. This will be a baseline measurement.
   d. Start the compression pump, make a video of the velocity graph of the PW measurement. Repeat this for 7 min, look at the US time on the screen. The first video is t_0 and the last measurement is t_7, in total this makes a set of 8 videos. Make sure the whole compression pump cycle is recorded within the video.
   e. After the 7 min, let the subject sit down again for 5 minutes. Meanwhile, prepare for the next measurement. Give instructions to the subject to control the compression of the cuffs with the hand pump and manometer. The pressure should stay between 38 and 42 mmHg.
4. Constant compression, upright position, over time
   a. Meanwhile type “Left CFV constant compression” on the US screen.
   b. Let the subject stand up. Make sure the subject is within the marked position and in a stable position.
   c. Find the CFV and measure the blood velocity using PW, make an image from the velocity graph. This will be the baseline measurement.
   d. Let the subject blow up the cuffs until the compression value is sort of stable.
   e. Make an image of the blood velocity graph of the PW measurement when the cuffs are blown up. Repeat this for 7 min, look at the US time on the screen. The first image is t_0 and the last measurement is t_7, in total this makes a set of 8 images.
   f. After the 7 min, let the subject take off the cuffs.

Appendix III: Matlab script groin measurements

To analyze the data, a script made by Lennart van de Velde is used to obtain the velocity graph from the US blood velocity image. This script looks at the highest pixel value and sets the corresponding velocity value at that time. Performing this for every pixel, a graph with the velocity and the time is created.

Due to the thickness of the zero line of the US image, the zero-velocity value does not have the value 0. This could influence the results as the venous velocities. For this reason, the zero values are corrected to 0.

When the velocity graph is obtained, the MATLAB function `cumtrapz` is used to determine the blood displacement. The function `cumtrapz` is a numerical integral which uses the trapezoidal rule is. This works by approximating the region under the velocity graph as a trapezoid. The area of a trapezoid can be calculated by taking the average value of the vertical sides, in this case these two sides vary in length, and multiply this by the horizontal side. This results in that the area under the velocity graph is divided into several trapezoids with the same time width but differ in height.