To the Graduate Council:

I am Submitting herewith a thesis written by Michel A. Farah entitled "Pneumatic Compression Devices for the Treatment of Lymphedema." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Engineering Science.

John H. Forrester, Major Professor

We have read this thesis
and recommend its acceptance:

Accepted for the council:

Associate Vice Chancellor and
Dean of The Graduate School

PNEUMATIC COMPRESSION DEVICES FOR THE TREATMENT OF LYMPHEDEMA

A Thesis
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Michel Adel Farah
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DEDICATION

A mes parents Linda et Adel.

This thesis is dedicated to my parents, Linda Tabchoury and Adel Farah. You two have supported and believed in me from the beginning. It was your hard work and sacrifices that have given me the opportunity to go to college and to graduate school. You have taught by example, and have been more instrumental to my education than any professor, class, or book. For this, I am forever grateful. To say that this thesis, or any other accomplishment I may have in life, is mine alone would be ridiculous. If I achieve, it is due to the love, support, and faith you have in me. I have never accomplished anything alone, and will never do so, as you will always be a part of who I am and what I do. A special thanks to all of my grandparents, aunts, uncles, and cousins; this document is a mere reflection of your love and support.

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ABSTRACT

Lymphedema, if left untreated, or if treated inadequately, may lead to death if total obstruction of the lymphatic vessels occurs. The management of lymphedema is extremely variable in the medical profession, ranging from aggressive diagnostic procedures, which may aggravate the disease, to precipitous operations. Scattered between these two controversial extreme positions are quite a number of conservative methods, some of which are in conflict with the anatomy and physiology of the lymph vascular system and the pathology of lymphedema.

This investigation first reviews how lymphedema can be treated with success, generally free of any side effects, using different approaches and techniques. As a second part of the research, pneumatic compression therapy is discussed in particular, and the results of some preliminary studies on four different pumps are reported. Desirable pump characteristics for effective treatment of lymphedema are discussed.

The third and final aspect of the present investigation discusses a new approach which has been developed which may help determine if pneumatic compression therapy will be helpful on an individual basis. A mathematical model of the compression process of lymphedematous tissue has been developed, and combined with a proposed physical device which measures an applied force to a small area of skin and the subsequent displacement of the skin in order to predict the volume of fluid displaced in compression

treatment. The goal is to be able to predict the degree of lymphedema reduction in a limb by predicting the volume of the translocated fluid from the limb during the compression therapy, and relating this to the pressures applied to the limb during the compression treatment.

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CHAPTER I

INTRODUCTION

1.1 Magnitude of the Disease

Although lymphedema has afflicted children and adults for centuries, little understanding about diseases of the lymph trunks existed until relatively recently. Not until 1934 was primary lymphedema described as a clinical entity, and only in the past 25 to 30 years have therapists and clinicians begun to focus more vigorously on its treatment. According to the World Health Organization, lymphedema affects 250 million people worldwide [10]. Others estimate that one in every 25 will suffer from some form of lymphedema during their lifetime [32]. In the industrialized world, as cancer rates increase, so will the incidence of lymphedema.

Over the past 15 years, several successful treatment modalities have evolved. When lymphedema is diagnosed promptly and treatment begun early, patients can enjoy productive lives with few complications and little or no restriction of lifestyle. However, when lymphedema remains undiagnosed or untreated for prolonged periods of time, the outcome often is disabling, painful, costly and, at times, even life threatening. It is also serious because of the pervasive lack of medical expertise in diagnosis and treatment of

the condition and the tendency of clinicians to trivialize lymphedema in patients who have been treated for cancer.

1.2 Description of Lymphedema

Lymphedema, or "lymphoedema", is the swelling of soft tissues as a result of the accumulation of protein rich fluid in the extra-cellular spaces and occurs when there is a diminished capacity for the lymphatic system to transport lymphatic fluid from the tissues. This results in the long-term swelling of part or parts of the body. It occurs most frequently in an extremity (an arm or leg), but can be seen in any organ or region such as the head, neck, abdomen, and genitalia [22]. Lymphedema of the legs is often worse than that of the arms. The lymphatic drainage from the leg is more difficult than from the arm, which makes walking difficult.

Lymphedema is serious because of the disability it causes, because of the cosmetic deformities that are difficult to hide, because of the frequent complications that occur, and because of the continuous deterioration of the condition in untreated patients. One frequent complication is cellulitis, an acute inflammation caused by bacterial infection, which spreads diffusely through the subcutaneous and connective tissues. As lymphedema progresses the involved areas swell more and more. Mobility can be severely impaired as the affected area increases in girth, joint movement can be restricted and painful, and skin over the involved areas becomes taut and dry. These effects are not

only physically damaging, but also can cause embarrassment and can lead to depression, causing a general degradation in the patient's quality of life and health. If the lymphedema is severe, especially if more than one limb is involved, the patient is excessively heavy.

1.3 Physiology of Lymphedema

The lymphatic system has two primary immunology functions, activating the inflammatory response and infection control. Equally important, however, is its symbiosis with the hematological vasculature (e.g. the blood vessels and the blood forming tissue) in the regulation of tissue-fluid balance. This delicate balance is achieved through the unidirectional transportation of proteins from the tissue to the blood system. In conjunction with the vessel networks, the lymphatic system maintains the equilibrium between tissue-fluid filtration and reabsorption [12, 24].

If the lymphatic system is damaged or blocked, proteins continue to enter the tissues from the blood capillaries in the normal way, and a build-up occurs in the tissues the lymphatics should be draining. The accumulation of proteins in the tissues causes excess fluid to enter them and the tissues to swell. The swelling decreases the oxygenation of the tissues, interferes with their normal functioning, and causes them to heal more slowly than normal. To some extent proteins are also removed by some of the cells in the tissues (e.g. the macrophages) [18, 44]. These assist the lymphatic system and can partly take

over its role if it is blocked. However, in lymphedema the chronic excess proteins cause these cells to cease to function [10].

The blood and lymph systems complement each other, providing a fine balance between filtration and reabsorption [6]. Fluid leaves the capillaries and enters the tissues under the effects of hydrostatic pressure. Proteins act as the vehicles in the blood transport system, carrying oxygen and nutrients to the cells of the tissues and then removing metabolic waste from them [47]. At the venous end of the capillary, osmotic pressure (exerted by the plasma proteins remaining in the bloodstream) draws the fluid back into the capillaries. However, many protein molecules, too large to be carried in the venous system are returned to the blood system via the lymphatics [22]. Approximately 90 % of the tissue fluid returns via the venous system, and the other 10 % enters the lymphatic capillaries to combine with plasma proteins, cell debris, organic matter, foreign bodies and fat (from the intestine) to form lymph [13]. Thus, lymphatic fluid is high in protein but also carries fat, cell components, and other macromolecules. Normal protein circulation requires an adequately functioning lymphatic vessel system; without it, the interstitial tissue can become congested with lymphatic fluid. Because lymph contains the protein fibrinogen, coagulation and fibrosis can occur with long-standing lymphatic fluid transport deficiency, leading to the firmness and pitting seen in many cases of postoperative edema, particularly after cancer treatments or hip replacement surgery [10,47].

1.4 Statement of the Problem

When diagnosed early, lymphedema usually responds to treatment. Many patients, noticing swelling for the first time, become frustrated when their physician says that the arm is "not so bad" or "it could be worse". The notion that one arm or leg should be twice the size of the other before it deserves attention is not only unfair but potentially dangerous. There appears to be a severe lack of knowledge among clinicians of the methods of treatment of lymphedema and the importance of the treatment to the lives of the patient. Very few medical facilities offer a comprehensive treatment program.

For the reasons stated above, one objective of this study is to collect, organize, and summarize information related to the indications for treatment of lymphedema and to successful treatment programs. Because of the debilitating effects related to lymphedema of the extremities, the study will focus on that particular problem. As part of the study, a preliminary evaluation will be made of several pump types used for compression therapy. From data analysis of the experimental tests of different mechanical compression pumps, speculations will be made on which type of compression pump may be most beneficial for patients with various degrees of lymphedema of the extremity. Also, a mathematical model which may help to describe the problem will be developed and presented, giving future investigators a possible method for studying the problem in a more analytical framework.

1.5 Organization of the Study

Chapter I of this study contains information related to the extent of the clinical problem, background on lymphedema and its affects on human beings, physiological description of lymphedema, statement of the problem, and organization of the study. Chapter II contains a review of the literature relevant to this research, organized into seven sections. The first section deals with the anatomy and pathophysiology of the lymphatic system, and the drainage of the excess proteins in the lymphatics. The second section deals with the chain of events in lymphedema. The third section deals with the formation of lymphedema. The fourth section deals with the types of lymphedema which cause the lymphatics to fail. The fifth section deals with types of secondary lymphedema. The sixth section deals with the problem after the lymphatics are damaged, when lymphedema occurs, and the management to prevent further development of the disease. The seventh section deals with the management of lymphedema. Chapter III describes the methods used in treatment of lymphedema, and consists of sections containing information about each method, its procedure, and the benefits that will contribute to the treatment of a patient. Chapter IV summarizes the experimental testing and results of four pumps used in compression therapy. Chapter V presents a mathematical model of the compression process of lymphedematous tissue to observe the mechanical properties of the tissue, combined with a proposed physical device which measures the applied force to the skin and the subsequent displacement of the skin.

CHAPTER II

REVIEW OF LYMPHEDEMA

2.1 The Lymphatic System

The lymphatic system is made up of capillaries, vessels, and nodes [4]. The fluid dynamics within the capillary bed are maintained by the pressure gradients that are created by the capillary plasma hydrostatic and plasma colloid oncotic pressure and the interstitial fluid hydrostatic pressure [23]. The pressure gradient supports filtration of fluid and proteins from the intravascular circulation to the interstitial space and reabsorption by the lymphatic capillaries, which drain into larger vessels (Figure 1) [23].

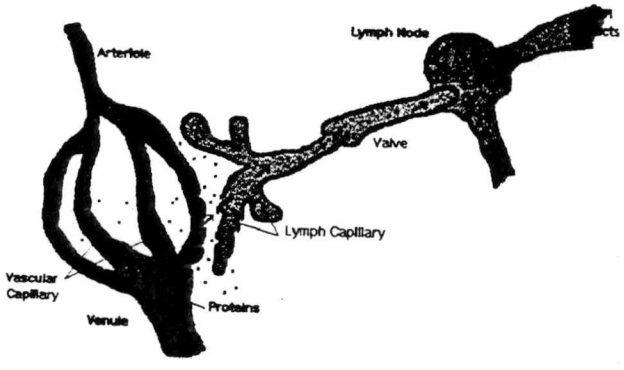


Figure 1. Microscopic View of a Lymphatic Channel. (From Humble, "Lymphedema: Incidence, Pathophysiology, Management, and Nursing Care". Continuing Education Vol.22 No.10; 1995).

2.1.1 Anatomy of the Lymphatic System: The lymph vessels are arranged in superficial and deep systems. The superficial vessels are very small, arranged in complex networks

in the dermis, i.e. the true skin, and have no valves. They connect with a deeper layer of larger diameter vessels that do contain valves and run alongside superficial subcutaneous veins. These in turn are linked to a still deeper layer of vessels that run just superficial to the muscle fascia and further help in the transport of lymph to the veins where the lymph system joins the blood circulation [25]. In the case of the lower extremity, the lymph vessels are arranged in a superficial and deep system with tricuspid valves every 2 to 3 mm (Figures 2, 3) [17, 25]. The superficial system is divided into medial and lateral groups. The medial lymphatics begin on the backbone of the foot and course along the great saphenous vein. These vessels end in the inguinal nodes. The lateral lymphatics begin on the lateral aspect of the foot, cross in front of the leg below the knee, and follow the medial lymphatics into the inguinal nodes [17, 25].

There are few lymphatics within the muscle compartments; lymphedema is luckily not an illness that affects these deeper muscle layers. Lymph is pumped into and along these lymphatic vessels by the movements of adjacent muscles, by the rhythmic smooth muscle contractions of the lymphatic vessel walls, as a result of negative intrathoratic pressure during inspiration, local muscle contractions, and the suction effect from the high-velocity blood flow of the venous system in which the lymphatic system terminates [4,46]. This pumping is aided by large numbers of valves located inside the vessels which allow the lymph to flow in only one direction (i.e. one-way valves in the lymphatics which prevent backflow of lymph). After passing different lymph node

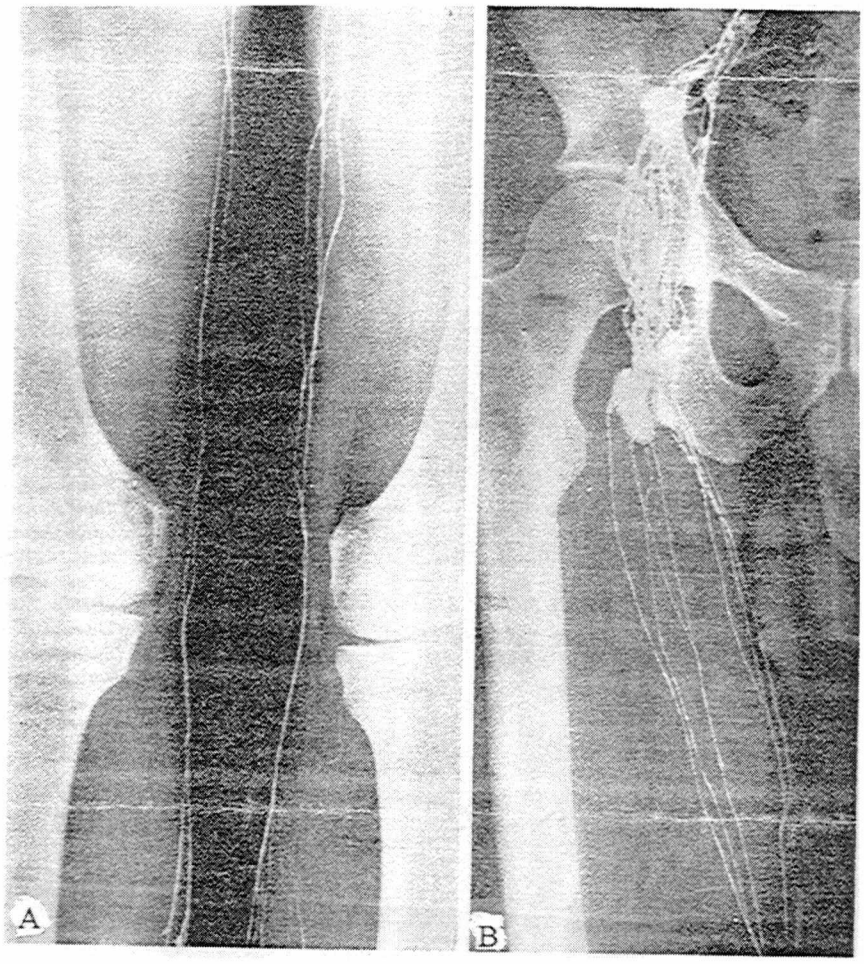


Figure 2. Medial Lymph Trunks of the Lower Limb. (A) medial trunks grouped closely together as they pass the knee joint; (B) vessels in the thigh are filled and spread out over the anteromedial aspect. (From Kinmonth, J.B.: The Lymphatics: Disease, Lymphography and Surgery. Baltimore, The Williams & Wilkins Co., 1972).

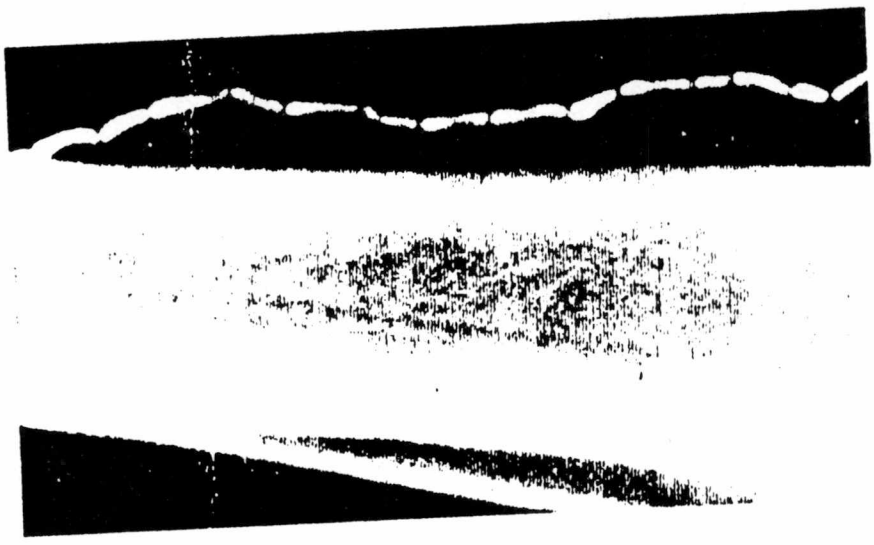


Figure 3. Enlarged Representation of the Limb Showing the Lymphatics. (From Kinmonth, J.B.: The Lymphatics: Disease, Lymphography and Surgery. Baltimore, The Williams & Wilkinks Co., 1972).

groups where foreign matter, e.g. bacteria, are filtered out and necessary immune reactions are activated, the lymph fluid finally empties into the venous part of the blood system, mainly via the thoracic duct [7]. The thoracic duct is the largest lymph vessel of the body. Under normal physiological conditions approximately one to two liters of lymph fluid drain in 24 hours via the thoracic duct into the right and left subclavain veins.

2.1.2 Major Components of Lymph: The lymphatic system comprises a complex network of vessels which provide an accessory one-way drainage route by which fluid can flow from the interstitial spaces, carrying macromolecules, including protein and bacteria, back into the bloodstream [30, 35]. The main task of the lymphatic system consists of the conveyance of substances which cannot be drained by the blood system, the so-called lymphatic loads which contains proteins, water, cells, and fats [15].

Proteins are utilized in the interstitial space for cell nutrition and immune defense. The quantity of plasma protein escaping physiologically from the blood capillaries into the interstitial space, approximately 50 % every 24 hours, has to be drained by the lymphatic system. Also pathological cases of increased protein in the interstitial space due to an increased permeability of the blood capillaries caused by inflammations of foreign protein contributes to the lymphatic loads. A fraction of the water, approximately 10 to 20%, escaping the capillary system via ultrafiltration is not reabsorbed by the blood capillaries. This water quantity drained by the lymphatic system adds up to approximately 1-2 liters a day, emptying into the venous system through the thoracic duct [15]. Cells and cellular debris that become free somehow in the organism are drained by the lymphatic system, such as cell debris resulting from neoformation or trauma. Mobile degenerated cells (i.e. cancer cells) unfortunately are also collected by the lymphatics, which then can be spread resulting in metastasis in other parts of the body [15,30]. Long-chained fatty acids are absorbed only in the lymphatic system of the intestines, and thus contribute to the lymphatic loads.

2.1.3 Pathophysiology of Lymphedema: Insufficiency or blockage of the lymphatic vessels can result in an increase in the hydrostatic pressure within the regional lymph vessel which leads to a decrease in the vessel wall integrity. This pressure increase results in a backward flow of lymph in some vessels, causing proteins and fluid to leak out into the interstitial space. Protein accumulation in the tissues result in increases in the

interstitial colloid pressure, leading to more fluid leakage [4]. The accumulated fluid can become a superb medium supporting bacteria growth, resulting in an increased risk for cellulitis. Infections normally result in increased blood flow, which causes increased hydrostatic pressure and capillary permeability, both of which will worsen the lymphedema in the affected extremity [4,23].

2.2 The Chain of Events in Lymphedema

The basic alteration in lymphedema is a low output failure of the lymph system (Figure 4). The disequilibrium between a normal lymphatic protein load (arising as a consequence of the continuous passage of plasma proteins across the wall of the blood capillaries) and a decreased lymph vascular transport capacity in combination with an inadequate tissue proteolysis results in a stagnation of plasma proteins in the interstitial space [15]. In the first stage lymphedema is pitting (e.g. the tissue is still soft and can be indented) and the swelling can be decreased, to some extent, by the elevation of the limb. Later, plasma protein stagnation triggers chronic inflammation. Fibrosis, abnormal hardening of a tissue, causes edema to lose its pitting character. In the second stage, elevation of the limb does not influence the swelling as before. Overproduction of connective tissue and hardening of the skin is dramatically hastened by recurrent attacks of cellulitis which lead into the third stage, lymphostatic elephantiasis (e.g. the swelling of a limb as a result of lymphatic obstruction).

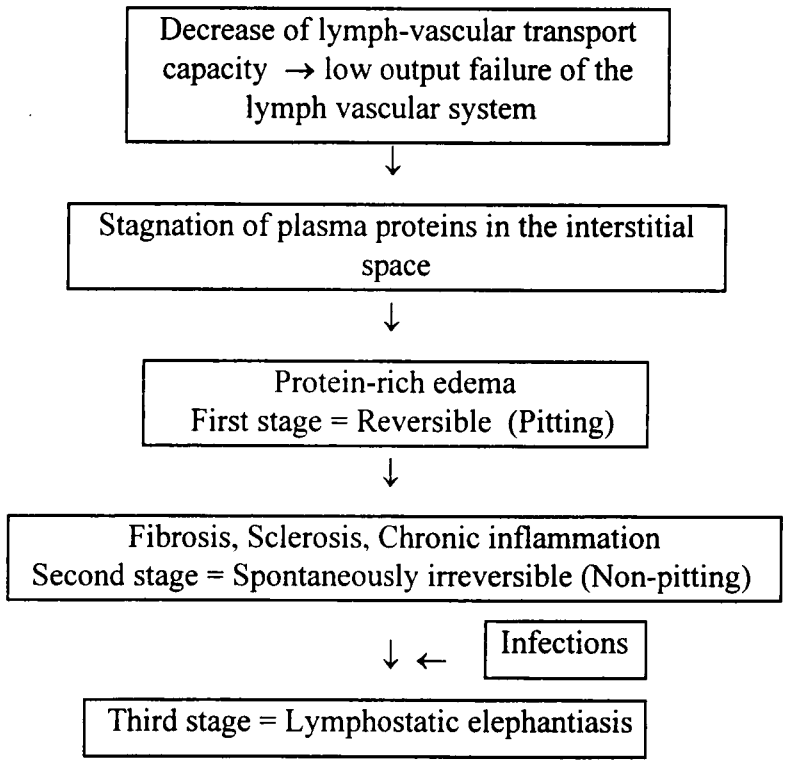


Figure 4. Chain of Events in Lymphedema

2.3 Formation of Lymphedema

The lymphatics help remove the excess fluid and protein which enter the tissues from damaged blood vessels in any inflammation (e.g. after injury). If they cannot remove it all, the part swells which leads to edema. However, this swelling is usually only temporary, because the tissues heal and the blood vessels no longer leak excessively [18, 22, 44].

2.3.1 Components of Lymphedema: There are four main components to lymphedema: excess protein in the tissues, edema, chronic inflammation, and excess fibrosis [30]. In

the early stages of lymphedema, tissue pitting will occur. As the protein-rich edema becomes invaded by fibroblasts, thickening and fibrosis of the skin and subcutaneous tissue results [17, 19]. This explains the non-pitting "brawny" nature of lymphedema, and the inability to pinch a fold of skin at the base of the toes or fingers. As the swelling progresses, limb shape becomes distorted and exaggerated skin folds develop [1, 17, 30]. The lymphatic system will become dilated and, under pressure, organize to form "blisters", which sometimes leak lymph and can be a portal of entry for infection [35].

2.3.2 Inflammation of Lymphedema: The excess protein in the tissues acts as a stimulus for chronic inflammation. One of the results of this is the formation of much excess fibrous tissue. The chronic inflammation causes more blood capillaries to form and to be dilated, making the limb feel hot. This heat, combined with the stagnant protein, provides a perfect site for bacterial growth (*Secondary Acute Inflammation*, S.A.I). The patient may be very ill, with constant infections, and need hospitalization [10, 44]. Fungal infections are also very frequent, and are often difficult to clear up. These infections, themselves, place greater loads on the lymphatics, and so aggravate the lymphedema. Any infection or other inflammation (e.g. after injury, sunburn) makes the lymphedema worse [10, 18, 44].

In an acute injury (e.g. a sprained ankle) the lymphatics are essentially normal. Although there is initial swelling, this is gradually reduced over a period of days to weeks. The

overload is only temporary although, depending on the severity of the injury, some fibrosis will occur. This may remain for months or even permanently.

When lymphedema first occurs it will pit if pressed with a thumb. It gradually becomes larger and harder and no longer pits. If lymphedema lasts for some years, the swelling gets worse and skin changes occur. There is loss of hair and alterations to the nails. The skin may get very thick, with huge folds and warts. Any lymphedema left untreated will gradually progress along this route. The subcutaneous tissues can become hard and fibrotic which impairs the flow of blood and oxygen to the area. This unhealthy state often leads to recurrent infections because the high protein lymph fluid is a good growth media for bacteria and fungi. Each subsequent infection can further damage the already impaired lymphatic system, and can be life threatening [18, 22, 44].

2.4 Causes of Lymphedema

There are two types of lymphedema, primary and secondary, which may cause the lymphatic system to fail. Primary lymphedema is caused by congenital absence or abnormalities in lymphatic tissue, and is relatively rare; there may be no pain at all, except during bouts of infection. Secondary lymphedema is generally caused by obstruction or interruption of the lymphatic system [1, 10, 22, 44].

2.4.1 Primary Lymphedema : Primary lymphedema occurs without any precipitating cause, and is due to inadequate or non-functional lymphatic vessels. Primary lymphedema affects women more often than men, and usually affects the lower extremities. Usually there are simply too few lymphatics; sometimes there are many lymphatics but they are very dilated and do not pump properly. Sometimes it is a combination of both. This lymphedema can appear before birth (*connatal lymphedema*), during puberty, which is most common for primary lymphedema (*lymphedema praecox*), or later in life, e.g. from 30-40 years old or older (*lymphedema tarda*). Occasionally there is a narrowing of one of the major lymph trunks, e.g. at the outlet of the thoracic duct. Primary lymphedema can also start following the onset of a secondary lymphedema in another part of the body, e.g. after surgery secondary lymphedema may initiate a primary lymphedema in the leg on the same side.

2.4.2 Secondary Lymphedema : Secondary lymphedema, affecting men and women equally, is precipitated by an event causing blockage or interruption of the lymphatic vessels which usually occurs at a proximal limb segment due to infection, malignancy, or scar tissue. It can cause great pain because the tissues are being torn apart. It is most often seen following:

(1) Surgery, especially for carcinoma with the removal of lymph nodes or a lot of tissue, which results in cutting many lymphatics. About 50% of patients who have had axillary node surgery will develop lymphedema [45].

(2) Radiotherapy, which kills tumor cells, destroys the lymph nodes, and blocks them with fibrous tissue proliferation.

(3) Accidental trauma tearing lymphatic vessels which may not rejoin when the blood vessels do. Any excess fibrous tissue caused by the damage can later shrink and constrict the lymphatic vessels.

(4) Parasites (e.g. filarial worms) which block the lymphatic drainage. The swelling may occur with parasite growth which damages the lymphatics and destroys their valves. It usually occurs only some years after the parasites die and break down, causing inflammation which blocks the lymphatics.

(5) Paralysis of a limb which prevents lymphatic pumping, causing wheel-chair edema.

2.5 Types of Secondary Lymphedema

There are several types of secondary lymphedema, each of which may be characterized by time of onset after medical treatment and associated clinical findings. The first type is acute, transient, and mild lymphedema that occurs within a few days of surgery as a result of the cutting of lymphatic channels. It usually responds within a week of onset after limb elevation and muscle pumping (e.g. making a fist and releasing it). The second type is acute and painful and occurs 4-6 weeks postoperatively as a result of acute lymphangitis or phlebitis (e.g. inflammation of one or more lymphatic vessels or veins). The third type of lymphedema is an acute erysipeloid often occurring after an insect bite or minor injury; it is an acute specific infectious disease in which there is a spreading of

the infection to other parts of the limb or the region. The fourth and most common type of lymphedema is usually insidious and painless and is not associated with erythema, which causes redness or inflammation of the skin and is the result of dilatation and congestion of superficial capillaries. This form is most frequently apparent 18-24 months after surgery [10].

Acute lymphedema is a temporary condition that lasts less than 6 months and is associated with pitting edema to the touch and no brawny skin changes. The following factors place the patient at risk for acute lymphedema: surgical drains with extravasation of protein into the surgical site; inflammation leading to increased capillary permeability; immobility of the limb that results in decreased external compression by the muscles; temporary absence of collateral lymphatics; and reversal of equilibrium at the capillary bed that results in accumulation of third-space fluid (i.e. the accumulation of extra cellular fluid outside the lymphatics and the blood capillaries) [4, 46].

Chronic lymphedema is the most difficult of all types of edema to reverse. A vicious cycle is started, wherein the deficient lymphatic system of the limb is incapable of compensating for the increased demand for drainage of fluid. This condition may occur subsequent to any one of the following: tumor recurrence or progression in the nodal area, infection and/or injury of lymphatic vessels, immobility, radiation therapy, surgery, contributing medical conditions leading to hypoalbuminemia (e.g. diabetes, kidney

malfunction, hypertension, congestive heart failure, liver disease), or inadequate postoperative instruction regarding prevention of lymphedema and venous obstruction due to thrombosis (blood clotting) [4, 10, 46].

2.6 Occurrence of Lymphedema

Once lymphatics are damaged, lymphedema may occur at any time. The onset is gradual in some patients and sudden in others. Sometimes it starts at once and lasts for life. Edema may occur for a few weeks, then disperse, and may or may not return; sometimes it appears years after the initial event. Bacterial entry is gained to the tissues through small breaks in the skin, e.g. fungal infections between the swollen digits due to a bee-sting, sunburn, or carrying heavy weights. Once the mechanical protection of the skin has been broken, the presence of bacteria triggers the inflammatory process as a second line of defense. Toxins released from the damaged tissue cells is evidenced by the redness and increased temperature of the inflamed area. Increased permeability of the blood vessels allows excess fluid and protein to flow into the tissues and cause edema. Apart from the acute phase which occurs briefly after blockage and then resolves, once lymphedema starts it may progress to a chronic state. This aggravation is usually slow in primary lymphedemas and rapid in secondary ones. It is usually a steady increase unless some inflammation occurs (e.g. infection, injury, burn), when it gets worse very quickly.

Factors that contribute to the development of lymphedema are irradiation of a dissected nodal basin, postoperative wound complications and subsequent cellulitis of the limb, and obesity. Patients at risk for lymphedema are those exposed to the following:

(1) Radiation therapy to the axilla following axillary node dissection. A 52% incidence of lymphedema among patients undergoing radiation after radical mastectomy has been reported, compared to a 25% incidence in groups treated without radiation [46].

(2) Breast cancer if they have received radiation therapy or had node dissection.

(3) Malignant melanoma (e.g. tumor arising from the pigment-producing cells of the deeper layers in the skin) of the upper or lower extremities if the patient has undergone node dissection and/or radiation therapy.

(4) Prostate cancer treated by whole-pelvic irradiation, surgery, or radiotherapy.

(5) Testicular cancer when the disease is advanced or when radiotherapy or surgery have been used as a treatment.

(6) Gynecologic cancers when the disease is advanced or when radical surgery with node dissection or radiation therapy has been used.

CHAPTER III

TREATMENT PROGRAMS

3.1 Introduction

Lymphedema is often a long term condition, resulting from a basic lack of adequate lymphatic function. It cannot be completely "cured" with current treatments but it can most certainly be greatly improved so that an affected limb often becomes essentially "normal", at least in size. Nevertheless, one must always remember the limb still has as an underlying deficiency, is at risk, and must be protected from injuries.

Determining the appropriate treatment for lymphedema depends greatly on the size of the limb and the nature or firmness of the edema. Currently the common belief is that multimodality treatment, rather than single-line therapy, most effectively manages lymphedema [10]. Successful lymphedema management takes an enormous amount of time and commitment from the patient and the treating clinician.

3.2 Historical Aspect of Lymphedema Treatment

In the second half of the 19th century a consensus existed concerning the treatment of lymphedema. The surgeons Esmarch and Kulenkampff stressed in 1855 that no surgery should be initiated before conservative therapy, consisting of hygienic measures, and

compression and elevation (which they found very effective, if the compliance of the patient was good) had been tried [15].

In 1892 Winiwater [15] gave the best description of the conservative treatment of lymphedema as it had crystallized from the experience of previous generations and his own experience. Winiwater was a surgeon but advocated, as the first choice of treatment, a conservative approach. The aim of treatment was, according to Winiwater, twofold:

> " The first aim is to increase the drainage of edema fluid; if this turns out well, overproduction of connective tissue will be halted. The second aim is to induce resorption of the exuberant connective tissue".

Winiwater's conservative treatment consisted of bed-rest, elevation of the swollen limb, compressive bandages, massage and remedial exercises. According to Winiwater, massage should be started on the root of the swollen extremity, the extremity itself was treated only later on. This complex physiotherapy of lymphedema, as it was practiced in the 19th century, has been forgotten. The view expressed in 1950 by Takats and Evoy [44] is typical:

> " Inspection of the fibrotic subcutaneous fat, the lacunar spaces filled with tissue fluid which undulates to and fro with gravity, palpatation of the thickened deep fascia which barricades the lymph-soaked tissue from the muscle spaces, and the histological study of soft tissue and lymph glands make it clear, that one is dealing with an irreversible process, and that the object of treatment can only be either an arrest of the disease so that further deterioration is prevented or the removal of as much of this tissue as possible without sacrificing the function of the limb."

In 1936 Vodder treated a patient who suffered lymphedema of both lower extremities. He started massage on one leg with centripetal effleurage, a kind of massage technique of

using long, whole-hand strokes in one direction only, with the aim of assisting the venous return of blood which then increases arterial blood supply. On the other leg he started massage at the root of the extremity. Decongestion occurred much faster on the side where massage was started centrally [15].

3.3 Treatment Options

Treatment of lymphedema aims to restore and maintain normal limb volume and shape. Determining the appropriate treatment for lymphedema depends greatly on the limb size, nature, and firmness of the edema. The most successful lymphedema treatment programs are discussed below.

3.3.1 Elevation: Often the suggestion made to a patient who develops lymphedema is to elevate the extremity, making use of gravity to assist proximal lymphatic flow. Elevation decreases the hydrostatic pressure gradient from the blood vascular system to the tissues. This reduces the outflow of proteins and fluids from the vascular system. Also in the elevated limb the hydrostatic pressure gradient in the lymphatics increases along the lymph trunk flow direction; this effect of elevation may also encourage an increased lymph flow. One of the methods of elevation is with the patient lying supine in bed, both arms are supported and fixed at a comfortable elevation of 80° and at an abduction of 25° as shown in Figure 5 [43]. Although elevation may be somewhat effective with mild edema, it most often provides only a temporary solution. For larger extremities, elevation

has even less impact. In fact, elevation alone has not been shown to be an effective treatment of lymphedema [43].

Performing exercises (e.g. ball squeezing) with the arm overhead has often been prescribed. Again, this leads to little, if any, sustained reduction in overall limb size.

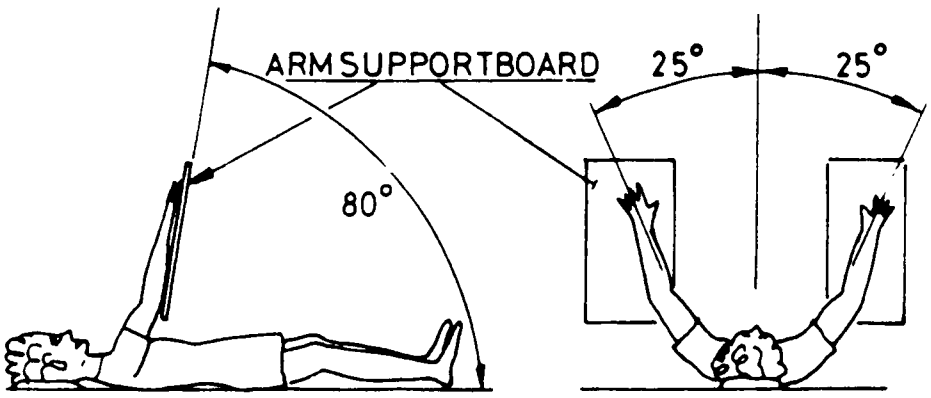


Figure 5. Position of Elevation. (From Swedborg : "Lymphoedema Post-Mastectomy" Scand. J. Rehab. Med. 25: 79-82; 1993).

Finally, the prolonged arm elevation must also be questioned. Perhaps the most beneficial effect of periods of elevation is to provide the patient with comfort and a decreased feeling of "heaviness" of the limb.

3.3.2 Exercise: Exercise has generally been accepted in the treatment of lymphedema. However, the specific type of exercise recommended can vary greatly. There does not appear to be any scientific literature comparing different exercise protocols of varying intensity and duration. Lymphatic fluid moves as the body moves; muscle contractions serve as a pumping force, which can facilitate lymphatic flow.

Many patients report sudden onset of lymphedema with over-use or over-stress of the limb. These stresses can vary in intensity and activities that are routine before any medical treatment or surgery prior to the existence of lymphedema often precipitate the condition [47]. Reconditioning the extremities through a controlled exercise program may be one way to help prevent the lymphedema that can occur with sudden, unexpected stress. Prescribed activities can range from simple flexibility exercises to gentle strengthening exercises using free weights. The patient should be encouraged to use his/her extremity as a barometer to tolerate the activities. If exercises are performed without an increase in the edema for several sessions, the exercise can progress. If at any time the extremity responds adversely (i.e. increased edema or pain), the intensity of the exercise should be decreased [15].

An aerobic program may also be a beneficial addition to the lymphedema treatment program, especially for the woman who has undergone breast surgery. It improves upper-body strength, flexibility, and posture. Swimming is helpful for both upper and lower extremity lymphedema [47]. A drop in intrathoracic pressure occurs with abdominal breathing and creates a suction force that can facilitate the lymphatic flow by extracting the fluids [47]. Excessive force, weight lifting or strain should be avoided by those with lymphedema and in the prevention of lymphedema because it may trigger or increase the severity of the condition. Care should be taken to avoid trauma such as fracture or sprain.

Trauma can precipitate the first episode as well as seriously aggravate existing lymphedema [15].

3.3.3 Compression Garments: Edema causes the skin to stretch, as the tissues hold more fluid. The idea of a compression sleeve or bandage is to provides a boundary to which the limb must conform. Although often unpopular with patients, they have been proven to be extremely important in providing external support to the skin and can be an effective way to reduce and control edema. The gradient compression forces inherent in most garments and created by bandaging push the lymphatic fluid into the lymph vessels from the interstitial space, which assists in the transport of excess fluid back to the circulation and helps move the fluid proximally. They make it more difficult, on the other hand, for nutrient solution to pass from circulation into the tissue. Furthermore, wearing a compression garment gives resistance to the contracting muscles beneath, which increases the interstitial pressure and thus the lymphatic flow. Therefore, wearing an appropriate compression garment is important during the treatment phase to maximize reduction and prevent the return of fluid between treatments. For continuous progress and control, the garment should be worn as long as the edema persists [15]. A compression sleeve or bandage should be worn during times of increased activity, as during an exercise program. To be maximally effective the garment should be fitted properly and replaced when worn out.

3.3.4 Manual Lymphatic Drainage: Manual lymphatic drainage is a special massage technique that uses the superficial lymphatic vessels of the skin to transport lymphatic fluid from an area of congestion to an area of functioning lymphatics. The massage is performed in the direction of normal lymphatic flow by using light and sequential strokes. This massage technique is very popular in Europe [15].

The addition of manual lymphatic drainage to a treatment program is considered essential if long-term results are desired [10,15]. The technique increases the lymphatic fluid transport capacity leading to increased lymphatic drainage from the areas of damage. Therefore, repeated manual lymphatic drainage can actually lead to anatomic changes that improve lymphatic flow, reduce the size of the extremity, and when combined with a properly fitting compression garment, help maintain the limb size.

3.3.5 Surgery: Surgical treatment for lymphedema patients is recommended only when total obstruction of the lymphatic vessels exists. Surgical therapy of lymphedema falls into two main categories: those designed to encourage lymph drainage from the lymphedematous limb, and those designed to remove the abnormal tissue.

Surgery is used to reconstruct or reconnect the lymph vessels, because the lymphedema will increase in the presence of total obstruction. During surgery the physician connects the dilated lymph vessels with the veins so that the fluid can come out of the lymphatic

vessels and pass to the veins so drainage will occur. If the venous systems are obstructed, as well as the lymphatic vessels, then the use of a small piece of the lymph vessel of a normal leg or hand will be necessary. The results are generally unpredictable; many of the procedures are long and require many hours of general anesthesia and the scarring that results interferes with later therapy. Regardless of the results, no known surgical techniques will cure lymphedema [37].

3.3.6 Diuretics: Diuretics remove water, yet lymphedema is caused by excess protein in the tissues, which retains the water. If the protein is removed, the water leaves via the blood system, hence the lymphedema is reduced (as is done by the benzo-pyrones). Diuretics concentrate protein in the tissues and increase its deleterious effects [9,11].

Diuretics are not recommended for lymphedema, except in emergencies, because their effect is transitory and over time they lead to increased colloid osmotic tissue pressure, increased fibrosis and increased swelling. However, if they have been taken over a period and then suddenly stopped, the body (i.e. the kidneys) does not cope, and takes a month to adjust. During this time there is an immediate worsening of the lymphedema [9,11].

3.3.7 Complex Physical Therapy: Complex Physical Therapy (CPT), or sometimes referred to as Complete Decongestive Physiotherapy (CDP), consists of a number of physical therapeutic approaches combined to treat lymphedema. A course of this

treatment technique normally lasts from 2 to 6 weeks, depending on the severity of the condition and the number of limbs involved. This treatment in conjunction with the benzo-pyrones is very popular in Australia and New Zealand [10]. Complex Physical Therapy consists of four main parts: (1) skin care to improve the skin condition and to prevent any infection which would add to the lymphatic load, (2) a special form of daily massage to increase lymph flow, which removes excess fluid and protein and opens collateral lymphatics so that unaffected regions can drain the affected one in the future, (3) compression bandages during the course of treatment to keep the reduced limb from rapidly resuming its former size, and (4) special exercises to supplement the massage.

Reduction will occur after treatment if the drainage from the blocked area to the normal adjacent areas has been improved by enlarging the size and/or number of the lymphatics which join one drainage area to the next. To maintain the reduction achieved after CPT, the patient must be willing to wear a good compression sleeve or stocking at all times, look after their limb and treat any infection promptly, and persevere with their exercises. With these precautions another course of the therapy, which can commence six months to a year after the first, may result in a further removal of the interstitial fluid [10].

3.3.8 Benzo-pyrones: In the early 1980's, Casley-Smith and coworkers at the University of Adelaide, Australia found that an excess of plasma proteins in rat subcutaneous tissues, without lymphatic obstruction, was sufficient to produce tissue changes characteristic of

chronic lymphedema within a few months [8, 10]. These changes included the presence of many macrophages and fibroblasts, and an increase in the numbers of blood capillaries and initial lymphatics [8]. Recently, much attention has been given to the pharmacological treatment of lymphedema through the use of benzo-pyrones. These drugs are the only treatment presently available for those who cannot tolerate or wear compression garments. Without compression garments, this kind of treatment is very slow but steady reduction is a virtue since a rapid one would leave huge cavities which would readily refill. This slowness allows the body to gradually remodel, so that the altered tissue takes the place of the garments [9].

Once excess tissue protein is absorbed, edema subsides and the fibrosis slowly resolves by remodeling. The benzo-pyrones reduce all high-protein edemas by causing the macrophages (scavenger cells in the tissues) to increase both their numbers and their normal proteolysis of the excess protein [8, 9, 11]. Thus increased colloid osmotic pressure is reduced via this alternative pathway for the removal of the excess protein. By decreasing the excess protein, fluid retention is reduced, the fibrous tissue recedes, the medium for bacterial growth also diminishes, and tissue edema decreases. Although the drugs are slow-acting, they have been shown to decrease lymphedema and the chronic inflammation that accompanies it over periods of at least 6 months [11].

The benzo-pyrones or Coumarin are the only known drugs which reduce the excess protein in the tissues with high protein edema including lymphedema. Benzo-pyrones as a group have very low toxicities, especially Coumarin (or 5,6 benzo-pyrone or 56 BaP). Only a few patients (2-5%) have side-effects from the benzo-pyrones, and these are only mild gastro-intestinal ones which disappear after about a month if the patient continues taking the drug regularly. No serious side-effects have ever been reported. Benzo-pyrones may be taken orally, or applied topically. They are useful for high-protein edema, and improve the results of physical therapy for lymphedema [10]. All trials show that oral benzo-pyrones alone usually work slowly in lymphedema. A few patients do get rapid benefits, especially those who have primary lymphedema. Topical benzo-pyrones work much more rapidly than the oral form, but only to a very small depth into the skin of 1-2 cm. It should be applied once to twice a day. The powder form is an excellent lubricant during the limb massage of the CPT treatment technique discussed in Section 3.3.7, and during the application of compression garments [8, 11].

Many clinical trials in Australia on a variety of high-protein edemas have been done on lymphedema from many causes [10]. Benzo-pyrones reduced lymphedema much more slowly than adequate physical therapy, but they did reduce them. In the trials done by Casley-Smith [11] on 31 patients with lymphedema of the arm and 21 patients with lymphedema of the leg, the patients received 400mg of Coumarin every day. Excess tissue volume was reduced by one-half over a six month period. The benzo-pyrones or

Coumarin convert a slowly worsening condition into a slowly improving one. In addition, the drugs considerably reduce the number of attacks of secondary acute infection, and considerably improve the patient's comfort and mobility. It is possible that when benzo-pyrones reduce limb volume down to a nearly normal level, the patients may well have retained these reductions after stopping drug treatment. While this drug is not yet approved for lymphedema treatment by the U.S. Food and Drug Administration (FDA), benzo-pyrones have been used for over 35 years in the treatment of lymphedema in Australia and in other countries all around the world [11]. If approved by the FDA, benzo-pyrones could be one more tool in the management of lymphedema.

3.3.9 Pneumatic Compression Therapy: Lymphedema is an accumulation of surplus fluid in the interstitial space, often with high protein content, causing a pathological increase in the interstitial pressure. Neither the skin nor the surrounding tissue offers sufficient resistance against this pressure. The principle of physics which states that fluids tend to flow from areas of higher pressure to areas of lower pressure also applies to the movement of fluids into and out of the tissues. If the blood or lymph in a major (transport) vein in the distal limb is to rise to the proximal limb, it must be subjected to a driving pressure greater than the hydrostatic pressure acting on it.

One of the most important treatments of lymphedema in the United States is the use of external mechanical compression via a pneumatic single or multiple-cell sleeve garment attached to a mechanical pressurizing pump [45]. Intermittent sequential pneumatic

compression is generally required when lymphedema is moderate or greater in severity, or long-standing. Pneumatic compression devices vary in size, complexity, and cost. A sleeve contains a series of air bladders attached to a pump, which first inflates the distal portion of the sleeve and then sequentially inflates the more proximal bladders. The purpose is to move lymph out of the tissues as the pressure wave progresses proximally. Pneumatic pumps provide compression at varying pressures depending on the severity of edema and the underlying pathology. The deflation phase of the compression cycle allows lymphatic and venous vessels to fill with fluid. Increased tissue pressure during the inflation phase compresses these vessels causing the fluids to flow in the direction of the dilated valves. External counterpressure during the inflation phase enhances muscle activity to accelerate interstitial fluid movement in the lymphatic system. In addition to compression, the pump simulates the activity of the muscle's pumping action.

Pneumatic compression pumps have been used for more than 20 years. The pneumatic massage device includes the sleeve that envelops the limb and the air control unit that supplies compressed air into the sleeve. The sleeve, as shown in Figure 6, consists of a series of pneumatic cuffs. When the first cuff is inflated, a part of the limb is pressed by a high pressure in order to make the lymph fluid move proximally in the limb. The rest of the cuffs are inflated sequentially. The deflation techniques differ from one pump to another, but in most of the pneumatic compression pumps the deflation does not start until at least the third cuff is inflated in order to prevent the lymph and venous blood from

flowing backward. This sequential inflation/deflation procedure occurs from the distal cuff to the proximal one, so as to displace the stagnant lymph toward the systemic circulation. The device thereby exerts a continuous massage action over the limb resulting in volume reduction of the limb girth.

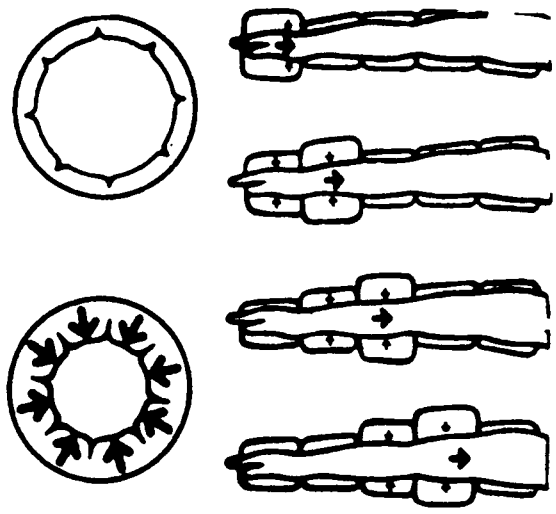


Figure 6. Principle of pneumatic Massage.

A retrospective study was completed in France concerning compressive therapy [31]. This study enrolled 7144 patients treated by compression devices alone or associated with manual lymphatic drainage. Cellulitis was seen in 10% of the patients, but in two thirds of these cases patients had had cellulitis previous to the therapy. Moreover, in three fourths of the 10% cases the compression treatment was used again without infection. Thus, compression therapy may have triggered an episode of cellulitis, but this occurs in very few cases (in fact, far less than 10% if we consider the number of treatments instead of the number of patients).

Twenty five patients (seven patients for upper-extremity and 18 for lower-extremity problems) underwent 24 hours of treatment at the National Institutes of Health Clinical Study Unit at the New England Medical Center in Boston, using a Lympha-Press pneumatic compression pump for lymphedema [50]. The pump utilized a short duration and high-pressure cycle, that provided a sequential milking pattern to the limb through multiple compartments. All extremities showed a decrease in circumference measurements with the maximal reduction occurring at the wrist (45%) for the upper extremities and at the mid-calf (47%) for the lower extremities. Lower-extremity leg volume was reduced by 45% [33]. The sequential compression device apparently reduced lymphedematous limbs rapidly and safely [34, 50].

The usefulness of compression devices for lymphedema is well known, and repeated treatments produce the best long-term results. But this method has certain disadvantages, among them the need for repetitive treatment, dependence on a heavy, cumbersome, and in general immobile machine, and considerable expense to acquire the apparatus. Another disadvantage is the difficulty of use or the discomfort produced by the multi-compartment sleeve in some patients. Still another disadvantage is that without the proper support, the skin will stretch to accommodate fluid. Therefore after compression pumping therapy the patient should wear a good compression sleeve or stocking, which may need changing every 6 to 8 weeks to adapt to the decreasing circumferences.

However, in management of lymphedema, sequential intermittent pneumatic compression has proven to be the best method of nonoperative treatment [50]. Compression therapy and garments provide a safe and effective treatment for lymphedema. This approach is noninvasive, has few complications, is usually well tolerated, and is widely available. Although inpatient treatment has been advocated [46], recent experience suggests that even the most aggressive therapy techniques can be performed on an outpatient basis.

CHAPTER IV

EXPERIMENTAL ANALYSIS

4.1 Introduction

As a part of this study, an evaluation and comparison of four commercially available pneumatic compression pumps (Wright Linear Pump model WLP 2, Jobst Extremity Pump System model 7500, Flow-Plus by Huntleigh model AC 330, and Bio-Compression System Pump model 2000) were included as a preliminary investigation of the relative effectiveness of treatment of lymphedematous legs using compression therapy. The four pumps were loaned to our laboratory at the University of Tennessee from CBF Inc., Knoxville, Tennessee, and were the only ones available for this study. For the Bio-Compression Pump, only an arm sleeve was available, but leg sleeves were available for the other three pumps. Two different techniques were investigated: the technique of using a single-cell sleeve and that with multi-cell compartments where the number of cells vary from one pneumatic pump to another.

4.2 Test Procedures

Experiments were conducted to determine if the pumps produced pressures in the sleeve consistent with those preset on the pump. To compare between the pump and sleeve pressures, pressures were read by the gage meter at the pump, and at the entries of each

cell in the sleeve using of pressure transducers (Grass Model PT300) and a four channel which physiological recorder (Grass Model 7400), as illustrated in Figure 7. The pressure transducers were connected to the pressure hoses at the entrance to each cell by a three-way stopcock. The transducers sensed the pressure signals of the incoming pressures during pressurization and thus the pressures inside the cells after steady-state was reached.

Before taking any measurements all the pressure transducers as well as the recorder were calibrated with a manometer using a 2.95 specific gravity liquid. The transducers were calibrated up to 125 mm of mercury.

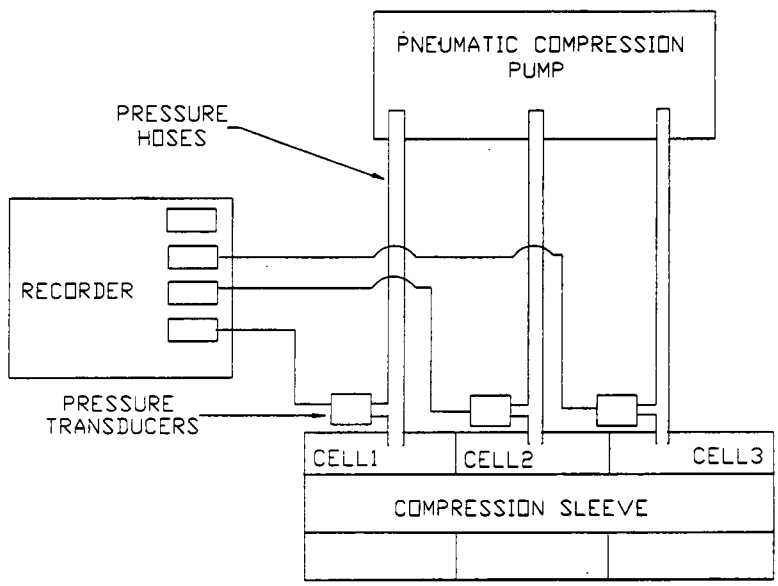


Figure 7. Experimental Setup for the Pressure Measurements.

4.3 Leg and Arm Models

In order to simulate the treatment of lymphedema of the leg using pneumatic compression pumps, a model leg was constructed close to the dimensions of a human leg affected with

lymphedema. As noted in Table 1, three legs were fabricated and used inside the pressured sleeves while collecting the test data for each pump. The lymphedema model leg was constructed of a prosthetic leg built up with Styrofoam to actual lymphedema leg dimensions according to a size chart provided by CBF. Inc. of Knoxville. The intermediate model leg was constructed similarly, using less styrofoam and the normal model leg was simply a prosthetic leg with no additional material added to increase its size. The model of the arm used with the arm sleeve for the Bio-Compression Pump was constructed of wood wrapped with foam such that the sleeve fit over the model.

Table 1. Leg Dimensions Used for the Testing

	THIGH (in) 30in from ground	CALF (in) 14in from ground	ANKLE (in)	FOOT (in)
Lymphedema Leg Circumferences by CBF	23-26	16-18	9-12	7-11
Lymphedema Model Leg Circumferences	24	18	12	10
Intermediate Model Leg Circumferences	21	16	11	9
Normal Model Leg Circumferences	19	14	9	8

The model legs were tested with the three pumps for which leg sleeves were provided to determine how critical the fit of the compression sleeve over the leg was while the sleeve was pressurized to the preset pressure. It was thought that a loose fit might adversely affect the procedure of the compression treatment, but on the contrary that was not the case. Figure 8 shows that for the Flow-Plus Pump the pressures obtained in the sleeve were nearly the same for all three models after only three cycles. This was typical for the other two pumps tested as shown in Table 2.

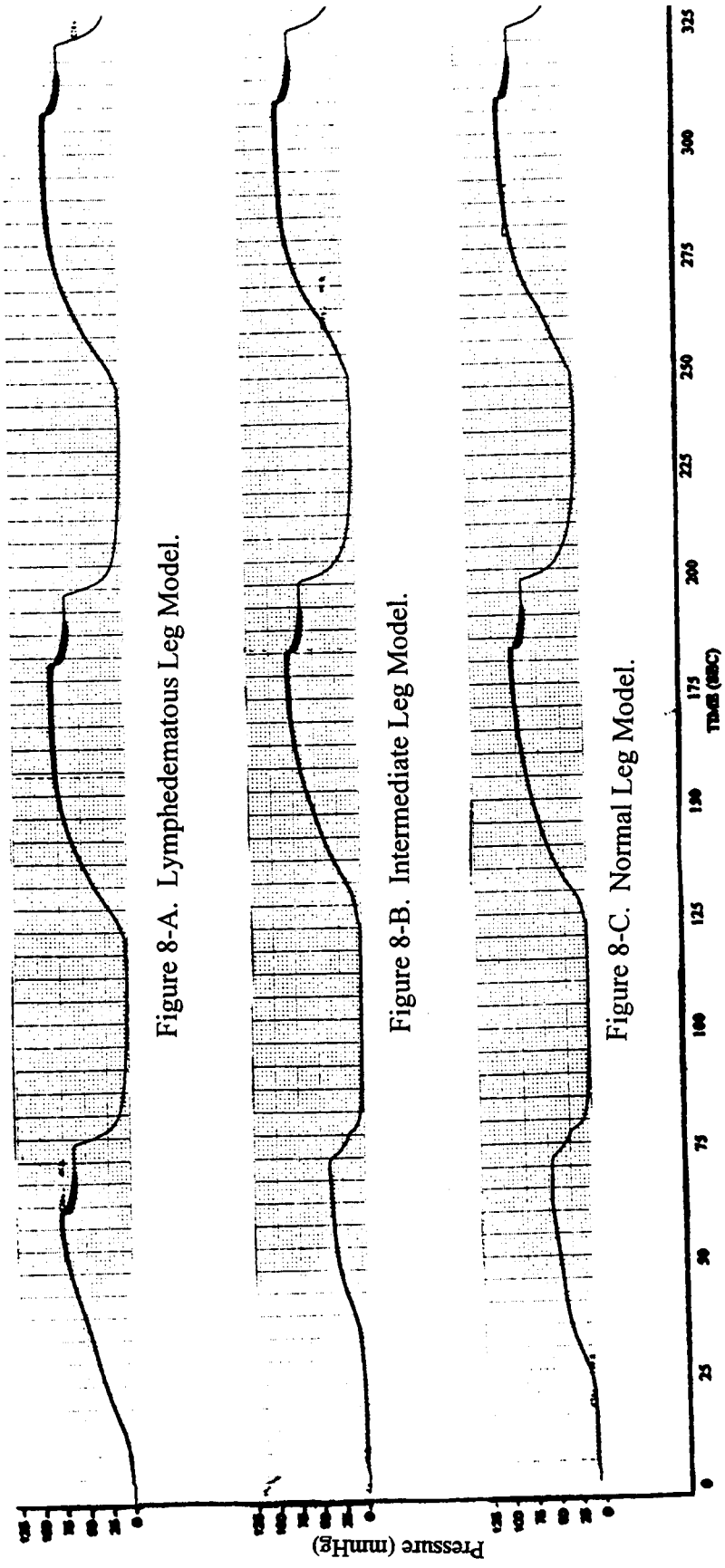


Figure 8-A. Lymphedematous Leg Model.

Figure 8-B. Intermediate Leg Model.

Figure 8-C. Normal Leg Model.

Figure 8. Compression Cycles for the Flow-Plus for the Three Leg Models. (Pressure Set at 90mmHg).

Table 2. Steady State Pressure in the Sleeve After Several Cycles for all the Models

		Max. Pressure Setting (mmHg)	Normal Leg (mmHg)	Intermediate Leg (mmHg)	Lymphedema Leg (mmHg)
Wright	Cell 1	100	87	88	88
	Cell 2	90	77	79	79
	Cell 3	80	70	72	72
Jobst	Cell 1	100	87	88	89
	Cell 2	100	85	85	85
	Cell 3	100	83	83	84
Flow_Plus		90	82	82	83

4.4 Wright Linear Pump

The Wright Linear Pump is a three-cell compression unit. The distal cell encloses the foot and ankle, the middle cell works the calf to the knee, and the top section encases the thigh. The outer wall of each cell is provided with a hose to receive air from the linear pump at preset times and pressures. With the Wright Linear Pump the limb is exposed to a distal-to-proximal pressure gradient. The technique employs a series of overlapping cells or compartments longitudinally spaced and sequentially inflated that apply a sequential pattern of compression to the limb, permitting a somewhat physiologic milking action approach to the lymphedematous limb.

The pump incorporates multiple ports. Hoses deliver pressures to individual cells. Each cell has a dedicated regulator to set the appropriate pressure to the specific cell disregarding the pressure in previous cells. Pressures are monitored and may be adjusted throughout the treatment cycle. The timing of the cell pressures is controlled and

monitored throughout the treatment cycle for each of the cells. The Wright Linear Pump applies a maximum pressure of 100 mmHg to the distal cell, 90 mmHg to the medial cell, and 80 mmHg to the proximal cell (Table 3).

Table 3. Maximum Measured Pressures for the Wright Linear Pump

Wright	Max. Pressure Setting (mmHg)	Max. Pressure Read at Pump Gage (mmHg)	Max. Pressure Measured at Sleeve (mmHg)
Cell 1	100	100	88
Cell 2	90	90	79
Cell 3	80	80	72

The Wright Linear Pump is completely programmable and the most versatile of the four pumps investigated. The pressure is set for the desired compression level, and the timing sequence can be set for each individual cell. Also, the total "ON" time for compression and the "OFF" time for relaxation (for the release to atmospheric pressure) can be set prior to the pump use. Each cell segment begins to inflate as the previous segment reaches its steady-state pressure. The inflated segments remain at the steady pressures reached previously during the course of the cycle. After all three segments have been pressurized, the pressures are held for the specific amount of time set earlier. The three segments are released or deflated simultaneously to the atmospheric pressure for the "off" time set prior to treatment (Figure 9).

There are no interconnection passages between the three segments in the sleeves of the Wright Linear Pump. When compression was applied to each cell alone by sealing off the other two there was no leakage or interconnection between the compartments. The

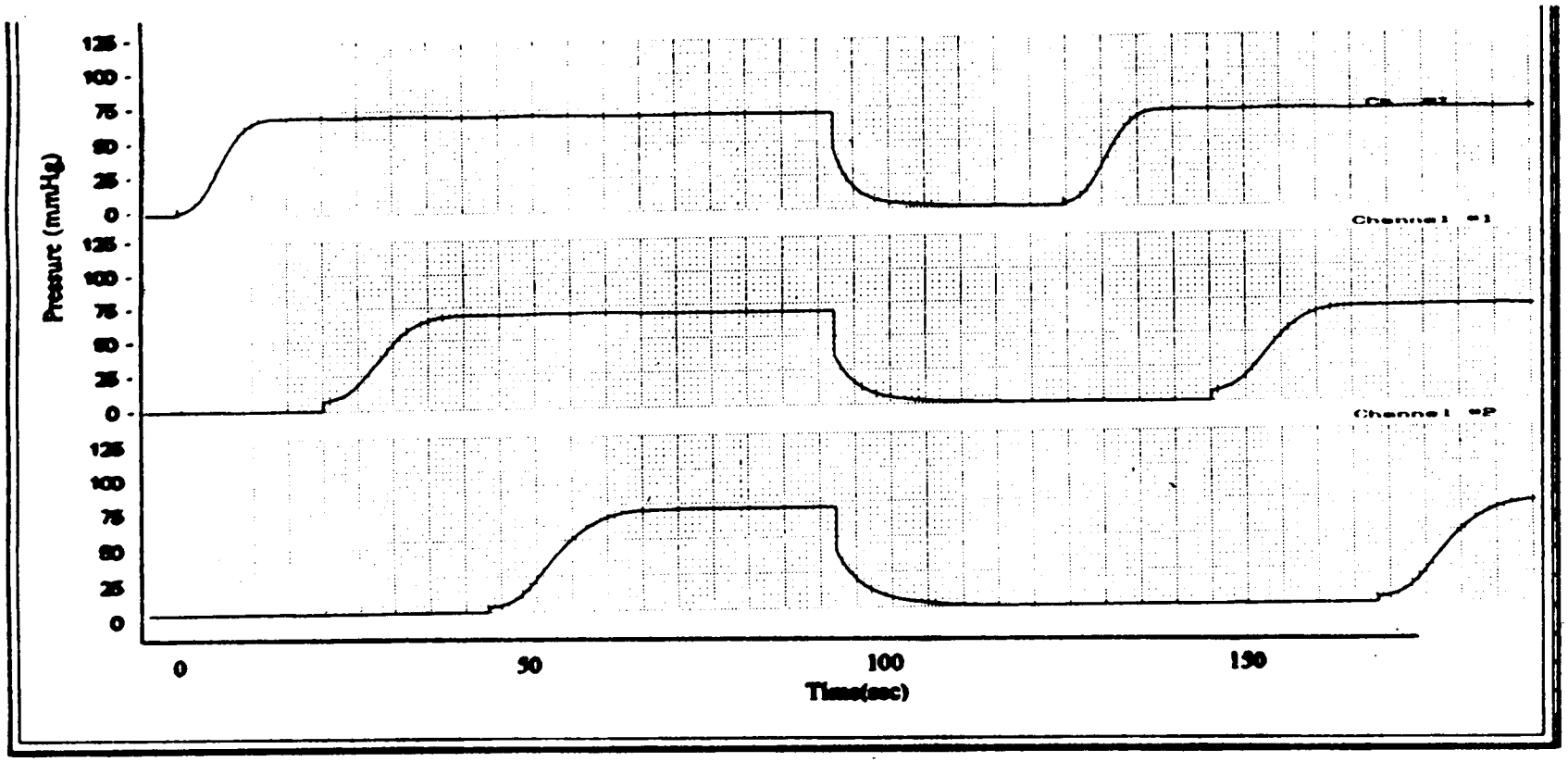


Figure 9. Compression Cycle of the Wright Linear Pump. (Intermediate leg model was used with compression levels set at 80mmHg for each cell. Channels 1, 2, and 3 from top to bottom show the pressures into the distal, medial, and proximal cells respectively).

compression cycle starts from the distal cell and travels toward the proximal cell. Even if the pump is turned off in the middle of the cycle, when it is turned back on the compression always starts from the beginning of the cycle at the distal cell.

Klein [25] describes a 48-hour treatment program "The Wright Linear Pump Protocol" whose purpose is to determine the clinical effectiveness of the Wright Linear Pump in individual cases, and to educate and acclimate the patient to its use. The first treatment period lasts two hours followed by an hour of rest and then two more hours of treatment. If treatment is tolerated without difficulty, treatment time is increased to consecutive four-hour periods, with a one hour rest period in between treatments. Treatment is then lengthened to consecutive sessions of six hours and then advances to eight hours. During the rest periods the involved limb remains elevated and is wrapped with compression bandages. The most common unfavorable reaction to the 48-hour treatment is pain in the treated limb following compression of the multi-cell sleeve. This problem generally is eased by slight pressure reduction (5 to 10 mmHg) of the particular compression cell in the region of pain.

According to Klein [25], the pump is set so that the distal cell has the highest pressure (up to 100 mmHg but no less then 80 mmHg), the middle cell is reduced to 20 mmHg less than that of the distal cell, and the proximal cell is reduced by another 20 mmHg (Figure 10). The time sequence remains constant. The duration of each cycle is 120 seconds, for

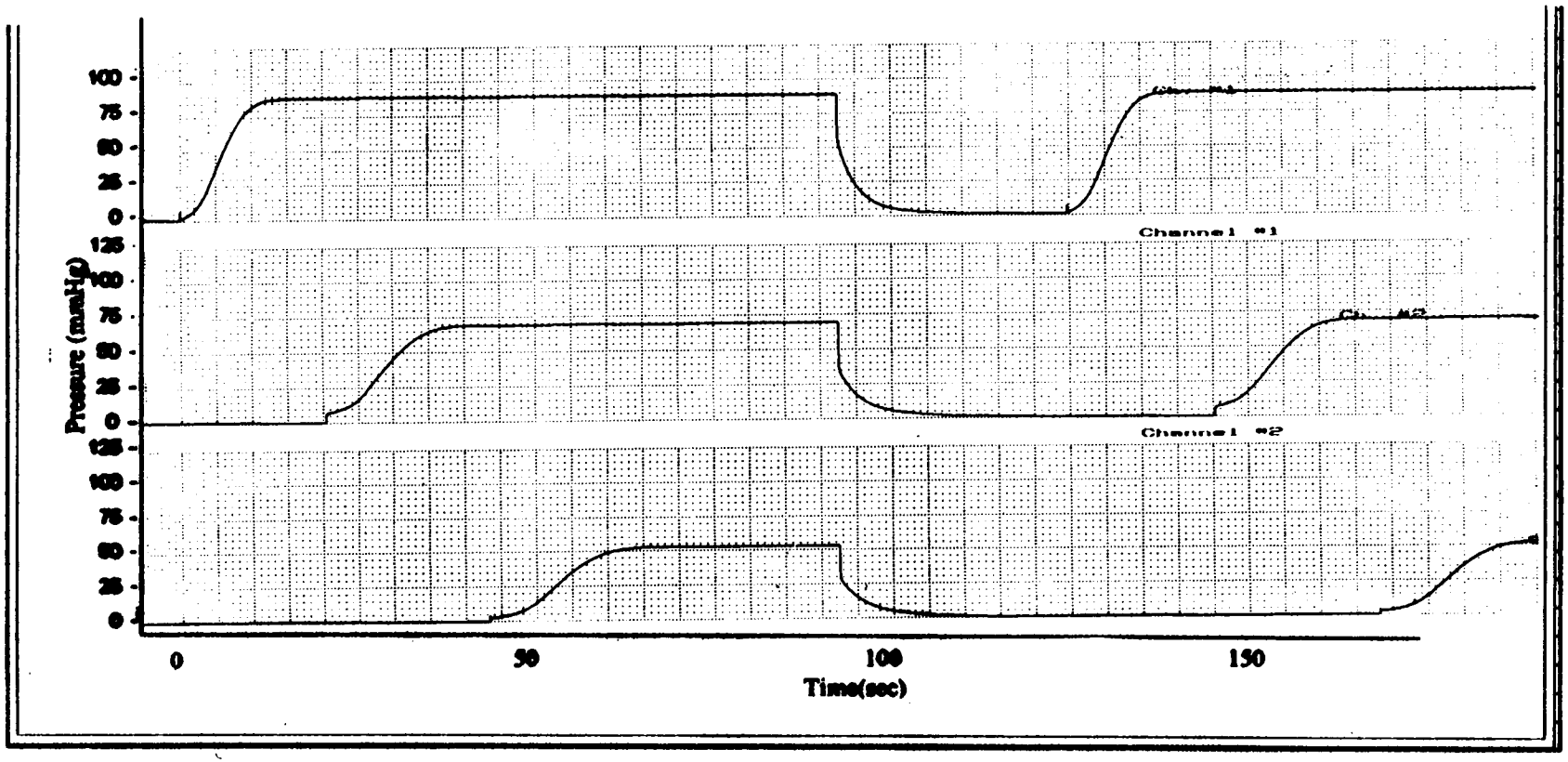


Figure 10. Compression Cycle of the Wright Using Klein's Protocol. (Intermediate leg model was used with compression levels set at 100mmHg for the distal cell, 80mmHg for the medial cell, and 60mmHg for the proximal cell. Channels 1,2, and 3 from top to bottom indicate the pressures into the distal, medial, and proximal cells respectively).

90 seconds of which the system is mechanically pressurized. There are two delay timers between the three cells so that the most distal cell is pressurized for a longer period than the middle cell which again is pressurized for a longer time than the proximal cell. The distal cell is pressurized first and is pressurized continuously for 90 seconds. Twenty seconds later, and accompanying the distal cell, the middle cell is pressurized for 70 seconds. Twenty seconds after the middle cell begins, and simultaneously with both the distal and middle cell, the proximal cell is pressurized for 50 seconds (Figure 10). At the end of this phase of the cycle there is a 30 second period during which all chambers are equilibrated to atmospheric pressure. The cycle is then automatically repeated.

Once the Wright Linear Pump is found to be effective and comfortable for the patient, it may be used periodically such as on a nightly basis for approximately an hour. During the day, the patient would then use a compression stocking to maintain a degree of external compression.

4.5 Jobst Extremity Pump System

The Jobst pump employs a series of three cells or compartments longitudinally spaced and sequentially inflated that apply a sequential distal to proximal pattern of compression to the limb in a manner similar to that of the Wright Linear Pump. As in the Wright Linear Pump, the distal cell encloses the foot and ankle, the middle cell works the calf to the knee, and the top section encases the thigh. The outer wall of each cell has a hose to

receive air from the Jobst pump at a preset pressure. Each cell segment begins to inflate as the previous segment nears the end of its 60-second inflation period. The first segment inflates for 60 seconds, then holds steady for the rest of the cycle (about 130 seconds), since the total inflation time is fixed at 190 seconds per cycle. As soon as the first segment holds steady the second segment starts to inflate for about 60 seconds and then holds steady for the rest of the cycle (about 70 seconds). As soon as the second segment holds steady pressure, the third segment starts to inflate, again taking approximately 60 seconds to reach steady-state. Then all three segments hold steady at the pressure levels they had reached earlier during the cycle for approximately 10 seconds before all three start to deflate simultaneously. From the data collected it appears that the first segment deflates faster than the other two, as shown in Figure 11. The total time of non-inflation or relaxation time is 50 seconds, followed by the re-inflation or pressurizing of the repetition cycle. The cycle repeats itself automatically and accurately until the pump is switched off. The maximum pressure that can be applied by the Jobst pump is 100 mmHg (Table 4).

Table 4. Maximum Measured Pressures for the Jobst Extremity System.

Jobst	Actual Pressure Setting (mmHg)	Max. Pressure Read at Pump Gage (mmHg)	Max. Pressure Measured at Sleeve (mmHg)
Cell 1	100	98	89
Cell 2	100	98	85
Cell 3	100	97	84

The disadvantages of the Jobst Pump System are: (1) the entire inflation/deflation timing cycle is preset and is not adjustable, (2) the timing of the pressure inflation and deflation

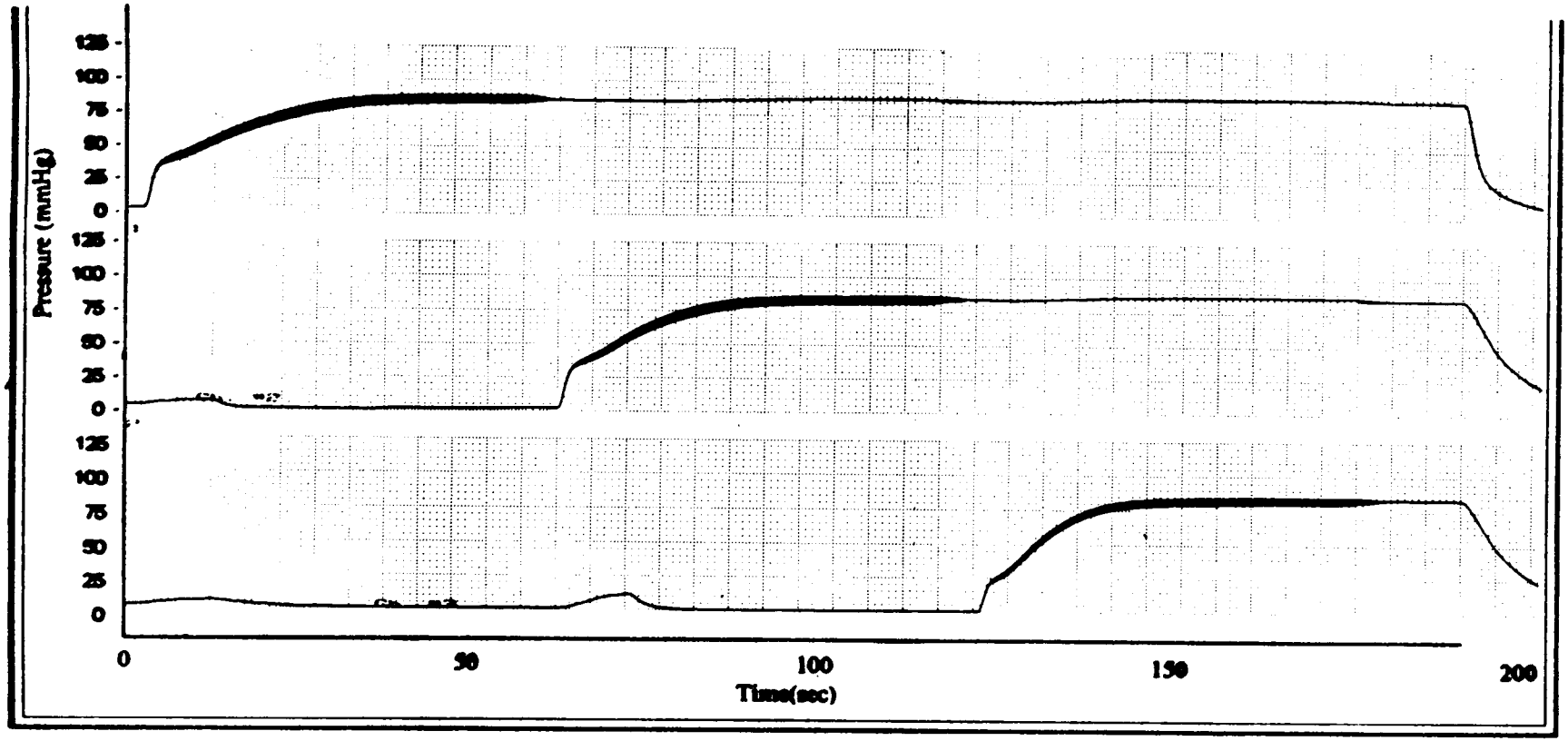
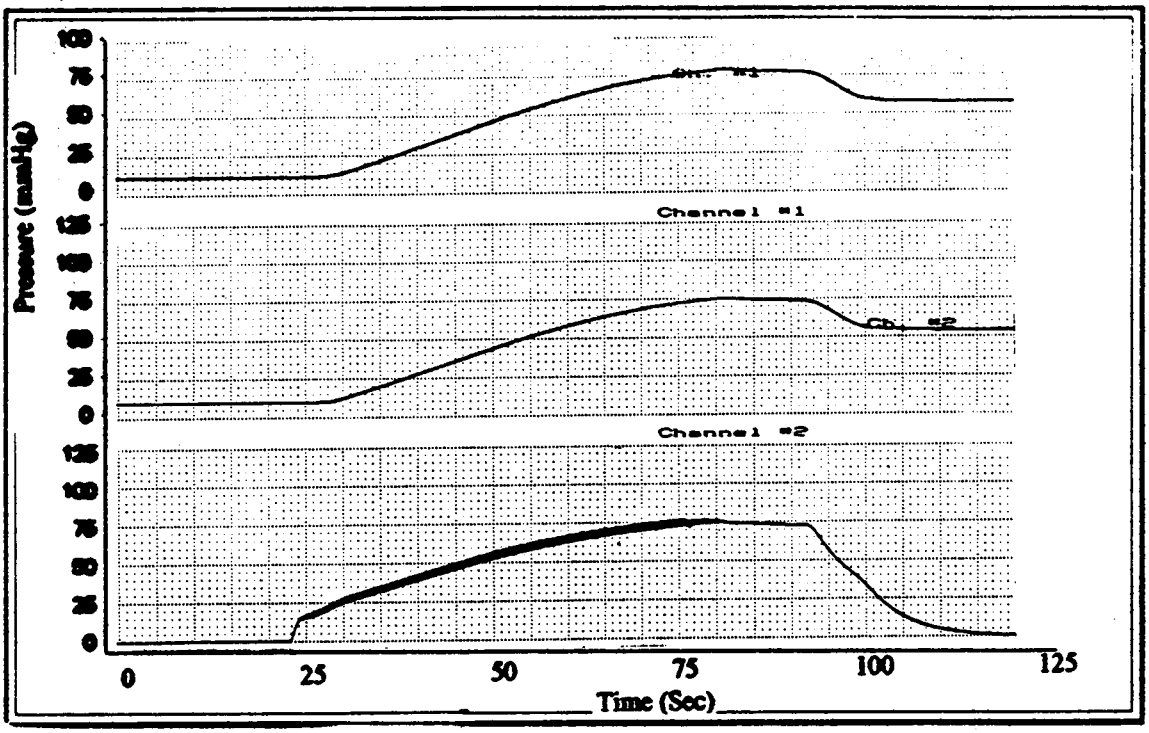


Figure 11. Compression Cycle of the Jobst Pump. (Lymphedematous leg model used with compression levels set to maximum at 100mmHg. Channels 1, 2, and 3 from top to bottom indicate the pressures into the distal, medial, and proximal cells respectively).

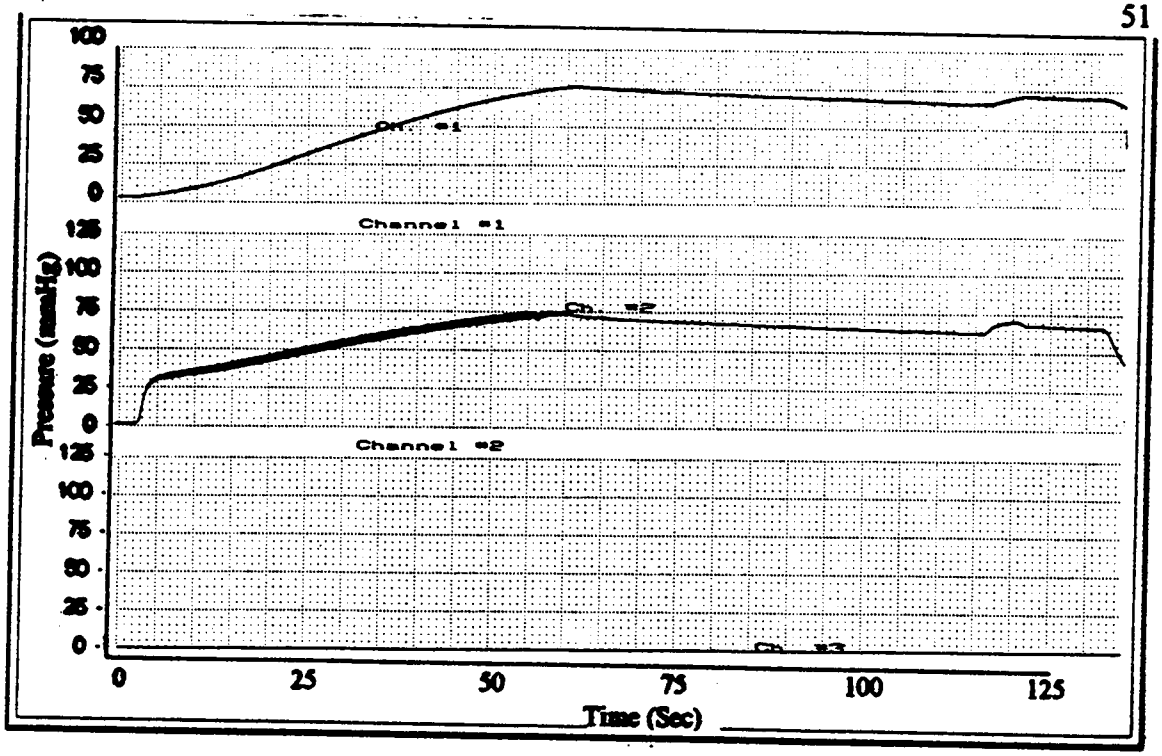
to each cell is preset and cannot be changed, (3) the individual cell pressures cannot be regulated; that is, once the pressure is set using the pump preset pressure control knob, the pressure is set equally for all three cells in the sleeve so one cannot obtain individual cell pressure adjustment. The Jobst Extremity Pump System has a single pressure setting, and therefore may not be intended to produce a pressure gradient between the cells once they are all inflated. Small pressure differences do exist, however, at times between adjacent inflated cells as a result of deflection of the intervening septum when the more proximal cell is inflated to the single set pressure (i.e. when cell 2 is inflated, the pressure in cell 1 rises slightly).

A test was conducted to determine if there was any interconnecting passages between the compartments. Pressure was applied to the proximal cell while the other two cells were sealed off (by blocking or shutting off the entrance to each cell). The three transducers read the same pressure in all 3 cells, which means that there are interconnecting passages between the cells allowing pressure to flow from the proximal to the distal cell. When the pressure was applied to the medial cell while the distal and proximal cells were sealed off, only the medial and the distal cells were pressurized; in other words the interconnecting passage is only from the medial to distal cell. When applying pressure to the distal cell with the medial and proximal cells sealed off, only the distal cell was engaged with no leaking to the other two cells (Figure 12-A, B, and C).

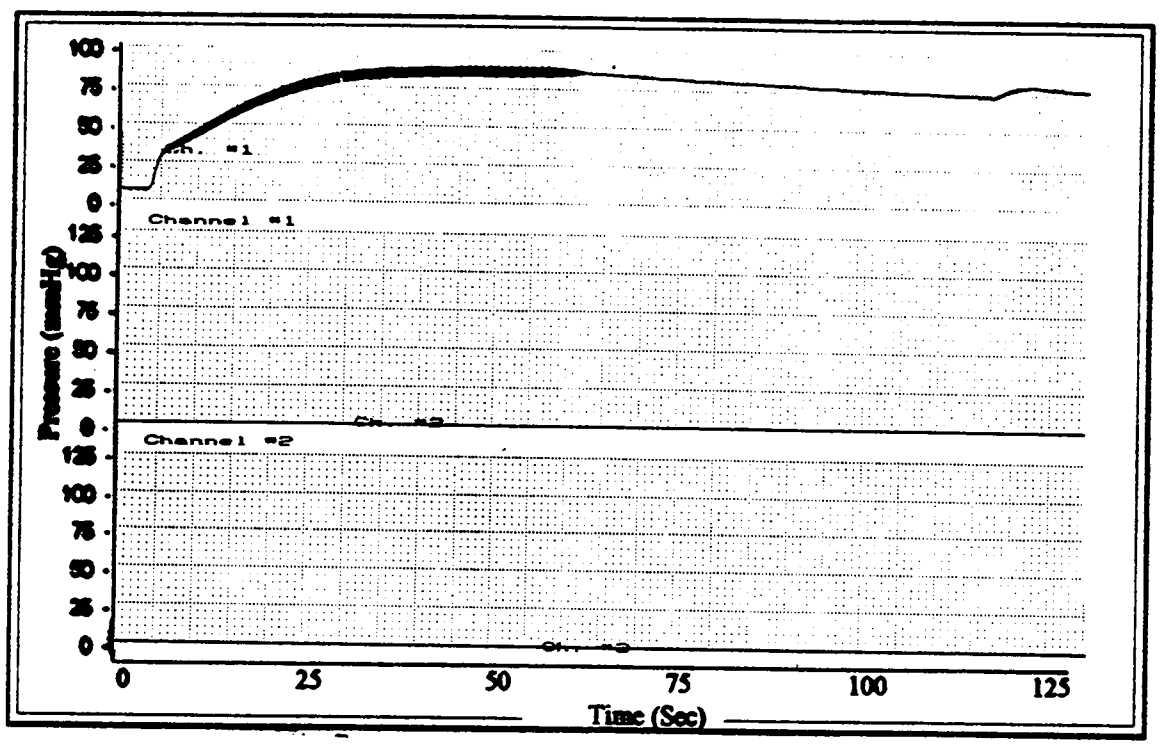


(12-A). Pressure into Cell 3. Proximal cell only (channel 3).

Figure 12. Jobst Extremity Pump Interconnection Passage System. (Lymphedematous Leg Model was used with pressure set to 100 mmHg).



(12-B). Pressure into Cell 2. Medial cell only (channel 2).



(12-C). Pressure into Cell 1. Distal cell only (channel 1).

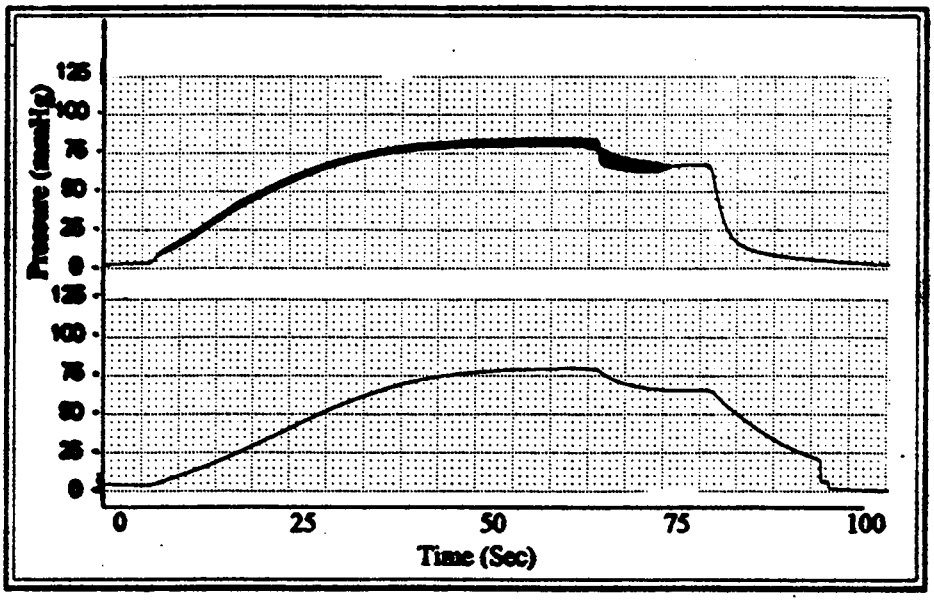
Figure 12. (Continued)

This test demonstrated that the valves between the cells permitted air to flow from the proximal to the medial to the distal cells. The valves thus prevent any significant reverse gradient pressure in case there is a misoperation. They also provide a route for all air to be exhausted from the appliance through the distal cell.

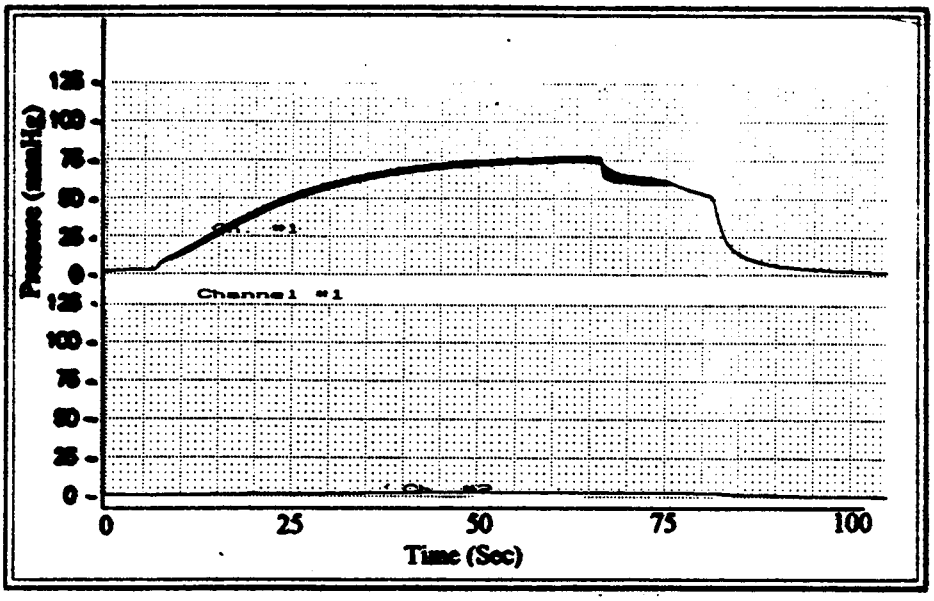
4.6 Flow-Plus by Huntleigh

The Huntleigh Flow-Plus device employs a single cell, encasing the entire limb section. The sleeve administers equal compression throughout the limb which fails to provide a directional flow to the body fluid; therefore, retrograde flow may be experienced to areas of relatively decreased tissue resistance in the extremity. The Flow-Plus pump is designed for a two minute cycle, one minute and 15 seconds for inflation and compression and 45 seconds for deflation and relaxation. The pump provides a maximum pressure of 90 mmHg. This cycle repeats itself automatically until the pump is switched off.

This design attempts to create a relative pressure gradient by applying the pressure into the distal section of the sleeve and exhausting the air through an orifice approximately 7 inches from the proximal end. While the sleeve was compressed to a specific pressure in the distal section of the sleeve, air was escaping to the atmospheric from the proximal end (Figure 13-A). Thus, the pressure measured at this end was essentially atmospheric. When the orifice in the proximal end was closed and pressure measured at



(13-A). Pressure measurement when proximal orifice is open to atmospheric.



(13-B). Pressure measurement when proximal orifice is closed.

Figure 13. Compression Cycle of the Flow-Plus Pump. (Lymphedematous leg with compression level set to maximum at 90 mmHg. Channel 1 is the actual pressure coming into the distal section, where channel 2 is the pressure exhausting to the atmospheric from the orifice in the proximal section).

the orifice, it was essentially identical to the pressure in the sleeve (Figure 13-B). There is no provision for regulation of the pressure inside the sleeve; in other words, one cannot determine the exact pressure inside the sleeve to monitor the treatment of lymphedema. It is believed, however, that the pressure is nearly uniform inside the sleeve.

4.7 Bio-Compression System Pump

The Bio-Compression System is a six cell unit including a single-cell interlayer. The first cell encases the hand and the wrist, the second cell encases the mid section of the forearm, the third cell encases the upper section of the forearm up to the elbow, the fourth cell encases the elbow, and the sixth cell encases the upper arm. The interlayer section comprises the fifth cell which extends the full length of the sleeve; it is intended to pressurize the interspace between the cells as shown in Figure 14. The outer wall of each cell is provided with a hose to receive air from the Bio-Compression pump at the preset pressure. There are no pressure regulators for each individual cell.

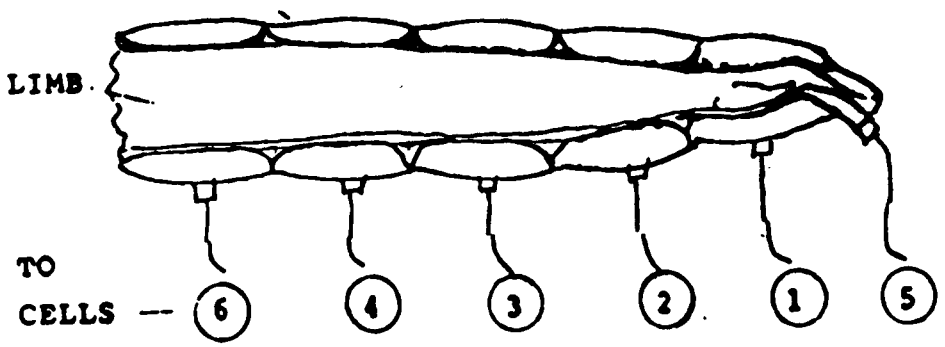


Figure 14. Schematic Representation of the Bio-Compression Sleeve.

The Bio-Compression device has two rates for compression settings, "LO" and "HI". The "LO" rate switch option produces a 60 second compression cycle and 10 seconds of relaxation time releasing all the cells to the atmospheric pressure (Figure 15). The "HI" rate switch produces a 25-second compression cycle with only 5 seconds of relaxation time (Figure 16). While the interlayer cell 5 and the proximal cell 6 were generally pressurized at the same time to lower values than the more distal cells, the pressures in cells 1 through 4 were more likely to cause a reverse gradient. When pressurizing the sleeve at a pressure setting of 100 mmHg using the low rate compression, all the cells 1 through 4 exhibited reverse pressure gradients at steady state conditions (Figure 15). Cell 1 reaches a steady state level at 75 mmHg before cell 2 reaches its maximum pressure of 87 mmHg which causes a reverse gradient; cell 2 reaches steady-state at 80 mmHg before cell 3 reaches the maximum pressure of 83 mmHg; and so forth (Table 5).

Table 5. Reverse Gradient at the "LO" Rate Pressure (Set at 100 mmHg)

Cell	Pressure at Steady State (mmHg)	Cell	Maximum Pressure After Previous Cell Reaches Steady State (mmHg)
1	75	2	87
2	80	3	83
3	80	4	82

When testing the pump at the "LO" rate compression of 100 mmHg the pump was pressurizing the sleeve to a pressure level higher then the actual setting of the pump as shown in Figure 15 and Table 6. The applied pressure exceeded the preset pressure.

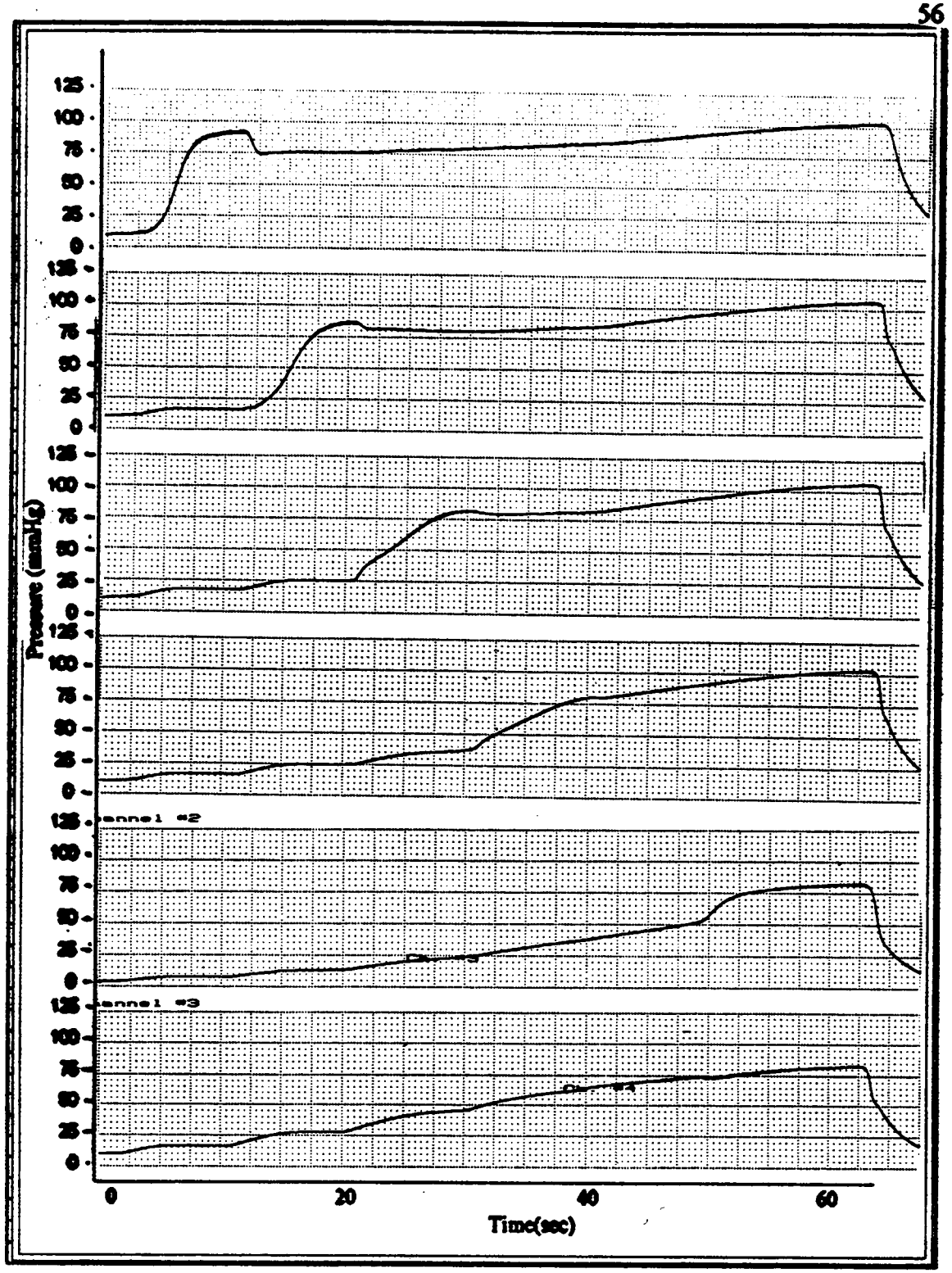


Figure 15. Compression Cycle of the Bio-Compression Pump for the "LO" Rate. (Arm model used with compression level set at 100mmHg. Channels 1, 2, 3, 4, 5, and 6 from top to bottom represent the pressures into the cells 1, 2, 3, 4, 6, and 5 respectively).

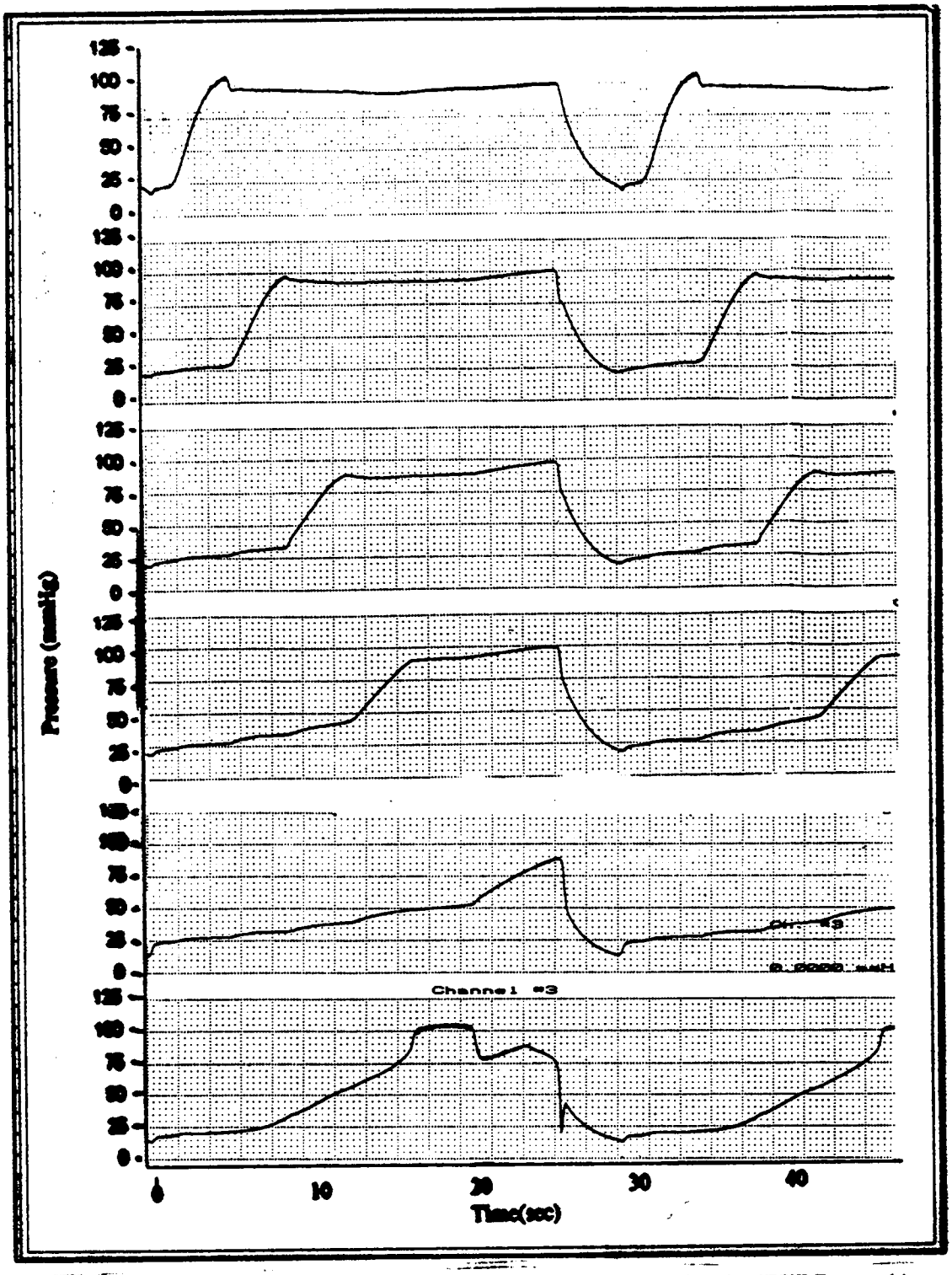


Figure 16. Compression Cycle of the Bio-Compression Pump for the "Hi" Rate. (Arm model used with compression levels set at 100mmHg. Channels 1, 2, 3, 4, 5, and 6 from top to bottom represent the pressure into the cells 1, 2, 3, 4, 6, and 5 respectively).

Table 6. The Compression Cycle at "LO" Rate Pressure

Bio-Compression	Pressure Setting (mmHg)	Max. Pressure Read at Pump Gage(mmHg)	Max. Measured Pressure in the Sleeve (mmHg)
Cell 1	100	95	103
Cell 2	100	95	107
Cell 3	100	90	106
Cell 4	100	85	104
Cell 5	100	80	84
Cell 6	100	80	84

When the Bio-Compression pump is turned off and then after awhile turned back on, the compression cycle starts from the point where it was stopped, it can start from the middle of the cycle causing a reverse pressure gradient. Thus the pump should be turned off only during the relaxation phase of the cycle so that when turned back on, it is ready to start a new cycle.

Results and conclusions from the four pump tests will be summarized in chapter VI, after introducing in chapter V a new method for evaluating the pneumatic compression treatment for lymphedema.

CHAPTER V

MATHEMATICAL MODEL

5.1 Introduction

Most of the fluid in the edematous tissue is free to move within the tissue under the action of applied loads [21]. Under compression, the deformation of the solid matrix and the flow of interstitial fluid gives rise to relative motion which exerts an action and reaction drag force that governs predominantly the observed viscoelastic properties of the tissue under compression [21, 27]. The translocation of the fluid under compression differs between normal and edematous tissues, depending on the resistance to outflow and the quantity of fluid stored [21]. Resistance to outflow is directly proportional to fluid viscosity and inversely dependent on the dimension of the channel through which fluid flows [21]. The increased fluid volume due to lymphedema is accompanied by a lower viscosity of the interstitial fluid [21, 27].

In order to obtain a somewhat quantitative measure of the nature and extent of the lymphedema, a mechanical model of the lymphedematous tissue can be proposed and evaluated. The intent is to obtain a measure of the expected translocated fluid due to an applied force on the skin. Such a model has been developed in this investigation and is described in the following sections.

5.2 Mechanical Properties of the Tissue

The mechanical properties of skin have been related to its water content under many different conditions. The flexibility, elasticity, and breaking strength of skin have been shown to vary with water content [39]. The interstitial space contains free fluids like water, solid elements like collagen and elastin, and gel-like ground substances [21]. Together all these components determine the mechanical behavior of tissues. Collagen and elastin, and their structural arrangement, determine the elastic properties of the skin; the ground substances determine the viscoelastic properties of skin, while the structure of the components of skin determine its function [14, 21, 27]. Excess fluid reduces the viscosity of its gel-like fluid ground substances [14, 27]. Therefore, the structural and mechanical changes produced by edema depend upon its severity and the rapidity with which it develops. The mechanical properties of a gel-like fluid is likely to vary with its water content, and, therefore, the mechanical properties of edematous tissue differ from that of normal tissue, and could be expected to vary with the degree of the edema.

In 1971, Guyton discussed that the fluid flow through the tissue spaces is normally restricted by solid elements which are packed one upon the other and by the high viscosity of the gel-like fluid matrix embedded in a network of collagen fibers [21]. A mechanical model which characterizes the rate of flow on extension and compression as a function of two viscosities, that of the free fluid and that of the gel-like fluid (Figure 17),

represents the equivalent of the anatomical model of skin described by Guyton in 1971 which consists of fluid, solid fibers as collagen and elastin fibers, and gel.

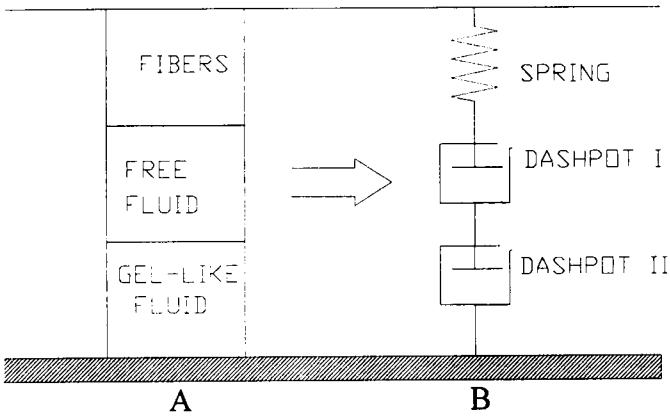


Figure 17. Schematic Representation of Skin. (A) Anatomical model. (B) Mechanical model. Dashpot I contains low-viscosity fluid like water, Dashpot II contains high-viscosity gel like fluid.

5.3 Mechanical Model of Lymphedema

The mechanism of fluid flow upon compression of edematous skin, is explained by the model shown in Figure 18, which is a modification of the earlier model shown in Figure 17. When the tissue is compressed rapidly, its elastic components are compressed rapidly. The resistive force of tissue under compression should be measured because it may be related to the mobility and the volume of interstitial fluid translocated due to compression. As the skin is compressed, the springs are compressed. Spring S1 will in turn compress dashpot 1 to translocate the low-viscosity free fluid. In edematous tissues, the viscosity of the free fluid is lower than in the normal tissues, the amount of free fluid is greater and the space d between the fibers (corresponding to the spaces between the piston and the wall of the cylinder) is greater than that in normal tissues [21], which

makes fluid flow easier. When dashpot 1 space is emptied (free fluid is completely out), the flow of the gel-like fluid from dashpot 2 space becomes predominant (gel-like fluids do not contain free fluid). In edematous tissues the viscosity of the gel-like fluid becomes lower than that of the normal tissues. The high viscosity of the gel-like ground substances present in the tissue is considered an indication of creeping phenomenon. When the compression is released, the pistons are returned to their initial positions with the action of spring S2. High compliance of edematous tissue corresponds to a small compressive force in spring S2, which results in a slow recovery process after the withdrawal of the applied compression [20].

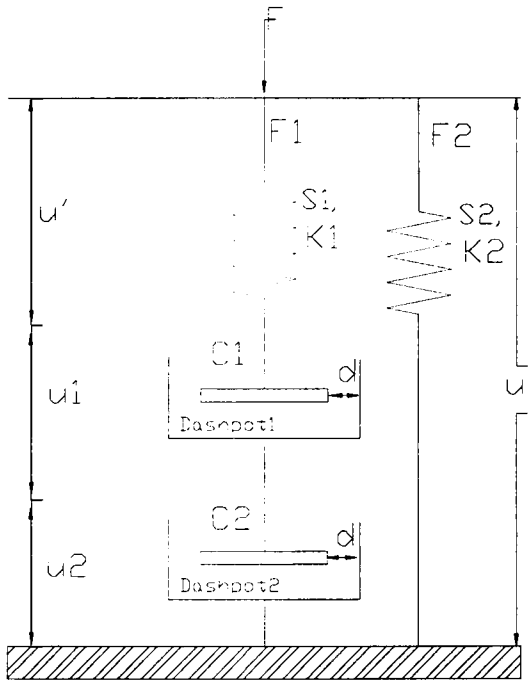


Figure 18. Mechanical Model of the Viscoelastic Material.

5.4 Mathematical Approach

The mechanical model of the viscoelastic material is shown in Figure 18, where this model is a modification of the standard linear solid (Kelvin model) as described by Fung [16]. The linear springs produce instantaneously a deformation proportional to the load, while each dashpot produces a proportional velocity at any instant. If the force is suddenly applied at the instant of time t=0, the springs will be suddenly deformed to u_0, but the initial dashpot deflections would be zero because there is no time to deform. The applied force is distributed as F_1 and F_2 over both springs. Thus:

$$\begin{aligned} &(a)- \quad u = u_1 + u_2 + u' \\ &(b)- \quad F = F_1 + F_2 \\ &(c)- \quad F_2 = k_2 u \\ &(d)- \quad F_1 = c_1 \dot{u}_1 = c_2 \dot{u}_2 = k_1 u' \end{aligned} \tag{5-1}$$

where k_1 and k_2 are the spring constants of the elastic tissue components S1 and S2, $\dot{u}$ is the velocity, and u the compression depth. The displacement u is broken down into u_1 of the free fluid dashpot, u_2 of the gel-like fluid dashpot 2, and u' of the spring S1.

Substitute Eq(5-1c) and Eq(5-1d) into Eq(5-1b) to obtain:

$$F = k_2 u + k_1 u' \tag{5-2}$$

Substitute Eq(5-6a) into Eq(5-2) to obtain:

$$F = k_2 u + k_1 (u - u_1 - u_2) = (k_1 + k_2) u - k_1 (u_1 + u_2) \tag{5-3}$$

which, when differentiated with respect to time, gives:

$$\dot{F} = (k_1 + k_2)\dot{u} - k_1(\dot{u}_1 + \dot{u}_2) \tag{5-4}$$

Hence

$$F + \left[\frac{c_1 c_2}{(c_1 + c_2)k_1}\right]\dot{F} = (k_1 + k_2)u - k_1(u_1 + u_2) + \left[\frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1}\right]\dot{u} - \left[\frac{c_1 c_2}{(c_1 + c_2)}\right](\dot{u}_1 + \dot{u}_2) \tag{5-5}$$

From Eq(5-1d) $c_1\dot{u}_1 = c_2\dot{u}_2 = k_1 u'$, so that

$$F + \left[\frac{c_1 c_2}{(c_1 + c_2)k_1}\right]\dot{F} = (k_1 + k_2)u - k_1(u_1 + u_2) + \left[\frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1}\right]\dot{u} - \left[\frac{c_2}{c_1 + c_2}k_1 u' + \frac{c_1}{c_1 + c_2}k_1 u'\right]$$

Thus

$$F + \left[\frac{c_1 c_2}{(c_1 + c_2)k_1}\right]\dot{F} = (k_1 + k_2)u - k_1(u_1 + u_2) + \left[\frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1}\right]\dot{u} - k_1 u' \tag{5-6}$$

Substituting $u' = u - (u_1 + u_2)$ into Eq(5-6) gives:

$$F + \left[\frac{c_1 c_2}{(c_1 + c_2)k_1}\right]\dot{F} = (k_1 + k_2)u - k_1(u_1 + u_2) + \left[\frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1}\right]\dot{u} - k_1 u + k_1(u_1 + u_2) \tag{5-7}$$

Thus

$$F + \left[\frac{c_1 c_2}{(c_1 + c_2)k_1}\right]\dot{F} = k_2 u + \left[\frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1}\right]\dot{u} \tag{5-8}$$

Let $\tau_\varepsilon = \dfrac{c_1 c_2}{(c_1 + c_2)k_1}$ and $\tau_\sigma = \dfrac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2)k_1 k_2}$

Then

$$F + \tau_\varepsilon \dot{F} = k_2 (u + \tau_\sigma \dot{u}) \tag{5-9}$$

For a suddenly applied force F_0 and displacement u_0 the initial condition obtained from Eq(5-3) is

$$F_0 = (k_1 + k_2) u_0 \tag{5-10a}$$

Using the definitions of τ_ε and τ_σ, k_1 and k_2 are replaced in Eq(5-10a) becomes

$$\tau_\varepsilon F_0 = k_2 \tau_\sigma u_0 \tag{5-10b}$$

The differential equation Eq(5-9) is solved (as shown in Appendix A) for the case where F(t) is a unit step function [1(t)] where the unit-step function is defined as

$$1(t) = \begin{cases} 1 & when \quad t \geq 0 \\ 0 & when \quad t < 0 \end{cases}$$

The solution of the differential Eq(5-9) is the creep function u which represents the displacement produced by a sudden application at t=0 of a constant force of unity magnitude. The solution (Appendix A) is given as

$$u(t) = \frac{1}{k_2}\left[1 - \left(1 - \frac{\tau_\varepsilon}{\tau_\sigma}\right) e^{-t/\tau_\sigma}\right] 1(t)$$

Substituting for τ_ε and τ_σ then

$$u(t) = \frac{1}{k_2}\left\{1 - \left(1 - \frac{k_1}{k_1 + k_2}\right)\exp\left[-\frac{k_1 k_2 (c_1 + c_2)}{c_1 c_2 (k_1 + k_2)} t\right]\right\} 1(t) \qquad (5\text{-}11)$$

To determine the viscoelastic coefficients that best fit the experimental results, a technique suggested by Schmid-Schonbein [38] is followed. Consider the error ε between the calculated displacement $u_c(t)$ from Eq(5-11) and the measured displacement $u_m(t)$, discussed in Section 5.6 and plotted in Figure 20, at different times k:

$$\varepsilon(k_1, k_2, c_1, c_2) = \sum_{k=1}^{n} \left| u_c(t_k) - u_m(t_k) \right|^2 \qquad (5\text{-}12)$$

The best fit of the viscoelastic model to experiment is obtained when the error is minimized. A necessary condition is:

$$\frac{\delta\varepsilon}{\delta k_1} = \frac{\delta\varepsilon}{\delta k_2} = \frac{\delta\varepsilon}{\delta c_1} = \frac{\delta\varepsilon}{\delta c_2} = 0 \qquad (5\text{-}13)$$

This leads to four equations for the four unknown viscoelastic coefficients. To solve the problem one needs to determine $u_m(t)$ for a given F_0. To accomplish this, a device needs to be designed and constructed which applies a constant force F_0 to the tissue while measuring the displacement u as a function of time.

An alternative method of determining the viscoelastic coefficients in Eq(5-12) is to solve Eq(5-8/9) for the relaxation function F(t) while specifying a unit step function u(t)=1(t). Using the same derivation and the initial condition obtained in Eq(5-10a) the solution is obtained similarly to that described for the creep function and is

$$F(t) = k_2\left\{1-\left(1-\frac{k_1+k_2}{k_1}\right)\exp\left[-\frac{(c_1+c_2)k_1}{c_1c_2}t\right]\right\}1(t) \qquad (5\text{-}14)$$

This solution is analogous to that given by Fung [16] for his linear standard model.

5.5 A Proposed New Approach for Evaluating Compression Treatments

At the compressed skin area A, tissue pressure increases locally, which causes the flow of interstitial fluid out of the compressed volume. Let the skin be compressed u_0 by a force F_0 and held constant at u_0. The volume translocated at any time can be denoted by V(t). The elastic components start to expand after being compressed for a distance

$u_1 + u_2 = \frac{V(t)}{A}$. Therefore

$$V(t) = A(u_1 + u_2) \qquad (5\text{-}15)$$

where u_1 and u_2 are the displacements of dashpot 1 and dashpot 2. A decay of the force F(t) is proportional to the quantity of fluid translocated from the compressed site by substituting Eq(5-15) into Eq(5-3):

$$F(t) = (k_1 + k_2)u_0 - k_1\frac{V(t)}{A} \qquad (5\text{-}16)$$

By dividing Eq(5-16) by Eq(5-10a) we get the normalization of the recorder force:

$$F_n(t) = \frac{F(t)}{F_0} = 1-\left(\frac{V(t)}{Au_0}\frac{k_1}{(k_1+k_2)}\right) \qquad (5\text{-}17)$$

Hence

$$V(t) = Au_0 \frac{(k_1 + k_2)}{k_1}\left(1 - F_n(t)\right) \tag{5-18}$$

At t=0, V(t) = 0 (i.e. no fluid has been translocated), so $F_n(0) = 1$. At any time $0 < t < \infty$ the volume translocated =V(t).

The flow rate can be obtained from the differentiation of Eq.(5-18).

$$\frac{dV(t)}{dt} = -Au_0 \frac{(k_1 + k_2)}{k_1} \frac{dF_n(t)}{dt} \tag{5-19}$$

Thus the volume of interstitial fluid flowing away from the compressed area (Eq 5-18) and the rate of volume flow (Eq 5-19) can be determined by measuring the temporal variation of tissue resistive force during compression, since we already determined the viscoelastic coefficients of the mechanical model in Section 5.4.

5.6 Proposed Force/Displacement Measurement Technique

Measurement of fluid translocation is useful in selecting and evaluating the effectiveness of lymphedema treatment, as well as in determining the viscoelastic properties of the edematous tissues. A new approach has been developed to help determine the volume of the translocated fluid to be expected due to the compression therapy.

The experimental apparatus is visualized as shown in Figure 19. A force transducer is fixed on the shaft of a stepper motor, and has a cylindrical pressure head of diameter D. The motor is controlled by a microprocessor mounted on a rigid stand. The stand should

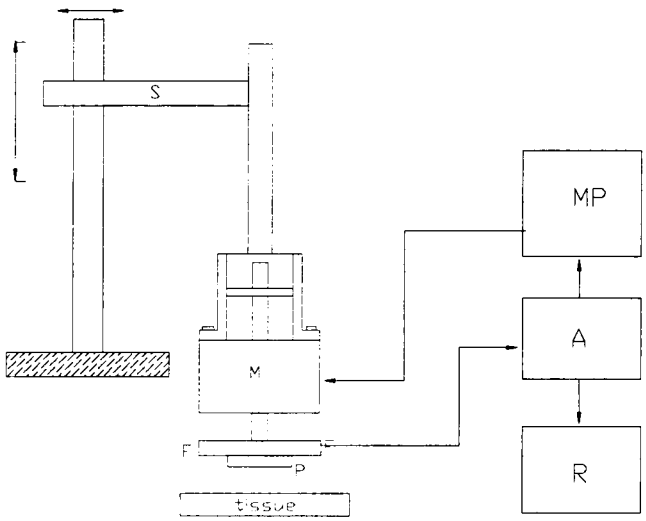


Figure 19. Schematic Diagram of the Apparatus for Applying Compression and Detecting the Corresponding Force: (S : stand; M: motor; F: transducer; P: pressure head; MP: microprocessor; A: amplifier; R: recorder).

be adjustable to be able to locate the apparatus parallel to the skin surface at nearly any point on the body. When the motor starts it will move the force transducer toward the skin with a constant velocity. As soon as the force transducer touches the surface of the skin the microprocessor causes the motor to compress the tissue with a specific constant velocity to avoid damaging the tissues (Figure 20). The predefined depth u_0 of the compression should be adjustable, the depression will then be sustained and the force required to do this is measured. The duration of compression should be small, approximately 20-30 sec, in order to get good readings without any risk of patient

movement. After the elapse of the determined compression period, the motor automatically retreats to the original position with a lower velocity (Figure 20). The signal from the force transducer should be continuously recorded at every depth and time. Measurements can be automatically repeated with variable intervals between the measurements.

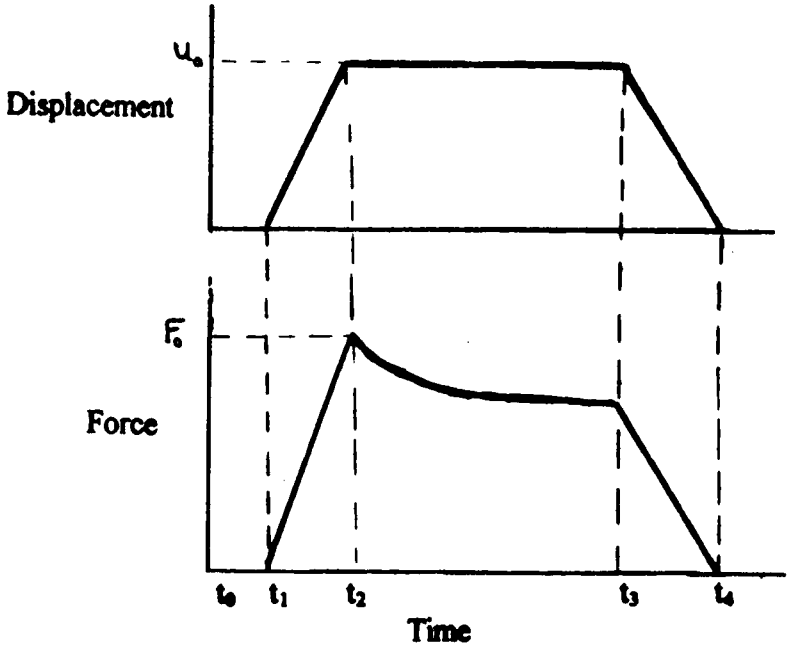


Figure 20. Proposed Displacement and Force Measurements. At t_0 the motor moves towards the structure under test; at t_1 the force transducer touches the skin and fast compression starts; at t_2 compression stops and the transducer remains stationary until t_3; the transducer is retracted, leaving the skin surface at t_4.

5.7 The Degree and Reduction of Lymphedema

5.7.1 Volumetric Measurement Technique: One of the methods used to find the degree and reduction of lymphedema was discussed by Swedborg [41]. The patient inserts

his/her arm or leg into a cylindrical container filled with water to the outlet. The leg or arm is slowly slid against the cylinder wall until the fist or foot is pressed against the bottom of the container. The displaced water is collected and weighed to obtain the volume of the translocated fluid. The degree of edema from the displaced water D_v, and the reduction of edema R_v are calculated from:

$$D_v = 100\left(\frac{V_e - V_n}{V_n}\right) \tag{5-20a}$$

$$R_v = D_{vb} - D_{va} \tag{5-20b}$$

Where:

V_e= volume of the edematous extremity before treatment

V_n= volume of the contralateral normal extremity

D_{vb}= degree of edema before treatment

D_{va}= degree of edema after treatment.

5.7.2 Translocated Fluid Measurements Technique: Results from the present study can be presented by "degree of lymphedema" and "reduction of lymphedema" parameters similar to those discussed above (Section 5.7.1). In Section 5.6, a method of determining force/displacement measurements of lymphedematous tissue was discussed. For every patient several sites should be measured on the edematous limb before and after the treatment. Similar locations on the contralateral, unaffected limb should be found and evaluated. The volume of the fluid translocated from the compressed skin can be

calculated from the previous derivations for the new approach discussed in Section 5.5, assuming that the pressure head caused a cylinder-like depression in the tissue (which is nearly the situation in the case of pitting edema, where the surface tension of the skin is low).

Referring to Eq(5-18) we know that

$$V(t) = Au_0 \frac{(k_1 + k_2)}{k_1}\left(1 - F_n(t)\right)$$

where A is the area of the compressed tissue (or the area of the pressure head), u_0 is the predefined depth, and k_1 and k_2 are two of the viscoelastic coefficients discussed in Section 5.4.

The function V(t) is integrated over the interval (0,T) and then divided by T to give the mean value of V(t) in the interval. The degree and reduction of edema from translocation measurement, D_t and R_t respectively is then defined as:

$$D_t = \frac{1}{T}\int_0^T V(t)dt \quad (\text{x}100) \tag{5-21a}$$

$$R_t = D_{tb} - D_{ta} \tag{5-21b}$$

where indexes b and a indicate before and after treatment respectively. It is believed that the parameters D_t and R_t may help the clinician better define a treatment program for the patient.

CHAPTER VI

CONCLUSION

6.1 Management of Lymphedema

All patients who have undergone axillary node dissection or radiation are at risk for developing lymphedema. Management should begin, therefore, preoperatively with patient education in which lymphedema is thoroughly explained and suggestions offered for postoperative precautions that may reduce the risk of complications. Foremost among these precautions are the avoidance of injury to the limb (including needle punctures, lacerations and abrasions, insect stings and bites, and solar or thermal burns) and identification of infection [3, 12]. Even the most innocuous of injuries, such as finger sticks for glucose monitoring in diabetics, can provoke edema [3]. Patients are instructed to use gloves that extend to the forearm when cooking or gardening. The limb should be protected with sun block and insect repellent when outdoors. It is also wise to recommend the avoidance of prolonged and energetic work with the extremity, to take special precautions on long airplane flights, and to avoid hot temperature environments.

Because the recovery rate is increased when lymphedema is detected early [28], patients should be taught to monitor their limbs for any changes in size or sensation and to recognize the early signs of edema. The following symptoms should be reported to their

care providers: feelings of tightness in the extremities, rings or shoes that don't fit, decreased strength, pain, aching or heaviness, redness, swelling, or signs of infection. Vigilance on the part of the patients combined with close follow-up by surgeons and primary care physicians should provide adequate surveillance for the onset of lymphedema, and thereby ensure prompt and early intervention.

6.2 Treatment Programs for Lymphedema

The most beneficial treatment programs for lymphedema include elevation of the limb which decreases the hydrostatic pressure gradient from the blood vascular system to the tissues. However, to be effective in reducing edema long term, elevation must be combined with other forms of treatment. A compression garment is very important in the treatment program of lymphedema; the garment provides some external support to the skin and can be effective in controlling edema after the limb has been reduced in size. Also the compression garment or bandage should be worn during times of increased activity, as during an exercise program.

Compression garments must be combined with other treatment techniques, such as pneumatic compression and massage techniques, for effective management of lymphedema. Massage techniques are very helpful for patients who cannot tolerate pneumatic compression pumps. The massage is performed in the direction of normal lymphatic flow by using light and sequential strokes. The technique increases the

lymphatic fluids transport capacity leading to increases in lymphatic drainage. In addition to massage, or as an alternative to massage, limb reduction may be obtained through external mechanical compression via a pneumatic single or multiple-cell sleeve, using a pressurizing pump. These devices intermittently inflate and deflate the sleeve which delivers a uniform pressure over the limb or desired limb segment. Pneumatic compression pumps provides a safe and effective treatment for lymphedema; this approach is noninvasive and is usually well tolerated.

The benzo-pyrones, used in some other countries but not in the United States (since they are not FDA approved), reduce all high-protein edemas by increasing the numbers of macrophages and their normal proteolysis. Thus, they remove the excess protein, and thereby the edema which is caused by it. Finally, surgery has been advocated in some cases of lymphedema, but this has not resulted in significantly better results.

In summary, it is noted that successful management of lymphedema depends on the proper blend of treatment modalities. The combination that works best may be different for each patient.

6.3 Experimental Results of the Pneumatic Pump Tests

An evaluation and comparison of four pneumatic compression pumps (Flow-Plus by Huntleigh, Bio-Compression System, Jobst Extremity System, and Wright Linear Pump)

was made to determine their characteristics. Based on the test results speculations can be made related to the most effective methods for treatment of lymphedematous limbs using compression therapy. Two different techniques were investigated, the technique of using a single-cell system and that of the using a multi-cell system, where the number of cells varied from one pneumatic pump to another. The Flow-Plus pump uses a single cell system which applies pressure into the distal section of the sleeve with an open orifice in the proximal end of the sleeve in order to create a pressure gradient inside the sleeve; this produces an unregulated pressure inside the sleeve which makes it difficult to control the treatment program (Section 4.5), so the Flow-Plus pump may not be an effective pump for compression therapy.

The Bio-Compression pump is a 6-cell unit. The pump might cause backflow instead of gradient pressure over portions of the cycle since at times it applies higher pressures to the more proximal cells then to the distal ones. The Bio-Compression pump incorporates two rates of compression: "LO" which is a slow long cycle, and "HI" which is a quick fast cycle. Pressure adjustments within each cell of the sleeve are not possible with the Bio-Compression System (Section 4.6). Since it is believed a "milking action" on the limb will expedite the movement of lymphedematous fluid, the Bio-Compression System pump may not be effective for compression therapy.

The Jobst Extremity System employs a series of three overlapping cells sequentially inflated which apply a sequential distal to proximal pattern of compression to the limb. The compression cycle time is fixed at 190 seconds and the pressure can vary from 0 to 100mmHg. The compression cycles are repeated automatically and accurately until the pump is switched off. The Jobst pump prevents backflow simply by having one way interconnecting passages between the cells, from proximal to distal cells. However, pressure adjustments within each cell of the sleeve are not possible with the Jobst Extremity System (Section 4.4).

The Wright Linear Pump is a 3-cell unit which exposes the limb to a distal to proximal pressure gradient. The pump is completely programmable; pressures can be monitored and adjusted for each cell during the course of the cycle. In addition, timing of the cycle as well as the pressurizing time for each cell can be monitored and changed during the course of the therapy (Section 4.3). According to all the experimental testing it is believed that the Wright Linear Pump is the most effective pump for pneumatic compression therapy, since it is the most versatile in allowing the time of each pressure cycle to be set for each cell and in providing a true pressure gradient from distal to proximal.

6.4 Mathematical and Physical Models to Assess Lymphedema

The effectiveness of pneumatic compression treatment does not depend on the degree of swelling but depends on the mobility of the edematous fluid [14, 20, 27, 39]. The distal sites of the lymphedematous limb have softer edema than that of the proximal sites, and thus one should be able to obtain greater reduction of lymphedema at the distal sites of the limb. In addition to limb size, the fluid mobility should be measured so when using pneumatic compression devices the pressure in the sleeve sections can be adjusted to the mobility of the fluid underneath in order to obtain a more effective treatment. The fluid mobility in subcutaneous pitting edematous tissue is significantly different from that in normal tissue.

The measurement of fluid mobility and analysis of the viscoelastic parameters may help determine the degree of edema and be clinically important parameters for the treatment of edema. The proposed technique of determining the volume of the translocated fluid in terms of the applied compressive force as discussed in Section 5.5 (Eq.5-17) depends upon determining two elastic coefficients (spring 1, and 2) of the four viscoelastic material parameters and an applied force/displacement history. The force/displacement history is obtained by applying a force to an area A of skin and measuring the displacement as described in Section 5.6. The viscoelastic parameters are determined from the mathematical model of the mechanical system devised to simulate the translocation of lymphedematous fluid due to external compression, as discussed in

Section 5.4. Once the volume of translocated fluid is determined the "degree of lymphedema" and "reduction of lymphedema" parameters can be calculated as discussed in Section 5.6.

The method summarized above of predicting fluid translocation appears to be rapid and convenient once the apparatus is designed and set up to measure the compression force and displacement. The advantage of such a technique is the ability to make measurements of the fluid translocation volume at any site, which may lead to prediction of the degree of edema and to the reduction of edema. Information as to whether compression treatment is applicable to a patient and if so, how effective the treatment is, may possibly be obtained from such measurements. Any changes in tissue resistance values cause changes in flow rates and changes in the translocated volume of fluid. The viscoelastic properties of tissue vary in different stages of an edematous condition to give different volume flow rates, and the proposed approach may help elucidate some important parameters in treating lymphedema. In contrast, when using only the volumetric measurement approach to assess lymphedema, one determines only the degree of swelling in the limb. Thus, volumetric measurement indicates nothing about the complex changes in the mechanical properties of the tissues due to edema.

6.5 Recommendations for Future Work

There is an urgent need for information regarding lymphedema risk factors to be organized into an effective assessment tool. Dissemination of this knowledge to health care workers, particularly those caring for patients with cancer, will aid the targeting of those most at risk. A rating scale for risk factors would be a very useful aid in the screening of those patients most at risk of developing swelling. Education of these patients regarding measures that they can take to avoid precipitating swelling, and the need to obtain prompt treatment if swelling occurs, will ensure that patients with lymphedema are treated at an earlier stage and with less complications than in most present cases.

Although pneumatic compression therapy appears to be the most effective noninvasive physiotherapy technique for the treatment of lymphedema [40], opinions differ regarding the selection of pneumatic machines. The Wright Linear Pump, Jobst Extremity System, Flow-Plus, and Bio-Compression System employ different methods to compress the limb. Ideally, sleeve pressure, pressure duration at each cell, and the number of treatment sessions should vary from patient to patient depending on the mobility and translocated volume of the edematous fluid. Further clinical investigations are needed to determine the most effective treatments for lymphedema, especially investigation of the testing method for the new surface measurement technique discussed earlier in Section 5.6. The reliability of this technique is clearly dependent on the very stable mechanical and

electrical design of the measuring device. Reliable and accurate measurement techniques are essential to evaluate the changes in the viscoelastic properties of tissues due to treatment of the limb.

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APPENDIX

Derivation of the Differential Equation

The differential equation (5-9) is

$$F + \tau_\varepsilon \dot{F} = k_2 (u + \tau_\sigma \dot{u}) \qquad \text{(A-1)}$$

For a suddenly applied force F_0 and displacement u_0 the initial condition obtained from Eq(5-3) is

$$F_0 = (k_1 + k_2) u_0 \qquad \text{(A-2)}$$

Using the definitions of τ_ε and τ_σ (from Section 5.4)

$$\tau_\varepsilon = \frac{c_1 c_2}{(c_1 + c_2) k_1} \qquad \text{and } \tau_\sigma = \frac{c_1 c_2 (k_1 + k_2)}{(c_1 + c_2) k_1 k_2}$$

k_1 and k_2 are replaced in Eq(A-2) to give

$$\tau_\varepsilon F_0 = k_2 \tau_\sigma u_0 \qquad \text{(A-3)}$$

The differential equation Eq(A-1) is solved for the case where F(t) is a unit step function [1(t)] where the unit-step function is defined as: $1(t) = \begin{cases} 1 & when \quad t \geq 0 \\ 0 & when \quad t < 0 \end{cases}$.

Therefore using Eq(A-3), the initial condition becomes

$$u_0 = \frac{\tau_\varepsilon}{k_2 \tau_\sigma} \qquad \text{(A-4)}$$

Multiply both side of the differential equation Eq(A-1) by $\exp\left(t/\tau_\sigma\right)$ and divide by $k_2 \tau_\sigma$

$$e^{t/\tau_\sigma}\dot{u} + \frac{1}{\tau_\sigma}e^{t/\tau_\sigma}u = e^{t/\tau_\sigma}\left(\frac{F + \tau_\varepsilon \dot{F}}{k_2\tau_\sigma}\right) \qquad \text{(A-5)}$$

For the case where F(t)=1 for t ≥0

$$e^{t/\tau_\sigma}\dot{u} + \frac{1}{\tau_\sigma}e^{t/\tau_\sigma}u = e^{t/\tau_\sigma}\left(\frac{1}{k_2\tau_\sigma}\right) \qquad \text{(A-6)}$$

which can be written as

$$\frac{d}{dt}(e^{t/\tau_\sigma}u) = e^{t/\tau_\sigma}\left(\frac{1}{k_2\tau_\sigma}\right) \qquad \text{(A-7)}$$

Integrating both side of the Eq(A-7) gives

$$e^{t/\tau_\sigma}u = e^{t/\tau_\sigma}\left(\frac{1}{k_2}\right) + C \qquad \text{(A-8)}$$

The constant C can be obtained using the initial condition Eq(A-4) at t=0

$$C = \frac{1}{k_2}\left(\frac{\tau_\varepsilon}{\tau_\sigma} - 1\right) \qquad \text{(A-9)}$$

Substituting back into Eq(A-8) gives the displacement u

$$u(t) = \frac{1}{k_2}\left[1 - \left(1 - \frac{\tau_\varepsilon}{\tau_\sigma}\right)e^{-t/\tau_\sigma}\right] \qquad \text{(A-10)}$$

VITA

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