The Method and Apparatus for Peripheral Arterial Disease Treatment

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Keywords: Peripheral Arterial Disease (PAD) Treatment, Cardiosynchronized Sequential Antegrade Pneumocompression (CSAP), Enhanced External Counterpulsation (EECP).

Abstract: The paper is devoted to a new method of peripheral arterial disease (PAD) treatment - cardiosynchronized antegrade pneumocompression. The method is based on sequential compression of the lower extremities to create an enhanced antegrade pressure wave in the arteries in order to increase blood flow in the distal parts of the lower extremities. The main provisions of the method, the physiological model of exposure are considered. It is shown how to optimally synchronize the impulses with the cardiac cycle for the simultaneous achievement of a beneficial hemodynamic effect in the limbs and coronary vessels. The structure of the device for the implementation of the method based on the system for external counterpulsation CARDIOPULSAR is presented. The physiological effects of exposure (increased blood flow, ABPI, temperature of the extremities) were investigated. The results of treatment on volunteers were presented.

1 INTRODUCTION

Peripheral arterial disease of the lower limb arteries (PAD) occur in 2 - 3% of the population, accounting for more than 20% of cardiovascular diseases. *(Dormandy J. et al, Fowkes, F.G.R. et al)*.

Surgical treatments for PAD are widely used but non-invasive methods are also known, including sequential rhythmic pneumatic compression of the lower extremities using inflatable cuffs (not synchronized with the heart rate). In particular, the positive experience of using pneumatic compression in a peripheral wave mode is known (compression levels were exceeded the systolic blood pressure on the brachial artery by 10 - 20 mm Hg) *(Lipnitsky E.M. et al, Delis K.T., Knaggs A.L.)*. In this case the front duration of pneumatic pulses and the delay between successive pulses are on the order of several seconds.

There are also known methods and devices for the treatment of vascular diseases of the lower extremities based on compression of the vessels of the affected extremity with a single cuff synchronized with cardiac activity (ECG) *(Benjamin et al., Dillon RS.)*.

The widely used Enhanced External Counterpulsation method (EECP) *(Conti C.R)* uses separate cuffs for the shins, hips and buttocks. With the help of successive compression in the direction from bottom to top, a retrograde pressure wave is effectively created in the arterial system, which increases myocardial perfusion and a simultaneous release of pressure in the compression cuffs of the extremities, which reduces the systolic work.

Such an effect is capable of producing a whole chain of favorable physiological changes in the body *(Bonetti P.O. et al)*. An increase in coronary blood flow, in particular perfusion pressure, blood flow velocity and shear stress in the coronary arteries, results in the release of vasodilators (NO) and the release of angiogenesis factors (VEGF). Basically, the method is used to treat angina pectoris, coronary heart disease.

This paper describes a method and apparatus for the treatment of peripheral arterial diseases using cardiosynchronized pneumatic compression, which are a development of the previously proposed methods.

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2 METHOD AND EQUIPMENT

The authors proposed a method of treatment for PAD - cardiosynchronized sequential antegrade pneumocompression (CSAP) *(Sudarev A.M., Sudarev A.M., Korotich E.V.)*.

In this method, an effective formation of an antegrade (i.e. towards the distal extremities) wave is achieved by periodic compression of each affected limb separately in two zones - proximal and distal. Compression pulses in the distal zone are delivered after pulses in the proximal zone with a controlled delay.

This pressure wave should enhance blood flow in the distal areas, increases the hydrostatic pressure and shear stress in the vessels in the areas below the affected zones, and increases tissue perfusion. Arterioles and capillaries were chosen as the main targets of exposure.

To obtain the desired effect, a pressure is created in the cuffs that exceeds the level of systolic blood pressure, which leads to the collapse of the arteries and an intensive redistribution of blood to the surrounding regions (Bonetti P.O. et al). A pressure wave arises, propagating in both directions from the point of occlusion. Compression of the second cuff located distal to the first leads to an increase in the pressure wave. In this case, the compression of the first cuff is a "gate" for the blood pushed out from the sections of the vessels located under the distal cuff. The formation of pressure waves is schematically shown in Figure 1. This scheme of action is similar to a peristaltic pump.

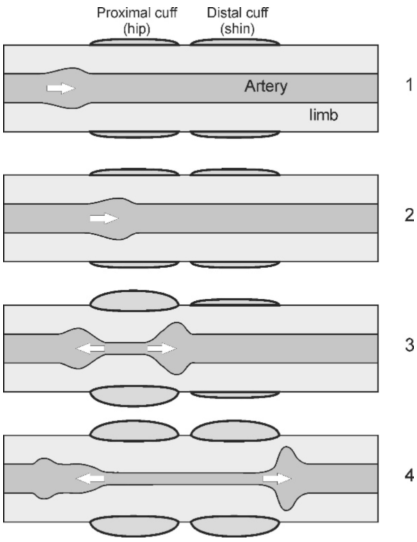

Figure 1: Impact mechanism.

For comparison, we present the schemes of exposure for EECP and CSAP (Figure 2, Figure 3).

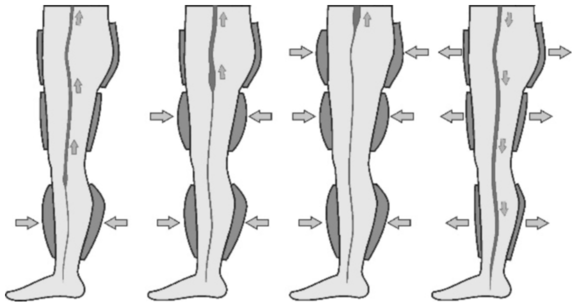

Figure 2: EECP diagram.

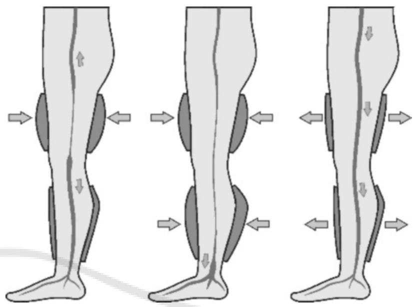

Figure 3: CSAP diagram.

In contrast to sequential rhythmic pneumatic compression, the external pressure slew rate value is fundamentally important, because the change in microcirculation in the distal regions, especially in the terminal arteries, arterioles and capillaries, depends on the compression slew rate in the proximal region. As shown in *(Conti C.R et al, Bonetti P.O. et al)*, with a decrease in the pressure pulse leading edge duration, the maximum attainable pressure in the outer regions increases. Accordingly, an increase in arterial pressure leads to an increase in capillary blood flow. With a slow slew rate, the pressure wave outside the compression zone is shunted by the collaterals and does not reach its maximum possible magnitude.

It was proposed to synchronize the compression pulses with the cardiac cycle in order to ensure the optimal superposition of the native pulse wave with the wave created by pneumatic compression for the most effective increase in perfusion pressure, and, accordingly, blood flow in the distal regions.

As will be shown below, this synchronization may be beneficial for two reasons: it increases the blood flow in the extremities, and it increases the blood flow in the myocardium with a simultaneous decrease in the systolic work. At EECP usage only the second goal is usually achieved.

For the maximum amplification of the wave propagating in the antegrade direction, the moment of the beginning of limb compression was proposed to be synchronized with the propagation of the natural pulse wave maximum through the compression zone. In this case, the superposition of these two waves is maximum. This moment corresponds to the ejection phase at the orifice of the aorta plus a delay in the propagation of the pulse wave from the orifice of the aorta to the site of cuff application. The delay of the impulse in the distal cuff relative to the proximal one should be of the order of the time of propagation of the pulse wave between the cuffs.

The timing diagram of the exposure is shown in the Figure 4.

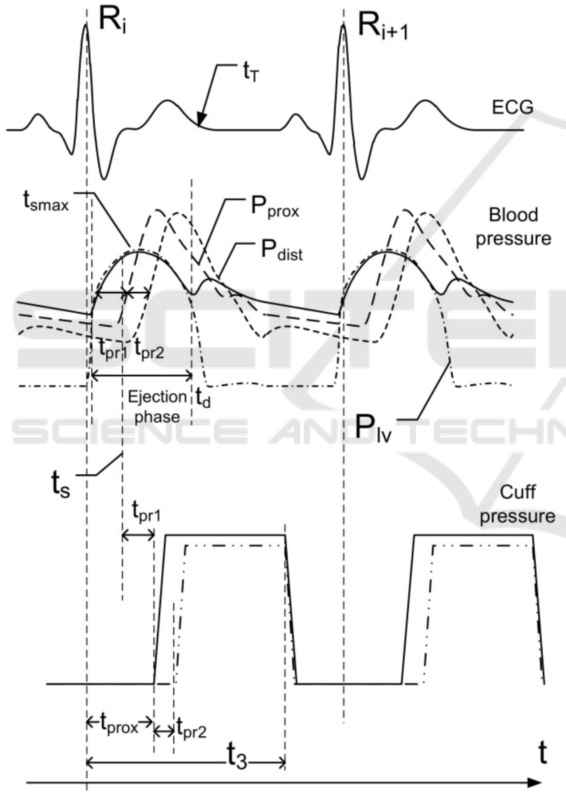

Figure 4: CSAP timing diagram.

Therefore, to maximize the antegrade wave, the time of the onset of the pulse in the proximal cuff is estimated as follows: $t_{prox} = t_s + t_{pr1}$, where t_s is the moment in the interval from the beginning of the ejection phase to the moment of the systolic maximum pressure t_{smax} at the aortic orifice, and t_{pr1} is the time of propagation of the pulse wave from the aortic orifice to the site of the proximal cuff. More accurate determination of t_{prox} could be made experimentally.

On average, t_{smax} (systolic maximum) is separated from the R-peak of the ECG by a time of the order of 0.15 ÷ 0.2 sec.

In this case, $t_{pr1} = L_1 / v$, where v is the speed of the pulse wave in large arteries (4–7 m/sec *(Caro C.G. et al)*), and L_1 is the distance from the aortic orifice to the site of the proximal cuff. When the cuff is applied to the hip, t_{pr1} is about 0.05 ÷ 0.1 sec. This gives t_{prox} (delay in the onset of compression in the hip cuff relative to the R-peak of the ECG) of the order of 0.2 - 0.3 sec.

The delay between pressure pulses in the proximal and distal cuffs is $t_{pr2} = L_2 / v$, where L_2 is the distance between the cuffs, which for t_{pr2} gives about 0.03 ÷ 0.06 sec.

When the vessels are compressed by the proximal cuff, a retrograde pressure wave is also formed, propagating towards the aorta. To increase coronary blood flow in this case (similar to the case of external counterpulsation) it is necessary that it reaches the aortic orifice during diastole. Thus, the lower limit for the beginning of the pressure in the proximal cuff is as follows: $t_{prox} \geq t_d$-t_{pr1}, where t_d is the end of the ejection phase (the aortic valve closure time is about 0.3 sec, approximately corresponding to the end of the T-peak of the ECG *(Caro C. G. et al)*), which gives the limit for t_{prox} - not less than 0.15 ÷ 0.25 sec.

The inflation of the cuffs should be carried out simultaneously before the onset of mechanical systole in order to ensure a decrease in the mechanical work of the heart, similar to the method of EECP *(Conti C.R et al)*.

The described method of exposure was implemented on the basis of the system for external counterpulsation CARDIOPULSAR™ (CONSTEL LLC, Russia) *(www.constel.ru)*.

The general scheme of the device in the antegrade pneumocompression mode is shown in Figure 5. The hip and shin cuffs are used as proximal and distal cuffs, respectively. To synchronize the pressure pulses in the cuffs, an electrocardiogram (ECG) signal was used. Pressure pulses in the cuffs, are given taking into account the delay of the incoming pulse wave in relation to the R-peaks of the ECG. To create the necessary time diagram of the compression effect on the lower extremities the software of the CARDIOPULSAR™ system was modified. A photoplethysmogram sensor placed on the toe was used to monitor changes in blood flow. This sensor can also be used to optimize the exposure timing.

An experimental study of the physiological effect of our proposed new method of pneumocompression (CSAP) was carried out.

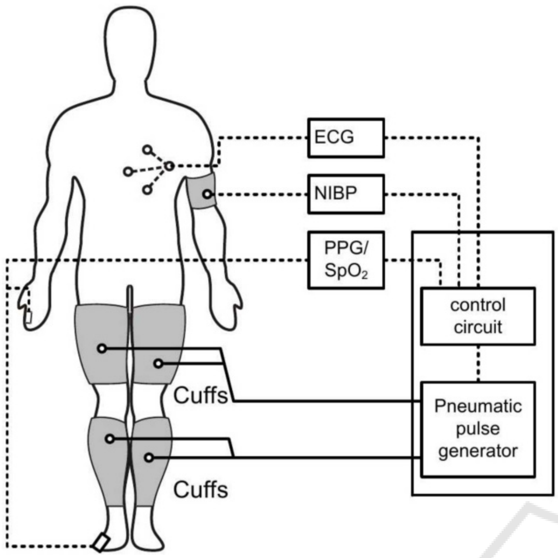

Figure 5: Device diagram.

3 EXPERIMENTAL STUDY AND RESULTS

To study the effect of the cardiosynchronized compression on the circulatory system of the extremities in practically healthy people and patients with PAD an experimental study was carried out to assess the change in blood flow in a toe.

The experimental studies involved volunteers: 4 apparently healthy adult men aged 22 to 50 years and 10 patients with atherosclerosis of the lower extremities, chronic vascular insufficiency of groups 2A and 2B aged 45 to 65 years.

Each episode included a standard 60 minute session.

The graphs (Figure 6 and Figure 7) show typical physiological signals without compression impact (Figure 6) and with impact (Figure 7): ECG signal, cuff pressure plots (hip and shin) and a photoplethysmograph signal (PPG) reflecting the pulse blood filling in the toe.

The difference between ECG signals (Figure 6 and Figure 7) is due to mechanical artifacts during periodic compression.

It can be seen that during the application of the compression, an increase in the pulse wave occurs. The characteristic increase in the PPG amplitude compared to the initial level is 2 to 4 times.

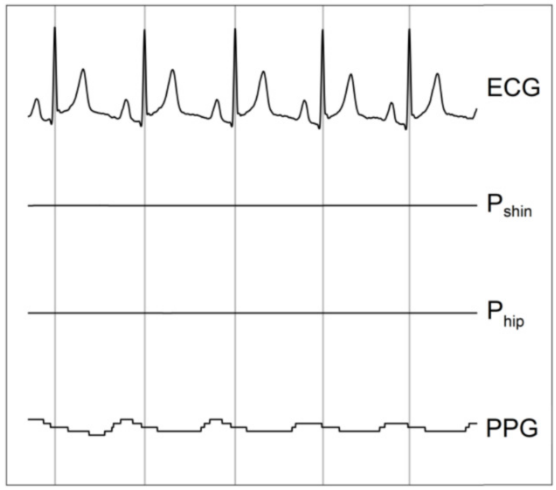

Figure 6: ECG, cuff pressure and PPG before exposure.

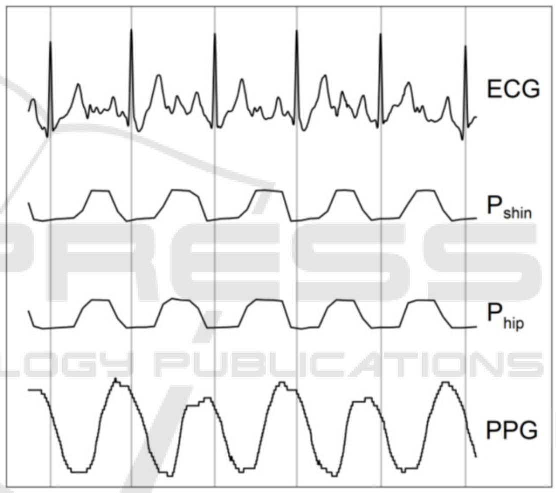

Figure 7: ECG, cuff pressure and PPG during exposure.

We studied the influence of the amplitude-time parameters of pneumatic pulses on the hemodynamic effects. Particularly the dependences of the increase in blood flow in the distal part of the limb (PPG amplitude on the toe) vs the amplitude of the compression pulses and their delay relative to the R-peak of the ECG, were investigated.

The dependence of the PPG amplitude on compression pressure was measured by a sequential increase in the amplitude of the compression pulses with a step of 10 mm Hg approximately every 20 sec. Typical dependences (on 4 subjects coded as S1, S2, S3, S4) in an experiments with a normal level of systolic pressure (<140 mm Hg) of the PPG amplitude vs compression pressure are shown on Figure 8 (solid lines show the interpolation of trends by fourth-order polynomials).

It can be seen that the dependences have a characteristic S-shape. The beginning of the growth of the PPG amplitude begins at compression pressures of 100-120 mm Hg. The maximum values are reached at pressures of 150-250 mm Hg, which corresponds to systolic blood pressure. These results indicate that the maximum effect is achieved with collapse of the arteries under the cuffs.

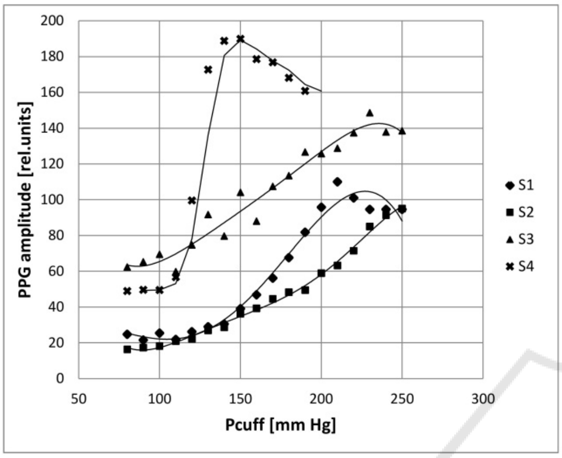

Figure 8: PPG amplitude on the toe vs cuffs pressure.

The amplitude of pneumatic pulses required to maximize blood flow in the distal regions are slightly more than systolic blood pressure. It could be explained by the fact that the actual mechanical stress of the underlying tissues is slightly less than the pressure in the inflatable chambers. The difference therefore depends on the type of compression cuffs (their geometric and design features).

The dependence of the shape and the resulting amplitude of the pulse wave on the delay in the onset of the pressure pulse in the proximal cuff was studied. The characteristic shape of the PPG signal at different delays looks is shown in Figure 9.

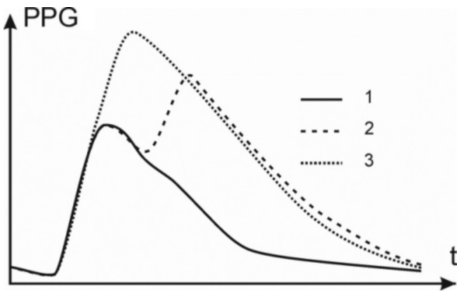

Figure 9: 1 - No action, 2 - long delay, 3 - optimal delay.

The dependence of the PPG amplitude on the toe on the delay between the R-peak of the ECG and the onset of compression in the femoral cuff was investigated experimentally. A typical dependence of the averaged PPG amplitude over approximately 20 cardiac cycles is shown in Figure 10. On the graph, the ordinate shows the delay between the R-peak and the moment when the pressure in the cuff has reached the amplitude value. In this case, the delay between the onset of impulses in the hip and shin cuffs was constant (40 msec). It should be noted that the reported values of the delay may have an error of the order associated with the inaccuracy of the formation of pressure pulses (10–20 msec) relative to the R-peak, as well as with the duration of the pulse front (approximately 70–90 msec).

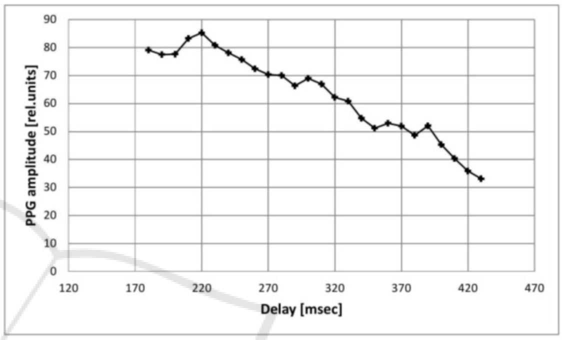

Figure 10: Dependence of the PPG amplitude on the delay between the R-peak and the moment of reaching the nominal pressure in the pulse in the hip cuff.

The graph repeats the characteristic shape of PPG (maximum (plateau) at low values and a smooth decline with increasing delay). This dependence characterizes the superposition of two waves in the distal regions: a natural pulse wave and a wave caused by compression (similar to the effects observed with external counterpulsation).

As a result, the shape and amplitude of the photoplethysmogram in the distal parts of the limb may be used as a feedback signal for more accurate adjustment of the exposure time diagram *(Sudarev A.M., Korotich E.V.)*, since the time of occurrence and the degree of actual compression of the tissues of the extremities by the cuffs depends on often uncontrollable factors: the delay in the measuring and acting tract, the design and degree of the initial tightening of the compression cuffs, the speed of propagation of the pulse wave, etc.

To achieve the maximum effect it is necessary to adjust the delay and the magnitude of the pneumatic impulse pressure achieving the maximum PPG amplitude and the approach of the moment of the maximum of the amplified blood flow wave to the systolic maximum of the natural wave. It should be noted that the decrease in latency should be limited, since the resulting retrograde wave should reach the aortic orifice in the diastolic phase. An excess value of the compression pressure leads to unwanted trauma to the underlying tissues without leading to an effect increase. This is evidenced by the saturation of the dependence of the increase in blood flow when the compression pressure is exceeded by more than 50-70 mm Hg above the systolic pressure levels (Figure 8).

To compare the hemodynamic effect in the distal parts of the limb in the CSAP and EECP modes, experiments were carried out in which the change in the PPG amplitude on the toe in these modes relative to the background level was compared. The gain was measured as $K_{ampl} = PPG_{exp} / PPG_{back}$, where PPG_{exp} is the amplitude of PPG during exposure, and PPG_{back} is the amplitude of PPG without exposure. In healthy volunteers (5 test subjects, 2 experiments carried out at different times), K_{ampl} in the CSAP mode was 1.8 ± 0.3 times higher than in the EECP mode.

Subsequently data on the greater efficiency of enhancing blood flow in the distal regions in the CSAP mode compared to EECP were repeatedly confirmed (in more than 100 patients with PAD) in clinical studies *(Atkov O. U. et al)*.

It is known that the distal parts of patients with PAD are often colder due to circulatory insufficiency. To investigate changes in limb circulation in two patients with PAD, a study was carried out using a thermal imager (IRTIS-2000, Russia).

The surface temperature of the skin, especially the limbs, measured by the thermal imager varies greatly depending on many factors. The experimental conditions (external temperature and long-term adaptation to the lying position) were selected in such a way as to minimize the natural temperature drift as much as possible.

The results of a typical experiment are shown in Figure 11and Figure 12.

The temperature of the toes increases markedly 10-30 minutes after the start of the procedure (up to 1-2 ° C). In addition, preliminary data show that the temperature of the feet increases after a course of procedures. An increase in foot temperature indicates an integral increase in blood circulation.

In the initial period of the study of the effectiveness of the treatment, a series of procedures was carried out in volunteer patients with PAD (diagnosis: atherosclerosis of the lower extremities, chronic vascular insufficiency, stages 2A and 2B by Fountaine), which made it possible to assess the change in the course of the disease and draw a conclusion about the clinical effect. The studies involved 10 patients. Each patient underwent 12 to 15 procedures, 60 minutes each.

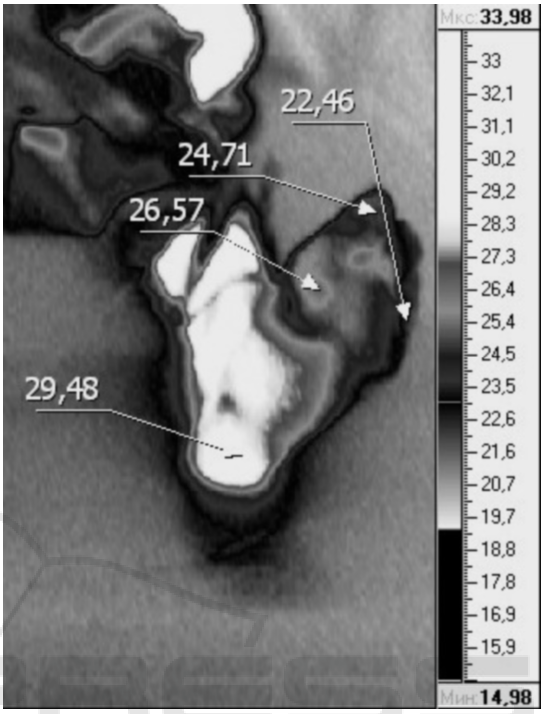

Figure 11: Thermal image before exposure.

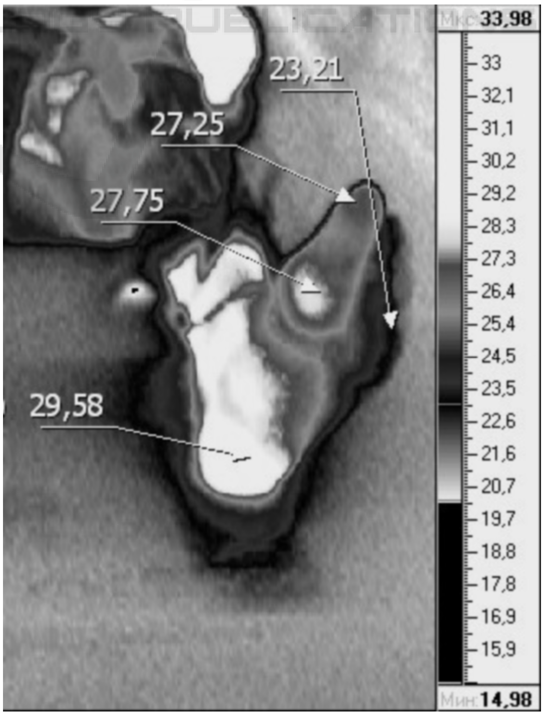

Figure 12: Thermal image (30 min after start of exposure).

All patients showed an increase in exercise tolerance (6-minute walk test until the onset of discomfort and pain in the shin muscles). The increase in distance was from 22 to 100% after the first two procedures.

The measurements of the ankle-brachial index (ABI) were also carried out, calculated as the ratio of arterial systolic pressure in the distal parts of the legs to systolic pressure in the brachial arteries. After a cycle of procedures in each of the patients, the index increased by 0.1 ± 0.05 with the initial values from 0.7 to 0.8.

In all patients with disease stages 2A and 2B, after the first procedure, subjective improvement was noted: discomfort in the limb, a feeling of coldness, especially in the distal parts, a feeling of cold in the legs, the need to keep the distal part of the limb warm during sleep, etc.

After receiving the first positive results, a multiclinic study of the effectiveness of the proposed therapeutic method was carried out on a large group of patients with multifocal atherosclerosis *(Atkov O. U. et al)*. This study showed that the use of the method and the CARDIOPULSAR device leads to an increase of pain-free walking distance, an increase of ankle-brachial pressure index (ABPI), and an improvement of microcirculation. The improvement of life quality estimated by DASI Activity Index and Edinburgh Claudication Questionnaire (ECQ) was also shown.

4 CONCLUSIONS

The method and device of pneumatic compression effect on blood circulation of the extremities for the treatment of PAD achieving an effective increase in blood flow in the distal regions have been developed.

The primary hemodynamic effects of exposure and the dependence of an increase of blood flow in the distal regions on the amplitude-time characteristics of pneumatic pulses were studied.

The results of clinical application of the method on volunteer patients suffering from PAD (obliterating atherosclerosis, endarteritis, diabetic angiopathy) have been obtained, which indicates its promising potential.

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REFERENCES

Atkov O. U., Zudin A. M., Shugushev Z. H ., Orlova M. A., Sudarev A. M., Korotich E. V., Maximkin D . A., Patrikeev A. V. (2015) Short-term results of cardiosynchronized consequential antegrade pneumocompression in patients with multifocal atherosclerosis *Rossijskij kardiologicheskij zhurnal (Russian Journal of Cardiology),* 3 (119): 82–88

Benjamin et al. (1978) Apparatus for promoting blood circulation*. Pat. US 4077402*

Bonetti P.O., Holmes D.R., Lerman A., Barsness G.W. (2003) Enhanced external counterpulsation for ischemic heart disease - What's behind the curtain? *Journal of the American College of Cardiology.; 41:* 11: 1918-1925

Caro, C. G., Pedley, T. J., Schroter, R. C. and Seed, W. A. (1978) The Mechanics of the Circulation, *Oxford University Press*. (527 pp.)

Conti C.R., (1999) EECP-Enhanced External Counterpulsation, *Journal of the American College of Cardiology.; 33*: 7: 1841-1842

Delis K.T., Knaggs A.L. (2005) Duration and amplitude decay of acute arterial leg inflow enhancement with intermittent pneumatic leg compression: an insight into the implicated physiologic mechanisms. *J Vasc Surg.;* 42(4): 717-25.

Dillon R.S. (1997) Fifteen years of experience in treating 2,177 episodes of foot and leg lesions with the circulator boot*. Angiology.;* 48: 17-34

Dillon R.S. (1996) Method for promoting circulation of blood. *Pat US 5514079*

Dormandy, J & Mahir, M & Ascady, G & Balsano, F & de Leeuw, Peter & Blombery, Peter & Bousser, M & Clément, Daboné & Coffman, J & Deutshinoff, A. (1989). Fate of the patient with chronic leg ischaemia. A review article. *The Journal of cardiovascular surgery*. 30. 50-7

Fowkes, F.G.R. & Housley, E & Cawood, E.H.H. & Macintyre, Colin & Ruckley, C.V. & Prescott, Robin. (1991). Edinburgh Artery Study: Prevalence of Asymptomatic and Symptomatic Peripheral Arterial Disease in the General Population. *International journal of epidemiology*. 20. 384-92.

Lipnitsky E.M., Amosov G.G., Morozov K.M., Zateryukin A.B., Platonov A.Yu., Vaidya A. (2007) Rhythmic pneumocompression for treatment of patients with chronic obliterating diseases of the lower-limb arteries *Angiologiya i sosudistaya hirurgiya (Angiology and vascular surgery). 13*: 3: 22-26 (in Russ.)

Sudarev A.M. (2013) Treatment for chronic obliterating diseases of lower limb arteries*. Angiologiya i* *sosudistaya hirurgiya (Angiology and vascular surgery)* 19, 1 . 26 -32 (in Russ.)

Sudarev A.M., Borodyanskaya E.S., D'yachenko A.I. (2010) Modeling of external counterpulsation gemodynamic effects by means of electrical analogs. *III Evrazijskij kongress po medicinskoj fizike i inzhenerii "Medicinskaya fizika - 2010"*; 4: 106-108 (in Russ.)

Sudarev A.M., Korotich E.V. (2016) Method and devices providing impact on cardiovascular system. *Pat. US US2013102939*