Abstract: The invention provides a system and method for cardiovascular training. The system of the invention includes one or more inflatable massaging sleeves and a device configured to generate one or more signals indicative of the state of vasodilatation. A processor is configured to determine one or more parameters of the inflation of the sleeves based upon one or more signals obtained by the device and to actuate a pump or compressor to generate an inflation of the one or more sleeves having the determined one or more parameters.
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.
METHOD AND SYSTEM FOR CARDIOVASCULAR TRAINING

BACKGROUND OF THE INVENTION
The following list of references is considered relevant for an understanding of the invention. The references are referred to herein by the number on the following list:


The term "ergoreflex" is used to refer to a strong, static (isometric) contraction of skeletal muscles or a rapid, powerful rhythmic dynamic (heterometric) contraction that causes a pronounced increase in arterial blood pressure, heart rate and respiratory rate. With the onset of contraction, signals are received by the cardiovascular centers from the motor areas of the brain where the voluntary contraction is initiated and from muscle receptors that sense the degree of activity of the contracting muscles.

The ergoreflex is modified in individuals with chronic heart failure (CHF), and this is thought to play a major role in the development of their symptoms and their long-term prognosis. Reduced exercise capacity with increased breathlessness and muscle fatigue is a major cause of morbidity in individuals with stable CHF who limit physical activity to avoid these symptoms. This results in de-conditioning and often leads to a vicious circle of progressively worsening exercise tolerance.

Several observations raise the possibility that changes in the periphery and not in the heart itself are important determinants of exercise performance in CHF. First, left ventricular function and systemic hemodynamic correlate poorly with exercise capacity. Second, although central hemodynamic improvement with drug therapy or heart transplantation is rapid, an increase in exercise capacity is delayed for weeks or months. Third, interventions acting on peripheral muscle metabolism such as physical training, can improve the exercise tolerance of CHF individuals without affecting their cardiac output. These findings suggest that in CHF individuals, an elevated ventilatory response to exercise may be related to an abnormally overactive ergoreflex.

Such an abnormally overactive ergoreflex has been clearly demonstrated in chronic heart failure individuals when forearm muscles and small muscles of the leg are activated. It has been proposed that the up-regulated ergoreflex plays a key role not only in the origin of the limiting symptoms in CHF but also in the progression of the syndrome by maintaining and stimulating compensatory mechanisms that are deleterious in the long term.

The central role of the periphery in the development of CHF symptoms leads to the development of the "muscle hypothesis". This hypothesis proposes another cycle of deterioration similar to those of neuroendocrine activation. A reduction in left ventricular function sets in motion a series of metabolic events that lead to wasting of skeletal muscle and resultant abnormalities of muscular metabolism and function. In response to early metabolic distress in exercising muscle, an exaggerated ergoreflex
activation occurs that is perceived by the individual as both muscle fatigue and dyspnea and that leads reflexively to excessive sympathetic vasoconstrictor drive to nonexercising vascular beds and an excessive ventilatory response to exercise. Persistent sympathetic activity may eventually lead to a progressive effect on remodeling of the left ventricle.

It was reported that enhanced ergoreflex in CHF individuals is attenuated by exercise training\textsuperscript{11}. The mechanisms by which exercise training improves physiology in CHF are not clear. This intervention has been shown to partially reverse early muscle acidosis and improve peripheral hemodynamics. It has been proposed that improvement in muscle function reduces the abnormal stimulation of the ergoreflex metabol-receptors, thus allowing the physiological balance to improve. The beneficial structural and metabolic changes, which are observed in skeletal muscles of trained CHF individuals, are thought to be the result of a significant improvement in blood supply to the trained muscle due to enhanced endothelial dependent vasodilatation.

A pivotal role of the endothelium in coordinating tissue perfusion has been recognized in heart failure. Studies demonstrate that endothelium-dependent dilation of blood vessels is impaired in heart failure, which may contribute to a reduction in muscle perfusion. Supplementation with L-arginine (a nitric-oxide precursor) improves abnormal vasodilatation in response to acetylcholine or an ischemic stimulus in heart failure individuals.

The impairment in endothelial-dependent vasodilatation is correlated with the degree of exercise intolerance and of the so-called New-York Heart Association class. Improvement in endothelial dysfunction is associated with improved exercise tolerance and the individual’s sensation of well-being.

In CHF individuals, regular aerobic exercise of the legs (cycle training) improved both basal and stimulated endothelial nitric-oxide (NO) formation and agonist mediated endothelium-dependent vasodilatation of the skeletal muscle vasculature. Correction of endothelium dysfunction was associated with a significant increase in exercise capacity. Previous studies have reported improved vascular endothelial function in the upper-limb after handgrip exercise training in CHF subjects. However, the increase in NO production and the subsequent vascular benefit may be generalized to the entire circulation rather than limited to the skeletal muscle bed directly involved in the training stimulus.
These observations are in agreement with another study that demonstrated post exercise improvement in endothelium-dependent vasodilatation in epicardial vessels, as well as in resistance vessels, in individuals with coronary artery disease. After 4 weeks of cycle training, the exercise group in this study had a 29% increase in coronary artery flow-reserve in comparison with the nonexercise control group. Furthermore, experimentally, repeated exercise induces a sustained increase in the expression of endothelial constitutive NO-synthase. It seems, therefore, that repetitive increases in flow, as a result of exercise training, induced a chronic adaptation of the NO vasodilator system. This improvement in flow-mediated dilatation was shown to reverse about 6 weeks after the cessation of forearm hand-grip exercise in CHF individuals. These data suggest, therefore, that an exercise program, at some as yet undetermined level, might be necessary to maintain the beneficial effect.

Intermittent pneumatic compression (IPC) of the limbs has been found to mimic the effect of muscle training on the vascular beds. Muscle contraction and IPC sleeve inflation were both found to significantly increase the shearing forces over the endothelial cells. When intermittent external pressure is applied to individual limbs, the sudden compression causes a forward pulsatile venous blood flow resulting in complete draining of blood at the compression site. The distention caused by the rush of blood volume imposes a compressive strain on the venous endothelial cells, while the increased flow velocity imposes an increased shear stress on the same endothelial cells.

Studies have shown that when cultured endothelial cell are exposed to mechanical shear stress (laminar flow at 16 to 20 dynes per cm²), endothelial nitric oxide synthase mRNA is up-regulated. Increased shear on the superior mesenteric artery of rats also increased nitric- oxide synthesis.

Moreover, when cultured endothelial cells were subjected to a 24% cyclic strain at 60 cycles/min, they exhibited a significantly increased endothelial nitric oxide syntheses activity when compared with stationary (unstrained) controls. In an in-vivo study of 80 male rats, vasodilatation was maximal by 30 minutes after initiation of IPC treatment. This vasodilatation effect was completely blocked by an inhibitor of nitric oxide (NG - monomethyl - L arginine), implying a positive role of nitric- oxide in vasodilation.

The rate of pressure development (dp/dt) produced by IPC devices was found to be an important factor in determining the modulation of distant microcirculation
induced by the treatment, while peak-pressure duration did not. The shorter the inflation time that is needed to reach the device target pressure, the greater the vasodilatation effect achieved. Assuming that the higher the dp/dt, the faster the peak flow velocity, the data are consistent with the hypothesis that increased shear stress on the vascular wall stimulates vascular endothelium to release NO causing vasodilatation.

The IPC effect on the human microcirculation was studied in intermittent claudication individuals. Improved walking ability, resting-ankle brachial index and post exercise ankle brachial index were reported in these individuals. Moreover, the treated group increased arterial calf inflow by 36%.

Some insight into the effect of IPC treatment in CHF individuals can be derived from studies that have been done on ischemic heart disease (IHD) individuals treated with Enhanced External Counter-Pulsation devices (EECP). These devices include an electrocardiograph (ECG) device in order to monitor the heart cycle and create an intermittent pressure on the lower part of the body that counteracts the pulsations of the heart and its acute hemodynamic effects thus simulating an intra aortic balloon pump.

It has been found that EECP improves peripheral endothelial function in individuals with advanced coronary artery disease. Moreover, it was shown that individuals who experience clinical improvement during EECP show an additional enhancement of their endothelial dependent vasodilation one month after completion of therapy. The EECP treatment thus appears to provide hemodynamic stimuli similar to those of physical exercise that contribute to the improvement in endothelial function. EECP was shown to improve exercise tolerance in CHF, to increase coronary flow reserve and to reduce high arterial blood pressure. However, this treatment device is very expensive, the individual is confined to bed during the treatment and the treatment must be given in special clinics under close supervision.

**SUMMARY OF THE INVENTION**

The present invention provides a method and system for cardiovascular training in an individual. The invention may be used, for example, for treating an over-active ergoreflex such as occurs in CHF, for increasing the coronary flow reserve in IHD and for reduction of blood pressure in hypertensive individuals. The invention is
particularly useful in cases of impaired exercise tolerance in which adequate muscle
training may be problematic and even impossible.

In accordance with the invention, intermittent compression is administered to
one or more body limbs of the individual. The state of vasodilatation of the individual is
monitored as the compression is administered, and the parameters of the compression
are modulated in accordance with the individual's state of vasodilatation.

The system of the invention includes one or more massaging sleeves for applying
intermittent pressure to a body limb of the individual. The massaging sleeves are typically
divided into a plurality of individually inflated cells along its length, with each cell being
connected to a control unit by a separate hose. The cells are inflated by a pump or
compressor that delivers a compressed fluid, preferably ambient air to each cell via each
cell's dedicated hose. The pump or compressor is actuated by a processor that is configured
to execute a desired temporo-spatial regime of inflation and deflation of the cells. For
example, the processor may be configured to operate the pump or compressor so as to
generate peristaltic contractions of the sleeve.

The system of the invention further comprises a device for monitoring one or
more parameters indicative of the individual's state of vasodilatation. The device may
be, for example, a finger plethysmograph, a peripheral pulse pressure signal, a pulse
oximetry signal, or an impedance meter that monitors changes in blood vessel
impedance. Signals generated by the device are input to the processor. This is in
contrast to the EECP systems which include a device that monitors the heart cycle. The
processor is configured to actuate the pump or compressor according to a control
algorithm in which the parameters of the inflation-deflation regime generated in the
sleeve are determined based upon measurements received from the device. The control
algorithm allows, preferably in real time, optimization of the pressure profile applied to
the body limb by the system in accordance with the individual's exercise level and
clinical status.

The system of the invention may include a remotely located service center that
communicates with the processor. Data received at the service center may be further
processed and then communicated to a medical caregiver. Analysis of the data may be
transmitted to the processor to be made available to the individual or a medical
caregiver adjacent to the individual. The service center may be manned by an operator
who may study and analyze the data received from the device. The operator may also be
capable of voice communication with the individual in order to advise the individual on using the apparatus, for example, the setting of the values of the various operating parameters of the inflation.

The processor may make a preliminary analysis of the input signals, thereby generating a set of analyzed data that is used by the processor to modify the parameters of the treatment. The data maybe transmitted to the service center for further analysis either automatically or by an operator), and the results of this analysis transmitted back to the processor of the system, and used by the processor to modify the parameters of the treatment. Thus, communication between the processor and the service center may be bi-directional. Data may be stored in a memory associated with the processor and/or the service center in order to detect rends in the individual's response to the treatment, and to evaluate to what extent the treatment is succeeding. The processor and/or the service center may provide a diagnosis of the individual's condition based upon the input signals.

In one possible control algorithm, an integer N operational stages are specified that are numbered from 1 to N. Each operational stage is characterized by a specific pump rate, rate of pressure development ,maximal pressure developed on the limb, and the duration of the maximum pressure. The higher the operational stage number, the higher the pump rate and the developed pressure. Moving from a low operational stage to a higher one increases the efficacy of the massaging, and therefore a higher level of vasodilatation is expected. An initial vasodilatation measurement VDM0 is obtained by the device in the absence of applied pressure while the individual is at rest. In one embodiment, the operational state is progressively increased until a vasodilatation measurement is obtained by the device that is greater than VDM0. In another embodiment, the operational state is progressively increased until a vasodilatation measurement is obtained by the device that is within a predetermined range.

The system of the invention may optionally include sensors for determining changes in the individual's tolerance to exercise, and hence his level of rehabilitation. Such sensors may include an ECG device for monitoring heart rate, a sphygmomanometer for monitoring blood pressure, and sensor for sensing respiratory rate. Measurements obtained by any one or more of such sensors can be communicated to the processor and stored in the memory, and possibly communicated to a remote service center.
Monitoring the maximal heart rate during treatment with the system of the invention provides information on both the individual's compliance with the exercise protocol, and for the individual's reconditioning and level of rehabilitation. Heart rate reduction at rest and during sub-maximal exercise is usually considered an improvement in the individual's exercise tolerance. Following the long-term changes of heart rate variability (HRV) during interventions that are believed to accelerate rehabilitation of the ergoreflex and improve the ischemic threshold is of clinical importance. This information may be used to change the treatment strategy.

Monitoring blood pressure during treatment with system of the invention can also be used to monitor the individual's level of rehabilitation. Peripheral resistance normally decreases during exercise. This occurs because of the tremendous increase in blood flow to working skeletal muscle. Vasoconstriction in non-exercising tissue is not enough to compensate for the vasodilatation in active muscles. However, blood pressure does not fall during exercise, it increases. Cardiac output increases greatly during exercise, which more than compensates, in normal individuals, for the fall in peripheral resistance. Systolic blood pressure usually rises steadily during exercise with only mild effect on the diastolic blood pressure. This situation leads to a significant increase in pulse pressure and mean arterial pressure during exercise. Failure to increase systolic and mean arterial blood pressures during exercise suggests heart failure. A fall in these pressures near the end of an exercise is particularly dangerous. Typically, diastolic pressure remains unchanged or slightly decreases (less than 10 mmHg) during exercise. A significant increase in diastolic pressure (>15mmHg or above ll0mmHg) is associated with a greater prevalence of coronary artery disease, and CHF.

Endurance training reduces resting and sub-maximal exercise, systolic, diastolic, and mean arterial blood pressures. Diastolic and mean arterial blood pressures are reduced also at maximal exercise, while training usually has no effect on maximum systolic blood pressure. Long term follow up of pressure parameters can therefore provide a reliable indication of the individual's rehabilitation progress.

The combination of a high heart rate and systolic blood pressure suggests a high oxygen demand of the heart. In fact the rate-pressure product (the "Duble Product") is a useful predictor of myocardial load. One of the goals of training is a gradual decrease in the individual's rest and exercise rate-pressure product.
Monitoring respiratory rate during treatment with system of the invention can also be used to monitor the individual's level of rehabilitation. Symptoms in individuals with heart failure are related to an excessive increase in blood lactate during low exercise levels, reduction of oxygen consumption at peak exercise and a disproportionate increase in ventilation at sub-maximal and peak workloads. The increased ventilation assessed by the hyperventilatory response to exercise and the increase in pulmonary dead space leads to rapid and shallow breathing during exercise. Over-active ergoreflex further contributes to this phenomenon.

Exercise training has the potential to improve these abnormalities. The changes are achieved primarily through peripheral mechanisms, with little or no effect on resting left ventricular function. Long term follow up of the individual's respiratory rate at sub-maximal exercise is an indicator of a level of reconditioning of the skeletal muscle and the level of rehabilitation of the heart failure individual. Reduction of the respiratory rate of the individual for a given workload is one of the targets of his rehabilitation program. This desired response is critical for the individual's well being sensation, and is of prognostic value.

Thus, in its first aspect, the present invention provides a system for cardiovascular training comprising:

(a) one or more inflatable massaging sleeves;

(b) a device configured to generate one or more signals indicative of a state of vasodilatation;

(c) a pump or compressor configured to deliver a pressurized fluid to the one or more massaging sleeves; and

(d) a processor configured to determine one or more parameters of the inflation of the sleeve based upon the one or more signals and to actuate the pump or compressor to generate an inflation of the one or more sleeves having the determined one or more parameters.

In its second aspect, the invention provides a method for cardiovascular training of an individual, comprising:

(a) providing a system for cardiovascular training, the system comprising:

(i) one or more inflatable massaging sleeves;
(ii) a device configured to generate one or more signals indicative of a state of vasodilatation;

(iii) a pump or compressor configured to deliver a pressurized fluid to the one or more massaging sleeves; and

(iv) a processor configured to determine one or more parameters of the inflation of the sleeve based upon the one or more signals and to actuate the pump or compressor to generate an inflation of the one or more sleeves having the determined one or more parameters.

(b) designating two or more operational stages of the pump or compressor, each operational stage being specified by values of the one or more parameters of inflation, and

(c) determining an operational stage of the pump or compressor based upon the state of vasodilatation.

In its third aspect, the invention provides a program storage device readable by machine, tangibly embodying a program of instructions executable by the machine to operate a compressor or pump configured to deliver a pressurized fluid to one or more massaging sleeves, comprising:

(a) determining an operational stage of the pump or compressor in a calculation involving an input from a device configured to generate one or more signals indicative of a state of vasodilatation; and

(b) operating the pump or compressor according to the determined operational stage.

In yet another of its aspects, the invention provides computer program product comprising a computer useable medium having computer readable program code embodied therein for operating a compressor or pump configured to deliver a pressurized fluid to one or more massaging sleeves, the computer program product comprising:

computer readable program code for causing the computer to determine an operational stage of the pump or compressor in a calculation involving an input from a device configured to generate one or more signals indicative of a state of vasodilatation; and
computer readable program code for causing the computer to operate the pump or compressor according to the determined operational stage.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Fig. 1 shows schematically a system generally indicated by 1 for cardiovascular training in accordance with one embodiment of the invention. Fig. 2 shows the system 1 in use by an individual 3. The system 1 includes one or more massaging sleeves 2 for applying intermittent pressure to a body limb of the individual. In the system 1, a massaging sleeve 2 is shown adapted for being applied to the individual's leg. This is by way of example only, and the system of the invention may include any number of massaging sleeves adapted for applying intermittent pressure to any one or more body limbs. For example, the system of the invention may include a massaging sleeve on each of the individual's calves, on each of his arms, on one or both thighs, on an arm and a calf, etc. The sleeve or sleeves 2 has an inner surface 4 and an outer surface 6 composed of a flexible, fluid impervious material. The sleeve or sleeves 2 may be divided into a plurality of cells 8 along its length. Eight cells 8, cells 8a to 8h, are shown in the sleeve 2. This is by way of example only, and the sleeve 2 may have any number of cells 8. Each cell 8 is connected to a control unit 10 by a respective hose 12. The hoses 12 may be enclosed in a common sheath 14, as shown in Fig. 2. Sections of the sleeve 2 may be non-inflatable, for example, a section 14 adapted to be applied around the individual's knee.

The control unit 10 contains a compressor 16 capable of compressing and pumping ambient air individually into each of the one or more cells 8 of the sleeve 2 via the hoses 12. The control unit 10 is preferably adapted to be worn by the individual, for example on the user's hip, as shown in Fig. 2. The control unit 3 also includes a processor 18 configured to actuate the compressor 16 so that the compressor 16 executes a desired temporo-spatial regime of inflation and deflation of the cells 8. For example, the processor 18 may be configured to operate the compressor 16 so that the compressor generates peristaltic contractions of the sleeve 2. In this regime of contractions, the distal most cell 8a is first inflated and then the next cell 8b is inflated. The cell 8a is then deflated while the cell 8c is inflated. This pattern continues until the proximal most cell 8h is inflated. This pattern of inflation and deflation is then repeated so as to force fluids inside the limb towards the proximal end of the limb. As another example, the processor 18 may be
configured to actuate the compressor 16 so as to create a regime of inflation and deflation that enhances the flow of the venous blood in the limb.

In a preferred embodiment of the invention, each of the cells 8 of the sleeve 2 are divided into two or more confluent compartments 20 that are inflated and deflated simultaneously, as disclosed in US Patent No. 6,447,467, which is incorporated herein in its entirety by reference. As explained in that patent, in this case, the sleeve may be worn under the individual's clothing, as indicated in Fig. 2 by the cut away trouser leg 22. This allows the individual to be ambulatory while using the system 1. In particular, the system 1 may be used while the individual is exercising, as shown in Fig. 2.

The system 1 further comprises a device 24 for monitoring one or more parameters indicative of the individual's state of vasodilatation. In the embodiment shown in Figs. 1 and 2, the device 24 is a finger plethysmograph that is applied to a finger of the individual for monitoring the peripheral state of vasodilatation. A reduction in sympathetic tone and improvement in endothelial function have been shown to produce an increase in finger pulse-wave amplitude (PWA) as measured by a plethysmograph. Alternatively, the device 24 may be, for example, a peripheral pulse pressure signal, a pulse oximetry signal, or an impedance meter that monitors changes in blood vessel impedance.

The system 1 may optionally include sensors 11 for monitoring one or more parameters indicative of the individual's tolerance to exercise. Such sensors may include an ECG device for monitoring heart rate, a sphygmomanometer for monitoring blood pressure, and sensor for sensing respiratory rate. Measurements obtained by any one or more of such sensors can be communicated to the processor 18 and stored in the memory 19.

Signals generated by the device 24, and/or device 11 when present, are input to the processor 18, either by a wired connection, or more preferably by a wireless connection, as shown in Figs. 1 and 2. For example, communication from the device 24 and/or the device 11 to the processor 18 may utilize a Bluetooth protocol. In the case of a wireless connection, the device 24 and/or the device 11 is provided with a transceiver 25, and the controller 10 includes a transceiver 27 connected to the processor 18. The processor 18 has a memory 19 for storing measurement values obtained by the devices 24 and 11, as well as the result of any calculations performed by the processor 18.
The processor 18 is configured to actuate the compressor 16 so as to execute a control algorithm in which the parameters of the inflation-deflation regime generated in the sleeve 2 are determined based upon signals received from the device 24. The control algorithm allows, preferably in real time, optimization of the pressure profile applied to the body limb by the system 1 in accordance with the individual’s exercise level and clinical status. The algorithm may be used for operating the system 1 either in conjunction with simultaneous exercise training, or without simultaneous exercise. The controller 10 may also include an alarm 21 that is activated by the processor when a potentially dangerous situation arises, as explained below.

The processor 18 may be configured to store in the memory 19 parameters relating to the use of the system 1. Such parameters may include, for example, treatment duration per session, total treatment duration per day, types of sleeves used, the control algorithm used during each treatment session and the characteristics of the final "optimal stage" that was achieved during that session. Evaluation of these parameters can provide information on the compliance of the individual with a prescribed treatment protocol.

The system 1 may include a remotely located service center 17. In this case, the processor 18 is configured to communicate with the remotely located service center 17. The service center 17 may be manned or unmanned. Communication between the processor 18 and the service center 17 may be via a wired or a wireless connection. For example, the controller may be adapted for connection to a mobile or wired telephone and data transmitted to the service center 17 over a telephone network. Alternatively, data in the memory 19 may be downloaded onto a PC and transmitted over the Internet to the service station 19. The data received at the service center 17 may be further processed and then communicated to medical caregiver. Analysis of the data may be transmitted to the processor 18 to be made available to the individual or a medical caregiver adjacent to the individual. The processor 18 may use results from the service center to modify the actuation of the compressor 16. The service center 17 may also assist the individual in using the system 1. The processor 18 and/or the service center 17 may be capable of generating a diagnosis responsive to a physiological variable of the user.

Fig. 3 shows a control algorithm carried out by the processor 18, in accordance with one embodiment of the invention. The control algorithm of Fig. 3 consists of an
integer N of operational stages that are numbered from 1 to N. Each operational stage is
categorized by a specific pump rate (frequency), rate of pressure development (dp/dt),
maximal pressure developed on the limb, and the duration of the maximal pressure. For
example, a typical operation state may be specified by a pump rate of 3 cycles of
inflation-deflation of the sleeve per minute, a pressure development rate of 200mm
Hg/sec, a maximum inflation pressure of 100 mmHg, and a duration of maximum
pressure of 2 seconds. The higher the operational stage number, the higher the pump
rate and the developed pressure.

As shown in Fig. 3, in step 30, an initial vasodilatation measurement VDM₀ is
obtained by the device 24 and input to the processor 18 with the individual at rest and
with the compressor not actuated. This initial vasodilatation measurement VDM₀, obtained
in the absence of applied pressure while the individual is at rest, is referred to
herein as the "baseline vasodilatation measurement", and serves as a reference.

When the system 10 is to be activated during exercise, the exercise is started
after obtaining VDM₀ with the compressor not activated. After a predetermined amount
of time, such as five minutes, of exercise, a vasodilatation measurement is obtained
from the device 24 (step 32). This vasodilatation measurement, obtained during exercise
in the absence of applied pressure is referred to herein as "the pure exercise"
vasodilatation state, and is indicated by VDMex. These first two measurements are
stored in the memory 19 of the processor 18 and later transmitted by the communication
subsystem to the service center 17. The relationships between these two parameters
(VDM₀ and VDMex) are important and reflect the rehabilitation status of the CHF
patient. In normal subjects, the endothelial-derived vasodilation in response to exercise
is very significant. However, this response is attenuated in unconditioned CHF patients.

In step 34, the operational state n of the algorithm is set to 1, and in step 35 a
counter k is set to 1. Then in step 36, the processor actuates the compressor 16 to
generate the inflation-deflation regime of the sleeve 2 as specified by the present value
of the operational state of the algorithm. The generation of the inflation-deflation state
specified by the present value of the operational state of the algorithm continues for a
predetermined amount of time, for example, such as 5 minutes of operation. Then, in
step 38 a vasodilatation measurement, indicated by VDMₙ, is obtained by the device 24
while the system 1 is operating in the current operational stage n and input to the
processor 18.
In step 40 it is determined whether \( VDM_n < VDM_0 \). If no, then in step 41 it is determined whether \( n = N \). If no, then the process returns to step 36 with the algorithm remaining at the current operational state until the system 1 is turned off or after a predetermined amount of time, for example, 30 minutes. If at step 41 it is determined that \( n = N \), then, in step 48 it is determined whether the counter \( k \) is equal to a first predetermined constant \( K_i \), which may be, for example, equal to 5. If no, then in step 50, the counter \( k \) is increased by 1 and the process returns to step 36. If yes, the operational stage is deceased by 1 to N-I (step 52). The processor 18 then actuates the compressor 16 to generate the inflation-deflation regime of operational stage N-I (step 54). The process terminates when either a predetermined condition is satisfied, for example, after a predetermined amount of time has lapsed, or when the system 1 is turned off.

If at step 40, it is determined that \( VDM_n < VDM_0 \), then the process continues to step 42 where it is determined whether the current operational stage \( n \) is equal to the maximal stage \( N \). If no, then the operational stage is increased by 1 to \( n+1 \) (step 43) and the process returns to step 36. If yes (i.e. \( n = N \)), then in step 44 it is determined whether the counter \( k \) is equal to a second predetermined number \( K_2 \), which may be, for example, 3. If no, then in step 46, the counter \( k \) is increased by 1 (step 45) and the process returns to step 36. If in step 44 it is determined that the counter \( k \) is equal to \( K_2 \), then, the alarm 21 is sounded (step 46) as a warning that the individual's level of exercise should be reduced. The process then continues (step 47). The process terminates when either a predetermined condition is satisfied, for example, after a predetermined amount of time has lapsed, or when the system 1 is turned off.

The algorithm preferably specifies a "default mode" based upon pressures, inflation rates, and inflation sequences that have been shown to induce endothelial dependent vasodilatation. The default mode may be determined from previous successful treatments of the same individual. When the VDM signal is lost, the processor 18 automatically switches to this mode.

Fig. 4 shows another control algorithm that may be carried out by the processor 18, in accordance with another embodiment of the invention. As with the control algorithm of Fig. 3, the control algorithm of Fig. 4 also consists of an integer \( N \) operational stages that are numbered from 1 to \( N \). Each operational stage is
characterized by a specific pump rate, rate of pressure development and maximal pressure developed on the limb. The higher the operational stage number, the higher the pump rate and the developed pressure.

The algorithm of Fig. 4 is used when it is possible to identify a target range of VDM measurements that can be considered "normal" or "acceptable" for the individual during a certain level of physical activity. This range is defined by the individual's physician, taking into account the individual's clinical status and the desired level of exercise training. This range is considered the "target goal" of the rehabilitation program, and can be changed according to the individual's progress.

The algorithm of Fig. 4 includes several steps in common with the algorithm of Fig. 3. In the algorithm of Fig. 4, after VDMn has been obtained in the step 38, the process continues to step 62 where it is determined whether the VDMn is in the target range. If yes, the process returns to the step 36. If no, then in step 64 it is determined whether the VDMn is above the target range. If yes, then in step 66 the operational mode is decreased by one and the process returns to step 36. If no, then VDMn is below the target range. In this case, the process goes to the step 42 where it is determined whether n=N. If no, then the operational stage is increased by 1 (step 43) and the process returns to step 36. If yes, then in step 49 it is determined whether the counter k is equal to a predetermined number K, which may be, for example, 3. If no, then in step 45, the counter k is increased by 1 and the process returns to step 36. If in step 49 it is determined that the counter k is equal to K, then, in step 46, the alarm 21 is sounded as a warning that the individual's level of exercise should be reduced. The process then continues (step 47). The process terminates when either a predetermined condition is satisfied, for example, after a predetermined amount of time has lapsed, or when the system 1 is turned off.

The operational stage at which the individual is within the target range (referred to herein as the "optimal stage") is recorded, stored in the memory 19 and transmitted to the service center 17. If during the rehabilitation program, the "optimal stage" decreases, this trend suggests good adaptation of the individual to the treatment. The level of the exercise can then be increased and accordingly a new target range for the individual can be set.

When, for example, the algorithm of Fig. 4 is implemented using the heart rate as the VDM, the target range may be defined as a percentage range of a maximal heart
rate previously determined for the individual. In this case, the system assists the individual to reach the desired designated heart rate despite his inability to perform the needed level of physical activity. Although in this case, the device is not programmed to optimize endothelial dependent vasodilation, it fits into traditional cardiac rehabilitation program concepts.

In the algorithms of Figs. 3 and 4, each operational stage may be specified by a pumping rate (f), rate of pressure development (dp/dt), a maximal pressure developed (P), and the duration that the maximal pressure is applied. The higher the operational stage number, the higher the pumping rate and the maximal developed pressure. Moving from a low operational stage to a higher one increases device efficacy and therefore a higher level of vasodilatation is expected.

The processor and/or the service center are configured to alter the parameters of the inflation of the one or more operational stages in the algorithm of Fig. 3 or 4, based upon the vasodilation state of the individual and/or based upon previous results obtained on the subject by the system and stored with either the memory or a memory associated with the service center.

Preferably, each of the above three parameters (pumping rate, rate of pressure development, maximal pressure, and duration of maximal pressure) are individually determined and optimized. A hierarchical scaling among these variables may be determined. The first one to be determined will be the variable that has the highest chance of affecting the clinical target. When the goal is to enhance endothelial function, for example, the first variable to be manipulated is preferably the dp/dt, the second is P and the third is f. All the changes are done on top of a baseline operational stage that can be either the "default mode" of operation or the "optimal stage".
CLAIMS:
1. A system for cardiovascular training comprising:
   (a) one or more inflatable massaging sleeves;
   (b) a device configured to generate one or more signals indicative of a state of vasodilatation;
   (c) a pump or compressor configured to deliver a pressurized fluid to the one or more massaging sleeves; and
   (d) a processor configured to determine one or more parameters of the inflation of the sleeve based upon the one or more signals and to actuate the pump or compressor to generate an inflation of the one or more sleeves having the determined one or more parameters.
2. The system according to Claim 1 further comprising a remote service station.
3. The system according to Claim 1 wherein the device is selected from the group comprising:
   (a) a plethysmograph;
   (b) a peripheral sphygmomanometer;
   (c) a pulse oximeter; and
   (d) an impedance meter.
4. The system according to Claim 1 further comprising one or more sensors monitoring one or more parameters indicative of the individual's tolerance to exercise.
5. The system according to Claim 4 wherein one or more of the sensors is selected from the group comprising a heart rate sensor, a sphygmomanometer, and a sensor for sensing respiratory rate.
6. The system according to Claim 1 wherein at least one massaging sleeve is divided into one or more individually inflatable cells.
7. The system according to Claim 6 wherein at least one cell is divided into two or more confluent compartments.
8. The system according to Claim 1 wherein the parameters of the inflation are any one or more of a pumping rate, a rate of pressure development, a maximum developed pressure, and a duration of maximum pressure.
9. The system according to Claim 1 wherein the processor is configured to actuate the pump or compressor in an algorithm comprising:
(a) designating two or more operational stages of the compressor, each operational stage being specified by values of the one or more parameters of inflation, and
(b) determining an operational stage of the pump or compressor based upon the state of vasodilatation.

10. The system according to Claim 9 wherein the algorithm specifies an integer \( N \) of operational stages numbered 1 to \( N \).

11. The system according to Claim 10 wherein, and the higher the operational stage, the higher the value of one or more parameters selected from a pumping rate, a rate of pressure development, a maximum developed pressure, and a duration of maximum pressure.

12. The system according to Claim 10 or 11 wherein the algorithm further comprises:

   (c) Setting the operational state \( n \) of the algorithm to 1;
   (d) actuating the pump or compressor to generate the inflation-deflation regime of the one or more massaging sleeves as specified by the present value of the operational state;
   (e) obtaining a vasodilatation measurement \( VDM_n \), while the system is operating in the current operational stage \( n \);
   (f) determining whether \( VDM_n \) is less than a baseline VDM;
   (g) increasing the operational stage by 1 and returning to step (d) if the \( VDM_n \) is less than the baseline VDM and \( n \) is not equal to \( N \); and
   (h) returning to step (d) if \( VDM_n \) is not less than the baseline VDM and \( n \) is not equal to \( N \).

13. The system according to Claim 12 wherein the algorithm further comprises:

   (i) setting a counter \( k \) to 1;
   (j) if the \( VDM_n \) is less than the baseline VDM and the current operational stage is equal to \( N \), determining whether the counter \( k \) is equal to a second predetermined number \( K_2 \), and
   (k) If the counter \( k \) is not equal to \( K_2 \), increasing the counter \( k \) by 1 and returning to step (d)

14. The system according to Claim 13 wherein the algorithm further comprises:
If the VDM\textsubscript{n} is not less than the baseline VDM and \( n \) is equal to \( N \), determining whether the counter \( k \) is equal to a first predetermined constant \( K_{i} \),

\begin{enumerate}
  \item if \( k \) is not equal to \( K_{i} \), increasing the counter \( k \) by 1 and returning to step (d);
  \item if \( k \) is equal to \( K_{i} \), decreasing the operational stage by 1 to \( N-I \); and
  \item actuating the pump or compressor to generate the inflation-deflation regime of operational stage \( N-I \).
\end{enumerate}

15. The system according to Claim 13 wherein the algorithm further comprises sounding an alarm if the counter \( k \) is equal to \( K_{2} \).

16. The system according to Claim 10 or 11 wherein the algorithm further comprises:

\begin{enumerate}
  \item Setting the operational state \( n \) of the algorithm to 1;
  \item actuating the pump or compressor to generate the inflation-deflation regime of the one or more massaging sleeves as specified by the present value \( n \) of the operational state;
  \item obtaining a vasodilatation measurement \( VDM_{n} \), while the system is operating in the current operational stage \( n \);
  \item determining whether \( VDM_{n} \) is within a predetermined target range; and
  \item returning to step (d) if the \( VDM_{n} \) is within the predetermined target range.
\end{enumerate}

17. The system according to Claim 16 wherein the algorithm further comprises:

\begin{enumerate}
  \item Determining whether the \( VDM_{n} \) is above the target range; and
  \item decreasing the operational stage by 1 if the \( VDM_{n} \) is above the target range and returning to step (d).
\end{enumerate}

18. The system according to Claim 17 wherein the algorithm further comprises:

\begin{enumerate}
  \item determining whether the current operational stage \( n \) is equal to the maximal stage \( N \) if \( VDM_{n} \) below the target range; and
  \item If the current operational stage \( n \) is not equal to \( N \), increasing the operational stage \( n \) by 1 and returning to step (d).
\end{enumerate}

19. The system according to Claim 18 wherein the algorithm further comprises:
(1) setting a counter \( k \) to 1;

(m) if the current operational stage is equal to \( N \), determining whether the counter \( k \) is equal to a predetermined number \( K \);

(n) If the counter \( k \) is not equal to \( K \), increasing the counter \( k \) by 1 and returning to step (d); and

(o) sounding an alarm if the counter \( k \) is equal to \( K \).

20. A method for cardiovascular training of an individual, comprising:

(a) providing a system for cardiovascular training, the system comprising:

(i) one or more inflatable massaging sleeves;

(ii) a device configured to generate one or more signals indicative of a state of vasodilatation;

(iii) a pump or compressor configured to deliver a pressurized fluid to the one or more massaging sleeves; and

(iv) a processor configured to determine one or more parameters of the inflation of the sleeve based upon the one or more signals and to actuate the pump or compressor to generate an inflation of the one or more sleeves having the determined one or more parameters.

(b) designating two or more operational stages of the pump or compressor, each operational stage being specified by values of the one or more parameters of inflation, and

(c) determining an operational stage of the pump or compressor based upon the state of vasodilatation.

21. The method according to Claim 20 further comprising specifying an integer \( N \) of operational stages numbered 1 to \( N \).

22. The method according to Claim 21 wherein, and the higher the operational stage, the higher the value of one or more parameters selected from a pumping rate, a rate of pressure development, a maximum developed pressure, and a duration of maximum pressure.

23. The method according to Claim 21 or 22 further comprising:

(d) Setting the operational state \( n \) of the algorithm to 1;
(e) actuating the pump or compressor to generate the inflation-deflation regime of the one or more massaging sleeves as specified by the present value of the operational state;

(f) obtaining a vasodilatation measurement $VDM_n$, while the system is operating in the current operational stage $n$;

(g) determining whether $VDM_n$ is less than a baseline VDM;

(h) increasing the operational stage by 1 and returning to step (e) if the VDM$n$ is less than the baseline VDM and $n$ is not equal to $N$; and

(i) returning to step (e) if VDM$n$ is not less than the baseline VDM and $n$ is not equal to $N$.

24. The method according to Claim 23 further comprising:

(j) setting a counter $k$ to 1;

(k) if the VDM$n$ is less than the baseline VDM and the current operational stage is equal to $N$, determining whether the counter $k$ is equal to a second predetermined number $K_2$; and

(l) If the counter $k$ is not equal to $K_2$, increasing the counter $k$ by 1 and returning to step (e)

25. The method according to Claim 24 further comprising:

(m) If the VDM$n$ is not less than the baseline VDM and $n$ is equal to $N$, determining whether the counter $k$ is equal to a first predetermined constant $K_1$;

(n) if $k$ is not equal to $K_1$, increasing the counter $k$ by 1 and returning to step (e);

(o) if $k$ is equal to $K_1$, decreasing the operational stage by 1 to $N-I$; and

(p) actuating the pump or compressor to generate the inflation-deflation regime of operational stage $N-I$.

26. The method according to Claim 25 further comprising sounding an alarm if the counter $k$ is equal to $K_2$.

27. The method according to Claim 20 or 21 wherein the algorithm further comprises:

(d) Setting the operational state $n$ of the algorithm to 1;
(e) actuating the pump or compressor to generate the inflation-deflation regime of the one or more massaging sleeves as specified by the present value \( n \) of the operational state;

(f) obtaining a vasodilatation measurement \( VDM_n \) while the system is operating in the current operational stage \( n \);

(g) determining whether \( VDM_n \) is within a predetermined target range; and

(h) returning to step (e) if the \( VDM_n \) is within the predetermined target range.

28. The method according to Claim 27 wherein the algorithm further comprises:

(i) determining whether the \( VDM_n \) is above the target range; and

(j) decreasing the operational stage by 1 if the \( VDM_n \) is above the target range and returning to step (d).

29. The method according to Claim 28 wherein the algorithm further comprises:

(k) determining whether the current operational stage \( n \) is equal to the maximal stage \( N \) if \( VDM_n \) below the target range; and

(l) If the current operational stage \( n \) is not equal to \( N \), increasing the operational stage \( n \) by 1 and returning to step (e).

30. The method according to Claim 29 wherein the algorithm further comprises:

(m) setting a counter \( k \) to 1;

(n) if the current operational stage is equal to \( N \), determining whether the counter \( k \) is equal to a predetermined number \( K \);

(o) If the counter \( k \) is not equal to \( K \), increasing the counter \( k \) by 1 and returning to step (e); and

(p) sounding an alarm if the counter \( k \) is equal to \( K \).

31. A program storage device readable by machine, tangibly embodying a program of instructions executable by the machine to operate a compressor or pump configured to deliver a pressurized fluid to one or more massaging sleeves, comprising:

(a) determining an operational stage of the pump or compressor in a calculation involving an input from a device configured to generate one or more signals indicative of a state of vasodilatation; and

(b) operating the pump or compressor according to the determined operational stage.
32. A computer program product comprising a computer useable medium having computer readable program code embodied therein for operating a compressor or pump configured to deliver a pressurized fluid to one or more massaging sleeves, the computer program product comprising:

   - computer readable program code for causing the computer to determine an operational stage of the pump or compressor in a calculation involving an input from a device configured to generate one or more signals indicative of a state of vasodilatation;
   - computer readable program code for causing the computer to operate the pump or compressor according to the determined operational stage.

33. A computer program comprising computer program code means for performing all the steps of any one of Claims 20 to 30 when said program is run on a computer.

34. A computer program as claimed in Claim 33 embodied on a computer readable medium.
START

30 Obtain VDM₀

32 Obtain VDMₑₓ

34 Set n = 1

35 Set k = 1

36 Activate compressor to generate inflation-deflation regime of current operational stage

40 VDMₙ < VDM₀?

41 n = N?

42 Yes

43 No

44 k = K₂?

45 Set k = k+1

46 Sound alarm

47 Continue

48 k = K₁?

50 Yes

54 Activate compressor according to operational stage N-1

52 Set n = N-1

END

FIG. 3
START

30 Obtain VDM₀

32 Obtain VDM₁ₓₙₜₑₚ

34 Set n = 1

35 Set k = 1

Activate compressor to generate inflation-deflation regime of current operational stage

36

Obtain VDMₙ

38

Is VDMₙ in target range?

39 Yes

Set n = n - 1

41 No

Is VDMₙ above target range?

42 Yes

n = N?

43 No

k = K?

44 Yes

Sound alarm

45 No

Continue

46

END

FIG. 4