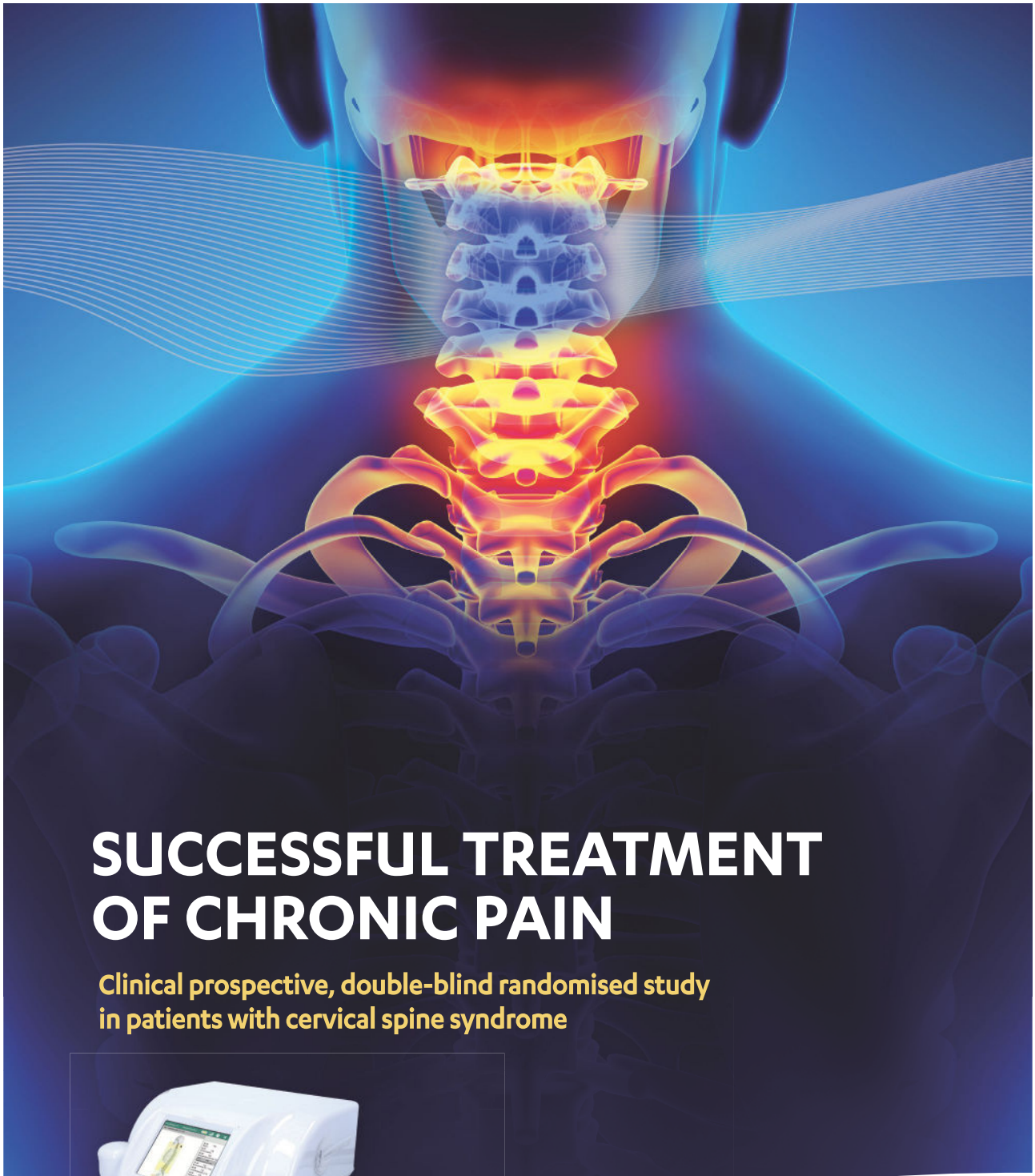

SUCCESSFUL TREATMENT OF CHRONIC PAIN

Clinical prospective, double-blind randomised study in patients with cervical spine syndrome

35 YEARS

RAYONEX
Biomedical GmbH

www.rayonex.de

Successful treatment of chronic pain

Clinical prospective, double-blind, randomised study

in patients with cervical spine syndrome

35 JAHRE RAYONEX Biomedical GmbH

www.rayonex.de

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Cover designed by: Kirchner Company GmbH, 50735 Cologne, Germany
Setting: Tanja Zoppe

Rayonex Biomedical GmbH
Sauerland - Pyramiden 1
57368 Lennestadt (Germany)
Tel: +49 2721 6006-0
Fax: +49 2721 6006-66
Email: info@rayonex.de
www.rayonex.de

Contents of the patient and user information

I. The Rayonex Biomedical GmbH

Rayonex Biomedical GmbH is headquartered in Lennestadt (Sauerland, Germany). It is a well-established medical device company that started over 35 years ago and currently operates in 45 countries around the world. Rayonex represents bioresonance according to Paul Schmidt, a cause-oriented treatment approach, that is named after the company founder and engineer Paul Schmidt. Rayonex Biomedical GmbH is certified to develop, produce and distribute medical devices according to DIN EN ISO 13485:2016 and is audited and certified by TÜV Nord on a yearly basis.

Extraordinary products deserve extraordinary presentation! This is why Rayonex Biomedical GmbH built their company buildings in the shape of a pyramid in 2006. The Headquarters (1), the Therapy and Consultation Centre (2) and the Paul Schmidt Academy (3) for education and further training are located in three of the seven Sauerland pyramids. The Galileo park (4-7), a leisure, science and mystery park houses its exhibition rooms in the other four pyramids.

Rayonex has always manufactured its products, which are Made in Germany, in these pyramids. Due to ever-increasing demand, Rayonex products are now manufactured in the Rayonex factory, which is located only a few hundred metres away from the headquarters. Production is carbon neutral and products are manufactured with high-precision through the use of robots.

In Germany alone, seven regional management teams and over 400 medical device advisers support our users locally. More information on our philosophy, Rayonex products from the areas of human medicine, veterinary medicine, TCM, building biology and wellness, as well as a range of educational and further training programmes can be found at www.rayonex.de.

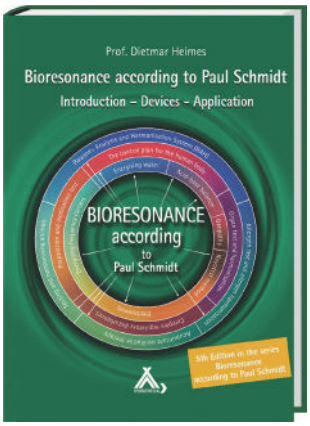
II. Bioresonance according to Paul Schmidt – explained in simple terms

The easiest way to explain bioresonance according to Paul Schmidt is through an example from nature. Surely the most ancient form of bioresonance is our sunlight. When our skin is exposed to sunlight it tans. This is not caused by our skin heating up but instead by the ultraviolet light that is found in sunlight, which has a frequency range in the high terahertz range. The typical frequency spectrum of sunlight can stimulate the production of melanin and thus supports pigment formation. The frequency spectrum of sunlight also stimulates the production of vitamin D in the body.

In 1975, Paul Schmidt discovered that not only does the sunlight's frequency spectrum impact the body, so too do other frequencies and frequency spectra. This marked the birth of bioresonance according to Paul Schmidt. Rayonex Biomedical GmbH continues to research other frequencies and frequency spectra and their effects on humans and animals to this day. To date over 1,800 frequency combinations have been created. These are set on modern bioresonance devices, such as the Rayocomp PS 1000 polar 4.0 med. or the Rayocomp PS 10 med. and are then used to stimulate patients. This is exactly what happens in the clinical prospective, double-blind, randomised study that can be found in Chapter VII of the patient and user information.

In summary, bioresonance according to Paul Schmidt is understood to mean stimulating the body in order to support self-regulation or reactivation.

Many books have already been published on the procedure and use of bioresonance according to Paul Schmidt. Dietmar Heimes's book is a bestseller in alternative medicine: Bioresonance according to Paul Schmidt - Introduction, Devices, Application. This is now available in 7 different languages.



III. Summary of the observational studies, scientific studies and studies on bioresonance according to Paul Schmidt (download at: www.rayonex.de/downloads/studien).

Rayonex has carried out several studies on bioresonance according to Paul Schmidt. The most informative of these is, of course, the new clinical prospective, double-blind, randomised study on pain reduction in patients with cervical spine syndrome (CSS). In addition to these studies, we would also like to draw attention to our reports portal: www.bioresonanz-erfahrungsberichte.de.

1. **Randomised, prospective, double-blind study to provide objective proof of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome (CSS)**
   Topic: Assessing neck pain, which is measured using the Neck Disability Index (NDI), before and after treatment with the Rayocomp bioresonance device and comparing this to the placebo and assessing the safety of the devices during use.

   Carried out using: Rayocomp PS 1000 polar 4.0 med.

   Results: "There was no change in the NDI (Neck-Disability-Index) of the placebo group, but a significant improvement in the NDI of the group treated with the Rayocomp bioresonance device ($p<0.001$)" (see page 15). "Based on the results of this clinical trial and when used for its intended purpose, no adverse effects were detected that could alter the risk profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. All things considered, the results confirmed the favourable safety profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. The device was shown to be safe when used according to the instructions". (see page 21)
   The final study report can be read in Chapter VII of the patient and user information.

2. **Dartsch Study**
   Topic: In vitro studies on the activation of cell metabolism
   in organic-specific cell cultures

   Carried out using: Mini-Rayonex

   Results: In summary, the in vitro studies carried out here confirmed something that had already been observed by users, which was that the Mini-Rayonex had stimulating effects. It is especially worth noting that cell metabolism stimulation increased significantly, by 30% to 45% regardless of the length of application. However, the device should be used for at least a few hours at a time.

3. **Fraunhofer Institute**

Topic: Studies on the effect of harmonising oscillations on cell cultures using Rayonex device technology

Carried out using: Rayocomp PS 1000 polar; Rayocomp PS 10; Thyreogym

Results: Due to their harmonising oscillations, all Rayonex equipment systems increase the metabolic activity of FIBROBLASTS by up to 8%.
The results relating to the repair of KERATINOCYTES are extremely interesting. Damaged cells showed significantly high levels of activity in the cell division phase. This was the case in particular for the Thyreogym, which registered an increase of up to 22% and the PS 1000 which registered an increase of over 40%.

4. **Bachelor thesis by Ms Gina Alberts**

Topic: Is bioresonance therapy helpful in identifying and treating the causes of chronic diseases in horses?

Carried out using: Rayocomp PS 1000 polar

Results: During the period of treatment, on average 53% of the horses showed improvements and 22% of the chronically ill animals were treated successfully. Thus, most of the levels of interference that were diagnosed and treated with bioresonance therapy, no longer produced any resonance frequencies.

5. **Dr. med. Thomas Vieth (Klinikum Chemnitz gGmbH, Clinic for Cardiology)**

Topic: Bioresonance according to Paul Schmidt in cardiology

Carried out using: Rayocomp PS 1000 polar 4.0 med.; Rayocomp PS 10 med.

Results: Both the health of patients and their ability to cope with stress improved. Clinical values in cardiology patients also significantly improved.

Bioresonance therapy according to Paul Schmidt was good and safe to use. It was optimally integrated into the everyday lives of the patients who were selected for this study and had severe health impairments (home therapy). The devices (Rayocomp PS 10 med.) can be independently and easily operated at home.

Most patients treated with this form of therapy reported symptom relief and a clinical improvement in their condition.

6. Case studies on the Rayocomp 1000 polar by Dr. Gerhard Brier, Cologne, October 1993

Topic: Do fine-matter therapy methods that employ the use of resonance frequencies have a healing effect on pathological changes in humans?

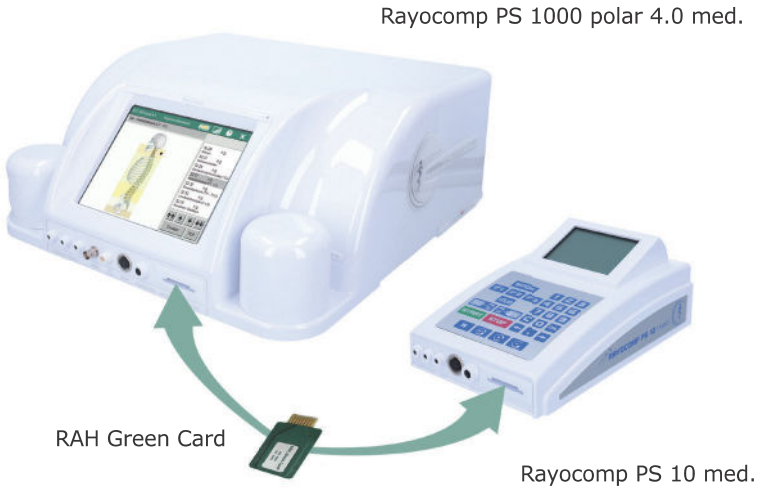
Carried out using: Rayocomp PS 1000 polar

- 514 patients in total
- 12 fields: Dermatology, orthopaedics, neurology, urology, ENT, rheumatology, oncology, circulatory disorders, psychiatry, gastroenterology, ophthalmology, pulmonology.

Results: Rayocomp therapy represents a proven and effective fine-matter aspect of therapy, which is underpinned by a different way of thinking about pathology and therapy, meaning in particular that it includes cellular energy-based modes of action.

IV. The importance of a double-blind, randomised study

Rayonex Biomedical GmbH manufactures two medical devices: the high-med. device, the Rayocomp PS 1000 polar 4.0 med., which can be used as a stationary device in a doctor's surgery and the portable Rayocomp PS 10 med., which is primarily for patients receiving therapy at home. Both devices complement each other perfectly. The therapy programs needed for treatment are compiled on the stationary Rayocomp PS 1000 polar 4.0 in the doctor's surgery. Patients are then either treated in the doctor's office or the programs are stored on a memory card (RAH Green Card) and the patients can then easily use them for treatment at home.



Due to the regulatory requirements for active medical devices, which applies to both of the Rayonex Rayocomp devices, a clinical evaluation must be carried out to prove the safety and effectiveness of the device. While in the past this evidence could be easily provided through reports, the new medical device regulation requires the submission of the highest level of scientific evidence of the effectiveness and safety of the device. This evidence needs to be in the form of a double-blind, randomised study and the study must receive a positive vote from the ethics committee.

What does this entail? In practice this means being able to objectively assess whether a procedure is effective and safe or not.

Therefore, two groups were created in the run-up to the study. One with the Rayocomp PS 1000 polar 4.0 med. taken from the production line and the other with inoperable devices, which were the placebo. Both devices looked and worked in exactly the same way. However, the dipole antenna system, which is normally used in the application of bioresonance treatment according to Paul Schmidt, was missing in the placebo devices. At the start of the study, a validated computer program randomly (randomised) determined which device each new patient would be treated with for the entire duration of the study. Thus, neither patient nor the clinical investigator (double-blind) applying the treatment knew during the study whether the Rayocomp PS 1000 polar 4.0 med. being used was therapeutically effective or not.

For this reason a randomised, double-blind study is considered to be the best type of study because unblinding (telling patients and investigators which devices really worked) only takes place after the results have been analysed.

At the end of studies like these, patients are usually careful about what they say and do not appear enthusiastic because they don’t want to say that the therapy helped them and then to find out that they had been treated with a placebo device.

This is why randomised, double-blind studies are held in such high regard. It is because results are based on completely objective, somewhat conservative accounts.

V. The Compact Program 71.60 used in the clinical prospective, double-blind, randomised study to provide objective evidence of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome.

Many chronic illnesses do not have one single cause but are the result of a wide variety of factors (e.g. genetic, lifestyle, environmental factors). The compilation of the therapy program for the study on cervical spine syndrome was selected in such a way that all possible causes were covered as multifactorially as possible due to the fact that individual tests were excluded from the study.

A number of different programs were created by experts in the field of bioresonance according to Paul Schmidt, which eventually gave rise to the study's compact program. The original compact program from the study and over 180 pre-existing compact programs are available on the Rayocomp devices.

All study participants received 10 treatment sessions with the compact program within a period of 70 days.

Below you'll find the contents of the compact program used in the study:

Energy supply:

- ❖ Frequency pattern of the pre-control
- ❖ Frequency pattern of the polarity balance
- ❖ Frequency pattern of the chakras
- ❖ Frequency pattern of the acupuncture meridians
- ❖ Frequency pattern of the ATP production

Causes:

- ❖ Frequency pattern of minerals, vitamins and hyaluronic acid, for example, to promote absorption or metabolization and counteract a deficiency.
- ❖ Frequency pattern of heavy metals
- ❖ Frequency pattern of spider and snake venoms
- ❖ Frequency pattern of environmental toxins
- ❖ Frequency pattern of relevant pathogens (bacteria, viruses, parasites and fungi)

Physiology:

- ❖ Physiological frequency pattern of the skeleton
- ❖ Physiological frequency pattern of the muscles
- ❖ Physiological frequency pattern of the immune system
- ❖ Physiological frequency pattern of the lymphatic system
- ❖ Accessory nerve
  (11th cranial nerve, motor nerve = damage causes paralysis of the trapezius and sternocleidomastoid muscles)
- ❖ Medulla oblangata (control organ in the brain. Receptors that regulate the acid-base balance among other things.

Pathology:

Frequency pattern that relieves the following list of possible symptoms of CSS:

- ❖ Pain (sense of pressure or pain on percussion) in the neck-shoulder area above the spine
- ❖ Pain in the musculature of the neck and shoulder due to hardening and tensions
- ❖ Sensory disturbances (tingling, numbness in the shoulder and neck)
- ❖ Signs of paralysis
- ❖ Headache
- ❖ Dizziness
- ❖ Visual and hearing disorders
- ❖ Tinnitus
- ❖ Whiplash

Frequency pattern that relieves the following conditions that may be related to CSS:

- ❖ Osteitis, osteomyelitis / Inflammation of the bones, cortical bone, bone marrow
- ❖ Osteoporosis / Bone loss
- ❖ Scoliosis / Lateral curvature of the spinal column
- ❖ Arthrosis / Joint degeneration
- ❖ Arthritis / Inflammatory joint disease
- ❖ Mycosis / Fungal infections
- ❖ Parasitic diseases of the skeleton

Detoxification:

Frequency pattern that supports detoxification of the cells and tissues and the lymphatic, renal, digestive and integumentary systems.

Pain/psyche:

Frequency pattern that relieves chronic pain combined with sleep disorders, limited physical and mental ability to cope with stress, reduced performance and depression.

The compact program used in the study, Compact Program 71.60 CSS, contains a total of 18 RAH programs that cover the contents mentioned above. These programs were stored on a memory card (Green Card) which must be inserted into the Rayocomp PS 1000 polar 4.0 at the start of the therapy session.

The order of the RAH programs and their respective therapy time when using Compact Program 71.60 CSS is as follows:

RAH 00.00	5 minutes	RAH 70.40	10 minutes
RAH 01.00	5 minutes	RAH 70.43	10 minutes
RAH 02.00	5 minutes	RAH 70.46	10 minutes
RAH 31.10	5 minutes	RAH 70.48	10 minutes
RAH 54.15	5 minutes	RAH 70.58	10 minutes
RAH 54.31	5 minutes	RAH 70.59	10 minutes
RAH 64.56	5 minutes	RAH 71.50	5 minutes
RAH 70.28	10 minutes	RAH 71.60	5 minutes
RAH 70.29	10 minutes	RAH 01.00	5 minutes

VI. Summary of the study results

Rayonex Biomedical GmbH is headquartered in Lennestadt. It is a well-established medical device company that started over 35 years and currently operates in over 45 countries around the world. Rayonex represents bioresonance according to Paul Schmidt, a cause-oriented treatment approach, that is named after the company founder and engineer Paul Schmidt. Rayonex Biomedical GmbH is certified to develop, produce and distribute medical devices according to DIN EN ISO 13485:2016 and is audited and certified by TÜV Nord on a yearly basis.

Rayonex manufactures two medical devices: the high-med. device, the Rayocomp PS 1000 polar 4.0 med., which can be used as a stationary device in a doctor's surgery and the portable Rayocomp PS 10 med., which is primarily for patients receiving therapy at home.
A clinical evaluation of active medical devices, including both Rayocomp devices, must be carried out in order to provide evidence of the safety and effectiveness of the devices.

The patient and user information presents the results of a clinical prospective, double-blind, randomised, study of the highest scientific level that aims to provide objective proof of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome.

The final report concludes that the devices are safe and effective to use. The following are citations from Chapter VII of the final report:

"There was no change in the NDI (Neck-Disability-Index) of the placebo group, but a significant improvement in the NDI of the group treated with the Rayocomp bioresonance device (p<0.001)."
"The placebo treatment did not achieve significant improvements in neck pain, headaches, back pain, shoulder pain or muscle tension, while treatment with the Rayocomp bioresonance device showed significant improvements (p<0.001) in all parameters (Figure 2, Figure 3, Table 10)."

"In terms of physical capacity, patients receiving the placebo treatment showed no significant improvement, while patients treated with the Rayocomp bioresonance device showed significant improvements (p<0.001) in all parameters (Table 11). The differences (all p < 0.001) are summarised in Table 12 and shown in graph form in Figure 7."

"The SF-36 parameters of physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health achieved no significant improvement in patients receiving the placebo treatment. Whereas, all of the parameters showed significant improvements (p<0.001) in patients receiving treatment with the Rayocomp bioresonance device. The differences (all p < 0.05) are summarised in Table 14 and shown in graph form in Figure 10."

"Overall, there were significant differences in how patients answered the question of whether they would recommend the treatment to others. All patients in the Rayocomp group said that they would recommend it, while only around a quarter of patients in the placebo group said the same. The results are summarised in Table 15."

"Furthermore, the study confirms that the Rayocomp PS 1000 polar 4.0 bioresonance device is safe. Based on the results and information provided in the manual, no adverse effects were detected during this clinical trial that could alter the risk profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. The favourable safety profile of the medical device was confirmed. It was shown to be safe when used according to the instructions in the manual."

This scientific study proves to patients and therapists alike that bioresonance according to Paul Schmidt is both safe and effective to use.

VII Final Clinical Study Report

Randomised, prospective, double-blind study to provide objective proof of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome

R-HWS

Clinical Study Report

Identifying the test product	Rayocomp PS 1000 polar 4.0 bioresonance device
Type of test	Prospective, randomised, double-blind, monocentric comparative study
Application method	10 therapy sessions within a period of 70 days
Patient population	52 patients with at least moderate pain in the cervical spine region
Sponsor	Rayonex Biomedical GmbH Sauerland-Pyramiden 1 57368 Lennestadt (Germany)
Basic study protocol	CIP R-HWS, V3.1 from 20/08/2019
Coordinating investigator	Dr. med. Axel Schussmann Zur Ohe 2 21406 Melbeck, Germany
Author of the report	Dr. Hans Werner Voß
Version and date	Version 1.2 • 20-02-2020

The study in this report was conducted in accordance with Good Clinical Practice (GCP), the Declaration of Helsinki, DIN EN ISO 14155 and all applicable national laws and regulations. The information in this report is strictly confidential. It serves exclusively to inform the sponsor, the investigators and the participating ethics committees and authorities. It may not be passed on to third parties without the express permission of the sponsor.

1 Contents

2 Summary

2.1 Name of the Trial

2.1.1 Title of the Clinical Trial

Randomised, prospective, double-blind study to provide objective proof of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome

2.1.2 Reference Number for Identifying the Clinical Examination

R-HWS

2.1.3 Version and / or Date of the Study Protocol

The basis for this report is version 3.1 of the Study Protocol from 20/08/2019.

2.1.4 Summary of the Revision History in Case of Changes.

1. Version 0.1 • Version 0.1 • 19-02-2019 first draft
2. Version 0.2 • Version 0.2 • 20-02-2019 version after sponsor and CRO review
3. Version 1.0 • Version 1.0 • 26-02-2019 version 1.0
4. Version 2.0 • Version 2.0 • 27-03-2019 version 2.0 after the ethics committee review
5. Version 3.0 • Version 3.0 • 05-08-2019 version 3.0
6. Version 3.1 • Version 3.1 • 20-08-2019 version 3.1 after the principal investigator's review

2.2 The Aim of the Test

The aim of this study was to collect data on the performance and safety of the Rayocomp bioresonance device when used for its intended purpose. The main aim was to assess the effectiveness of the device and to do this the Neck Disability Index (NDI) was used. Adverse events were recorded to assess the safety of the device.

2.3 Description of the Population Studied

The study population consisted of 52 patients who suffered from at least moderate pain in the cervical spine region.

2.4 Procedure

The Rayocomp PS 1000 polar 4.0 bioresonance device is a CE-certified medical device that provides pain relief in patients with CSS. The clinical trial consisted of 12 visits that took place over a period of 20-90 days. Details are described in Table 1. The sponsor provided the study site with four identical devices. These were labelled as described in

Section 4.1. Two of the devices were rendered inoperable before commencing the study (sham = placebo). The devices were labelled either R-HWS-A or R-HWS-B. Depending on the study arm, the patients were assigned to a treatment arm corresponding to the device number they had been allocated. The device was used according to the instructions in the manual.

2.5 Test Results

The aim of this study was to collect data on the performance and safety of the Rayocomp bioresonance device when used for its intended purpose.

The main aim was to assess effectiveness of the device using the NDI.

The secondary aim was to assess safety by recording adverse events. Performance, quality of life and a visual analogue scale for pain characterisation were also documented and analysed as secondary efficacy parameters.

In total, 17 male and 37 female patients between the ages of 27 and 84 were icluded in the study. 27 patients were assigned to the Rayocomp group (treatment with the Rayocomp bioresonance device) and 27 to the placebo group. The demographic data is summarised in Table 2.

The primary output measure was a change in NDI after treatment. Based on the results from Table 7, the differences are shown in Table 8 and Figure 1.

	Placebo (n=23)	**Rayocomp[1] (n=24)**
Difference in NDI [MV±SD (Median)]	0.6±5.4 (0.0)	24.1±9.9 (21.0)
Significance	**p < 0.001**	

The Mann-Whitney U test showed one statistically significant difference in the primary output measure in support of the bioresonance therapy according to Paul Schmidt.

All secondary aims substantiated this result. Significant differences were observed in performance, quality of life (SF-36) and the visual analogue scale for pain characterisation, which supports the bioresonance therapy according to Paul Schmidt. In total, three (3) of the 52 patients reported 10 adverse events. There were no reported problems with the product and there was no link between the adverse events and the test product. No further action was needed and the patients fully recovered. The degree of severity of all AEs were described as mild.

Severe adverse events did not occur.

1 Treatment with the Rayocomp PS 1000 polar 4.0

2.6 Conclusions

The Rayocomp PS 1000 polar 4.0 bioresonance device achieved significant improvements in all objective and subjective parameters compared to the placebo device.
This study is particularly important as it adopts a double-blind design involving a placebo device for comparison.
Furthermore, the study confirms that the Rayocomp PS 1000 polar 4.0 bioresonance device is safe. Based on the results and information provided in the manual, no adverse effects were detected during this clinical trial that could alter the risk profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. The favourable safety profile of the medical device was confirmed. It was shown to be safe when used according to the instructions in the manual.

2.7 Testing Timeframe

The study was conducted in accordance with §23b of the Medical Devices Act (MPG). As a result, no approval was required from the higher federal authority. The Lower Saxony ethics committee (EC) voted in favour of carrying out the study. The first patient was included on 27/05/2019. The last patient completed the study on 11/12/2019.

3 Introduction

The Rayocomp bioresonance device is a CE-certified medical device that provides pain relief in patients with CSS.

Bioresonance therapy according to Paul Schmidt is an energy treatment method based on physical knowledge and the assumptions of Traditional Chinese Medicine. It is assumed that the body reacts to certain electromagnetic oscillations. For example, the skin reacts to sunlight by increasing pigmentation levels (1).

The bioresonance system developed by Paul Schmidt was based on a frequency generator, which he used to conduct initial research into bioresonance in 1976.

Based on this research, Rayonex Biomedical GmbH developed the Rayocomp PS 1000 polar 4.0 bioresonance device. Initial studies involving cell cultures showed an increase in the metabolic activity of fibroblasts, keratinocytes and promyelocytes after treatment with the bioresonance device (2, 3). In case studies and single case reports, patients treated with the bioresonance device showed a subjective improvement in their level of pain (4, 5, 6, 7). No undesirable side effects, contraindications or risks were identified.

The study population was selected based on the intended purpose of the Rayocomp PS 1000 polar 4.0 bioresonance device. They were patients suffering from pain caused by restricted movement of the cervical spine.

Cervical spine syndrome has relatively non-specific symptoms, and yet it affects approximately 20% of the population (8, 9). It can cause pain, paraesthesia and dysfunction in the neck, shoulder and arm regions. Typical symptoms are dull pains in the arms, shoulders or neck that are hard to pinpoint. The muscles in the affected area may be hard and tight. Dysfunction or impaired movement of the joints may also occur. Tingling sensations and "formication" in the hands and arms caused by nerve irritation are also possible signs of cervical spine syndrome. These are eventually accompanied by headaches, dizziness, and visual and auditory disorders (tinnitus).

The NDI is an established, validated measuring instrument for quantifying the pain caused by cervical spine syndrome. The score is well researched and has been validated in the German-speaking world by Cramer et al. (10) When using visual analogue scales to record pain intensity, both the Saskatchewan study and the Hawley & Wolfe study showed a baseline of approximately 5 points in patients with neck pain. Consequently, this value can be used as an indicator of significant symptoms.

In addition to painful restriction of movement, neurological symptoms can occur in the form of paraesthesia or loss of strength in the upper extremities.

A possible cause of cervical spine syndrome are degenerative changes (wear and tear of the vertebral bodies or joints) in the cervical spine. This reduces movement in the cervical spine and causes the vertebral bodies to put pressure on nerve roots, which interferes with blood supply.
As cervical spine syndrome is a pain syndrome, it must be viewed in a psychosocial context (10, 11).
Headaches starting from the shoulder and neck region or in the cervical spine are often observed in people who sit at a desk for long periods at a time and spend a lot of time staring at a screen (12). Stress can exacerbate symptoms. If the muscles in the neck cramp up, this can cause headaches.

Slipped discs, vertebral blockages or spinal stensosis can also cause pain and inflammation, which can, in turn, cause severe muscle tension in the neck and shoulders.

A long-term effect could be the sensitization of nerves, which causes pain become chronic. This pain can become so intense that it makes those who are affected feel nauseous.

CSS can be classified according to course, localisation, pain radiation and cause. The aetiology is unknown in most cases. However, a distinction is made between degenerative, traumatic and functional causes. There is also a distinction between

temporal course (acute, chronic), location from which the pain radiates (local, radicular, pseudoradicular) and the area where the pain occurs (upper, middle, lower CSS).

Opinions differ on which therapies are suitable for treating CSS (9). Standard therapy recommends using movement training, mobilisation, manipulation, acupuncture, pain medication and low-level laser therapy to treat neck pain in patients without a serious pathology (10).

This involves the use of painkillers (paracetamol, ibuprofen) or muscle relaxants (diazepam, tetrazepam). Physiotherapy, relaxation exercises and massages are intended to improve mobility of the cervical spine and relax the muscles. In rare cases, the patient undergoes surgery. However, the effectiveness of this treatment method has not yet been clearly proven (8).

The aim of this study is to assess pain relief and whether the quality of life of patients with CSS improved when treated with the Rayocomp bioresonance device. Furthermore, the safety of the treatment will be investigated by recording the adverse effects that become apparent during the treatment.

The aim of evaluating the data collected in this study is to expand our knowledge of bioresonance therapy and to contribute to improving treatment of patients with CSS.

4 Test Product and Test Method

4.1 Description of the Test Product

The Rayocomp PS 1000 polar 4.0 (Rayocomp bioresonance device) is a Class IIa CE-certified medical device for alleviating pain associated with cervical spine syndrome (17). The Rayocomp bioresonance device is a biofeedback system from the product group UMDNS (10-396) in the non-active and active medical devices category. The technical documentation was last assessed by TÜV NORD CERT GmbH (Certificate No 08 232 012275) on 01/03/2017.

Rayocomp PS 1000 polar 4.0 is manufactured according to a quality control system approved by TÜV Nord, Essen, in accordance with DIN EN ISO 13485 and Appendix V of the Medical Device Directive (93/42/EEC). The devices used in the study were labelled accordingly.

The product label contained the following information:

- Name of the sponsor, contact information
- Name of the study
- Study-specific number
- The note: "Use only for clinical trial"
- The note: "Keep out of reach of children"

4.1.1 Intended Use of the Test Product

This study is a prospective, randomised, double-blind, monocentric study involving a CE-certified medical device (Rayocomp PS 1000 polar 4.0), i.e. it was a postmarket study to gather data on performance and safety.

The medical device was used for its intended purpose and for which it had been approved. An inoperable, sealed device was used as a comparison product (placebo). The patients and doctor were unaware that the device was inoperable without conducting specific tests.

4.1.2 Changes to the Test Product during the Trial

During the clinical trial there were no changes made to the materials, components, storage conditions or the manual.

5 Clinical Study Protocol

5.1 Aims and Hypotheses of the Clinical Trial

The aim of this study was to collect data on the performance and safety of the Rayocomp bioresonance device when used for its intended purpose.

The main aim was to assess effectiveness of the device using the NDI.

The secondary aim was to assess safety by recording adverse events. Performance, quality of life and a visual analogue scale for pain characterisation were also documented and analysed as secondary efficacy parameters.

The hypothesis was that treatment with the Rayocomp bioresonance device would result in significant improvements in pain.

5.2 Clinical Study Design

The clinical trial consisted of 12 visits that took place over a period of 20-90 days. Details are described in Table 1.

Table 1 Examination procedure

	Screening	Visit 1-10	Follow Up
Day	-21 to -1	1-3x/week	1 to 14
Inclusion and exclusion criteria	•		
ICF	•		
Pregnancy test in participants of reproductive age	•		
Demography	•		
Medical history	•		
VAS	•		•
NDI (Neck Disability Index)	•		•
SF-36	•		•
Performance	•		•
Pain medication	•		•
Adverse Events		•	•
Subjective assessment of the therapy success			•

5.3 Ethical Considerations

This study is a clinical trial involving a CE-certified medical device. In accordance with §23b of the MPG, approval from the higher federal authority was not required.

The clinical trial was conducted in accordance with the current version of the Declaration of Helsinki and the standard of "Good Clinical Practice" as outlined in DIN EN ISO 14 155 and ICH-GCP.

A written vote on protocol was held before commencing clinical trial. The clinical trial began only after it had received a positive vote from the ethics committees responsible for the participating site.

5.4 Data Quality Assurance

The study site was independently monitored for quality assurance purposes. This involved an initial visit, five routine visits and a final visit.

Monitoring served to check whether the statutory rights of the patients were being upheld and if the subjects were safe. It also ensured compliance with the Study Protocol, laws and guidelines (GCP, MPG, ISO 14155).

In addition to on-site monitoring, data quality was continuously being monitored through remote monitoring and feedback was provided to the site.

5.5 Subjects

5.5.1 Inclusion Criteria

- Gender: male and female
- Age: at least 18 years old
- Al least moderate pain (≥ 5 on the VAS) in the cervical spine region
- Neck Disability Index with at least moderate restriction (score ≥ 15)
- Patients must be able to understand the patient information
- Patients must be willing and able to meet the criteria of the study
- Written informed consent form

5.5.2 Exclusion Criteria

- Systematic or inflammatory musculoskeletal disease (e. g. muscular dystrophy, polymyositis)
- Trauma with fractures and surgical treatment
- Severe systemic disease with a life expectancy < 6 months (e.g. advanced heart failure, malignant diseases)
- Severe degenerative diseases with significant restricted movement (e.g. polyarthritis)
- Pregnant women, female patients who are breastfeeding or not using effective contraception
- Patients, who due to mental illness, are not able to understand the information about the study, give their consent or adhere to the guidelines of the study
- Patients deemed unsuitable by the principal investigator
- Alcohol or drug abuse
- Incapacitated patients
- People who have an employment relationship with or are dependent of the sponsor or investigator
- Incarcerated persons
- People taking part in another study

5.5.3 Sample size

Based on previously published data and within the scope of this study, a mean therapy improvement of 6 points with a standard deviation of 7 points was assumed for the primary output measure (Neck Disability Index). This resulted in a sample size of 52 patients and a drop-out rate of 10%. Details are described in Section 5.8.1.

5.6 Measures, Treatments and Their Allocation

The sponsor provided the study site with four identical devices. These were labelled as described in Section 4.1. Two of the devices were rendered inoperable before commencing the study (placebo). One of the sponsor’s employees, who was not blinded and was bound to secrecy, put a sticker with a marking and a study-specific number (R-HWS-A or R-HWS-B) on it on the test products before commencing the study. Depending on the study arm, the patients were allocated the corresponding device number. When the study ended, the sponsor took back the devices. The delivery and return of the devices was recorded in the investigator study file.

5.7 Simultaneous Administration of Medication

In general, no medications were excluded from the study. During the study, changes to the concomitant medication were recorded in the CRF.

5.8 Statistical Analysis

5.8.1 Calculating the Sample Size

The Neck Disability Index (NDI) was used as the primary output measure to calculate sample size. This corresponds to a score of between 0 – 50, or 0-100%. The NDI value in patients with CSS is often high. However, the literature on this is conflicting: The NDI in the study by Cramer et al. (10), which validated the German version of the NDI, was 32.75±13.09 points. Whereas, the study by Jorritsma et al. (14) indicated an NDI of 21.0±6.6 points. Improvements in the NDI were also varied: Jorritsma et al. achieved an improvement of 6.0±5.9 points in the NDI during therapy and observed improvements of 3-8 points in subgroup analyses. Whereas, the group studied by Vos et al. (15) were considerably less symptomatic and had an NDI baseline of 14.37±6.86 (14, 15).

These figures show that a mean therapy improvement of 6 points with a standard deviation (SD) of 7 can be assumed in a heterogeneous group. This resulted in a sample size of 23 patients per group. The drop-out rate was estimated to be 10%, which would leave 52 patients in the study.

Version 8.3 of nQuery was used to calculate sample size.

5.8.2 Method of Statistical Analysis

The primary data set was analysed according to the intention-to-treat principle.

Statistical analyses were carried out using the latest version of SPSS for Windows (SPSS Inc., U.S.A.). The metric variables are presented as mean and median values, while the measures of dispersion are specified as standard deviations and quartiles. The categorical or nominal data are calculated as absolute or relative frequencies.

The SF-36 questionnaire is analysed according to standardised specifications of the European publisher of scientific books, Hogrefe Verlag.

The Kolmogorow-Smirnow test is used to test the metric variables for normality of the distribution. When comparing the samples, statistical methods corresponding to the distribution pattern are used for normally distributed samples, while nonparametric tests are used for samples with a non-normal distribution.

The t-test is used to compare two independent, normally distributed samples. Before conducting the t-test, the Levene's test is performed in order to test the homogeneity of variance. If homogeneity of variance is proven, the Student's t-test is performed. If variances are unequal, the Welch test is used as a modification of the t-test. The Mann-Whitney U test is used as a nonparametric method for samples with a non-normal distribution. The Kruskal-Wallis H test is used for comparing more than two independent samples with non-normal distribution. One-way ANOVA, on the other hand, is used for comparing two independent, normally distributed samples. Two related, normally distributed samples are compared using the t-test for paired samples, while two related samples with a non-normal distribution are tested using the Wilcoxon test. The general linear model with repeated measures is used to compare more than two related, normally distributed samples, while the Friedman test is used to compare more than two related samples with a non-normal distribution. In contrast, categorical data is evaluated using the chi-squared test or Fisher's exact test.

All tests are followed by a two-tailed significance test, in which all statistical tests with a P value of < 0.05 are considered statistically significant.

6 Results

6.1 Testing Timeframe

The study was carried out between 27/05/2019 (first patient included) and 11/12/2019 (last patient completed the study). Prior to this, a vote was held by the ethics committee of the Lower Saxony State Medical Association (submitted: 26/02/2019; vote 14/03/2019, amendment submitted 26/08/2019; vote 10/09/2019).

6.2 Population and Test Product Availability

The study population was selected based on the intended purpose of the Rayocomp bioresonance device. They were patients suffering from pain caused by restricted movement of the cervical spine.
Cervical spine syndrome has relatively non-specific symptoms, and yet it affects approximately 20% of the population (8, 9). Thus, there is a well-defined and sufficiently large population.

The sponsor provided the study site with four identical devices. Details are described in Sections 4.1 and 5.6.

6.3 Demography

6.3.1 Demographic Data

In total, 17 male and 37 female patients between the ages of 27 and 84 took part in the study. The patients in the placebo group were, on average, approximately 5 years younger than the patients in the Rayocomp group (p = 0.18). 27 patients were assigned to the active group (treatment with the Rayocomp resonance device) and 27 to the placebo group.

The demographic data is summarised in the following tables.

Table 2 Patient characteristics

Patient characteristics	Placebo (n=27)	Rayocomp (n=27)
Age (years) [MV±SD (Median)]	57.4±12.7 (58.0)	62.1±12.7 (62.0)
Female sex [%; n]	70.4%; 19	66.7%; 18
Male sex [%; n]	29.6%; 8	33.3%; 9
Size [MV±SD (Median)]	172.7±7.5 (173.0)	171.0 ± 9.0 (171.0)
Weight [MV±SD (Median)]	77.6±14.1 (73.0)	73.5±14.0 (72.0)
BMI [MV±SD (Median)]	26.0± 3.9 (26.4)	25.0±3.9 (24.5)

All details can be found in the statistical tables in Sections 2.1 and 2.2.

Table 3 Smoker status

Smoker status	Placebo		Rayocomp	
	n	(%)	n	(%)
non-smoker (never smoked)	17	63.0%	20	74.1%
ex-smokers	6	22.2%	6	22.2%
current smoker	4	14.8%	1	3.7%

6.3.2 Medical History

There was no difference between the two treatment groups in terms of pre-existing conditions. The characteristics are summarised in Table 4 and do not differ between the groups.

Table 4 Pre-existing conditions

Pre-existing conditions	Placebo		Rayocomp	
	n	(%)	n	(%)
Diabetes mellitus	0	0.0%	3	11.1%
Cardiovascular disease	6	22.2%	7	25.9%
Pulmonary disease	2	7.4%	0	0.0%
Kidney disease	0	0.0%	0	0.0%
Gastrointestinal disease	10	37.0%	1	3.7%
Previous spinal surgeries	4	14.8%	3	11.1%
Other relevant diseases	4	14.8%	0	0.0%

At the start of the study the patients reported that their symptoms had persisted for more than three years. The length of time is similar in both groups.

Table 5 Duration of the symptoms

Duration of the symptoms	Placebo (n=27)	Rayocomp (n=27)
How long have they had the pain (weeks) [MV±SD (Median)]	165.1±195.3 (110.0)	180.4±296.8 (60.0)

The patient's current treatment is summarised in Table 6. There was no difference between the groups.

Table 6 Pain medication

Pain medication	Placebo		Rayocomp	
	n	(%)	n	(%)
WHO I (nonopioid)	18	66.7%	21	77.8%
WHO II (weak opioid + nonopioid)	2	7.4%	1	3.7%
WHO III (strong opioid + nonopioid)	0	0.0%	0	0.0%
Other	0	0.0%	0	0.0%

6.4 Breaches of the Study Protocol

Breaches of the Study Protocol were recorded in the monitoring reports. There were no serious breaches of the Study Protocol (see Section 6.5.4). During the study, the total duration of participation (10 treatments) was extended by a period of 20-90 days due to logistical problems caused by a number of changes to scheduling (Amendment 1).

6.5 Performance Analyses

6.5.1 Primary Output Measure

The primary output measure (effectiveness) was to assess neck pain, which was measured using the Neck Disability Index (NDI) before and after treatment with the Rayocomp bioresonance device. This was then compared to the placebo.

Table 7 summarises the development of the NDI before and after therapy in the respective treatment groups.

Table 7 Neck Disability Index before and after treatment

NDI before & after treatment	Placebo	Rayocomp
NDI before [MV±SD (Median)]	42.4±15.7 (42.0), n=27	41.0±10.8 (42.0), n=27
NDI after [MV±SD (Median)]	41.7±16.3 (38.0), n=23	16.4±2.0 (4,0), n=24

There was no change in the NDI of the placebo group, but a significant improvement in the NDI of the group treated with the Rayocomp bioresonance device ($p<0.001$).

The primary output measure was a change in NDI after treatment. Based on the results from Table 7, the differences are shown in Table 8 and Figure 1.

Table 8 Primary output measure

NDI before & after treatment	Placebo	Rayocomp
Difference NDI [MV±SD (Median)]	0.6±5.4 (0.0)	24.1±9.9 (21.0)
Number of cases	n=23	n=24
Significance	$p < 0.001$	

In the Mann-Whitney U test, there was one statistically significant difference in the primary output measure in support of the bioresonance therapy when compared to placebo.

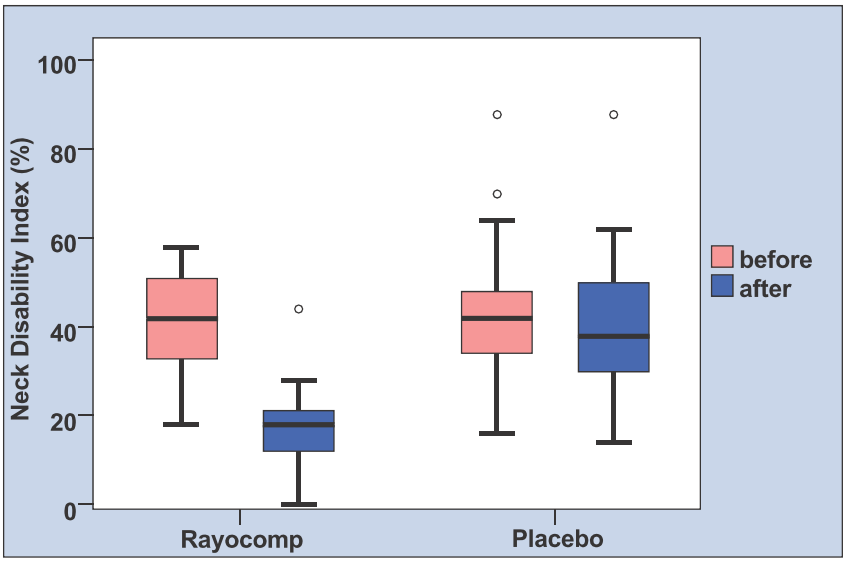


Figure 1 Disability Index before and after treatment

6.5.1.1 Secondary Target Criteria

The secondary target criteria were:

- The visual analogue scale (VAS) before and after treatment with the Rayocomp bioresonance device and its performance compared to the placebo.
- Quality of life measured in the SF-36 questionnaire, before and after treatment with the Rayocomp bioresonance device. This was then compared to placebo.
- Safety as measured by the incidence of adverse events

The results of the secondary output measures are summarised below.

6.5.1.2 Visual Analogue Scale (VAS)

A complete overview of the individual characteristics of the VAS can be found in the statistical report in Section 3.1. The overall difference for each parameter between the treatments is shown below in Table 9.

Table 9 VAS before and after treatment

VAS [MV±SD (Median)]	Placebo	Rayocomp
Neck pain (before)	7.0±1.0 (7.0), n=27	6.8±1.4 (7.0), n=27
Neck pain (after)	6.7±1.1 (7.0), n=23	3.0±1.1 (3.0), n=24
Headache (before)	5.1±2.9 (6.0), n=27	5.6±2.8 (6.0), n=27
Headache (after)	5.0±2.8 (6.0), n=23	5.6±1.8 (2.5), n=24

VAS [MV±SD (Median)]	Placebo	Rayocomp
Back pain (before)	5.5±2.4 (6.0), n=27	5.8±2.5 (6.0), n=27
Back pain (after)	5.1±2.4 (6.0), n=23	2.3±1.4 (2.0), n=24
Shoulder pain (before)	6.7±1.8 (7.0), n=27	6.7±1.9 (7.0), n=27
Shoulder pain (after)	6.6±1.9 (7.0), n=23	3.0±1.7 (3.0), n=24
Tension in cervical spine (before)	7.7±1.4 (8.0), n=27	7.6±1.2 (8.0), n=27
Tension in cervical spine (after)	7.3±1.5 (7.0), n=23	3.8±1.6 (4.0), n=24

The contrasting development of both treatment groups is shown in Figure 2 and Figure 3.

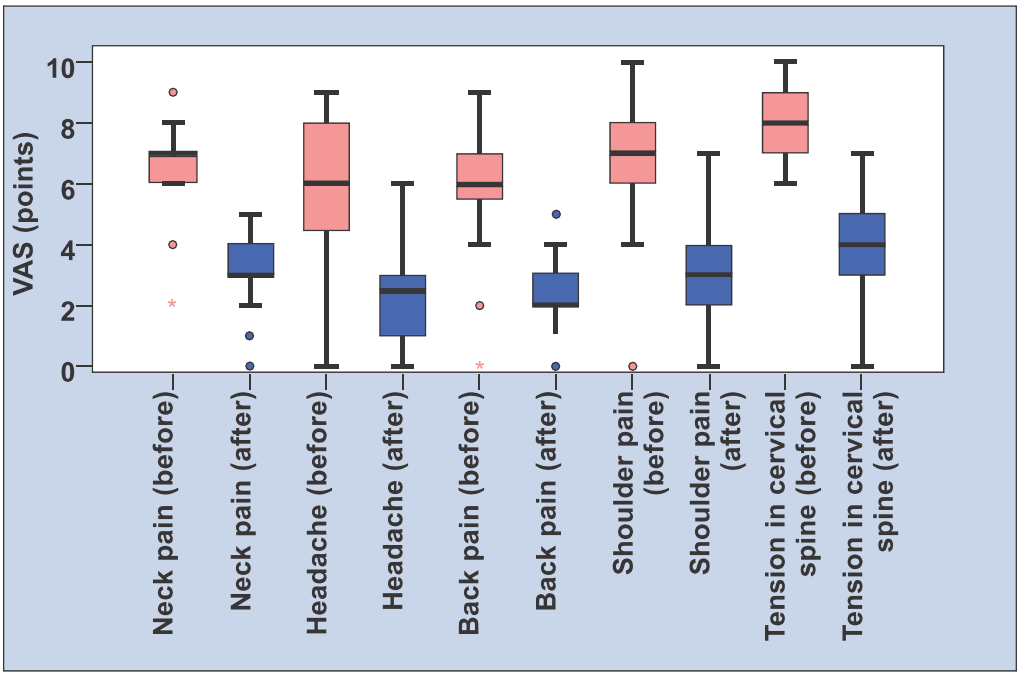


Figure 2 VAS before and after treatment (with the Rayocomp bioresonance device)

The placebo treatment did not achieve significant improvements in neck pain, headaches, back pain, shoulder pain or muscle tension, while treatment with the Rayocomp bioresonance device showed significant improvements ($p<0.001$) in all parameters (Figure 3, Table 10).

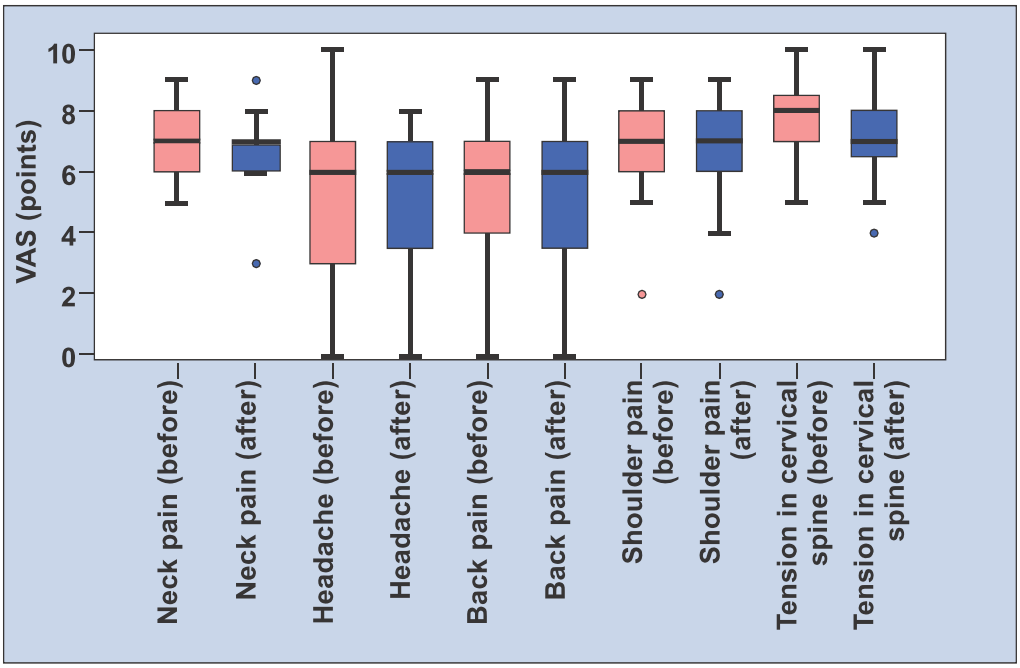


Figure 3 VAS before and after treatment (placebo)

Table 10 Difference in the VAS before and after treatment

VAS before and after treatment	Placebo	Rayocomp
Neck pain	-0.2±1.0 (0.0), n=23	-3.7±1.5 (-4.0), n=24
Headache	0.1±1.0 (0.0), n=23	-3.0±2.1 (-3.0), n=24
Back pain	0.0±0.8 (0.0), n=23	-3.5±2.0 (-4.0), n=24
Shoulder pain	0.0±1.2 (0.0), n=23	-3.8±1.6 (-4.0), n=24
Tension in cervical spine	-0.4±0.9 (0.0), n=23	-3.9±1.3 (-4.0), n=24
Significance	**p < 0.001**	

The differences are shown in graph form in Figure 4.

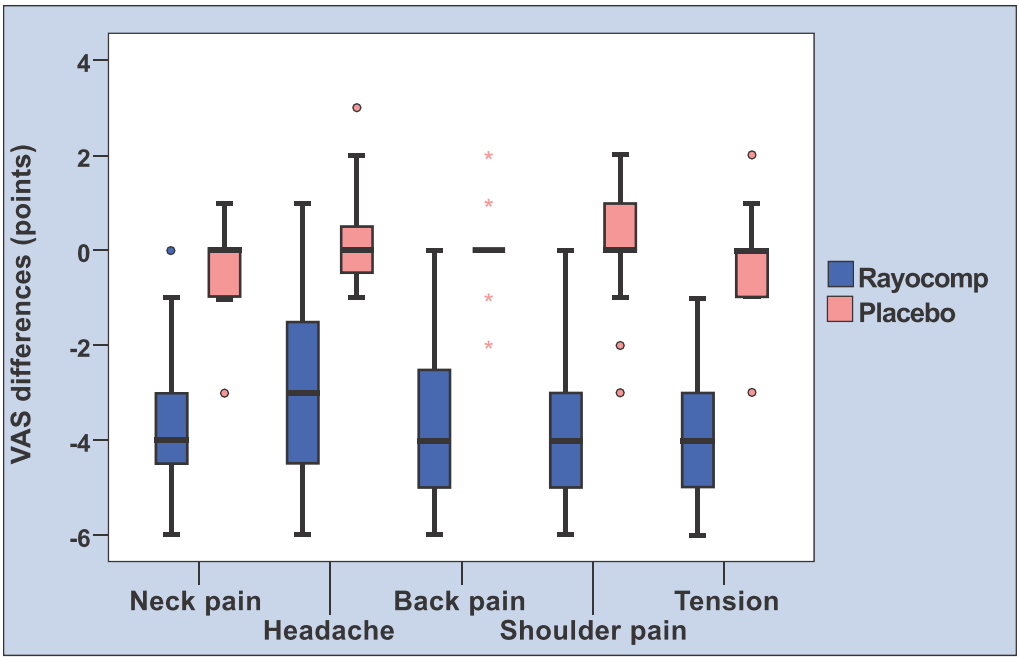


Figure 4 VAS differences before and after treatment

6.5.1.3 Performance

Performance in terms of the influence that the treatment had on physical activity was measured using a VAS before and after treatment.

The results are summarised below in Table 11 and the corresponding figures (Figure 5 and Figure 6).

Table 11 Performance before and after treatment

VAS [MV±SD (Median)]	Placebo	Rayocomp
Sport (before)	4.2±2.0 (4.0), n=25	4.4±1.9 (4.0), n=26
Sport (after)	4.1±2.0 (4.0), n=21	7.2±1.3 (7.0), n=23
Hiking (before)	5.9±2.8 (6.0), n=25	6.3±2.3 (6.0), n=24
Hiking (after)	5.5±2.8 (5.0), n=21	7.7±1.4 (7.0), n=21
Housework (before)	4.6±1.8 (4.0), n=27	4.8±2.2 (4.5), n=26
Housework (after)	4.3±1.5 (4.0), n=23	7.2±1.4 (7.0), n=23
Gardening (before)	4.1±1.4 (4.0), n=25	4.3±1.5 (4.0), n=24
Gardening (after)	3.8±1.4 (4.0), n=21	7.1±1.2 (7.0), n=21

VAS [MV±SD (Median)]	Placebo	Rayocomp
Swimming (before)	4.9±3.0 (4.0), n=19	4.1±2.0 (4.0), n=18
Swimming (after)	4.6±2.6 (4.0), n=16	6.9±1.7 (7.5), n=16
Biking (before)	5.2±2.4 (5.5), n=20	6.3±2.6 (6.5), n=24
Biking (after)	4.9±2.8 (4.0), n=16	8.1±1.5 (8.0), n=21
Everyday life (before)	4.8±1.9 (5.0), n=27	5.6±2.0 (5.0), n=27
Everyday life (after)	4.4±1.9 (4.0), n=23	8.2±1.1 (8.0), n=24
Disability (before)	4.0±2.3 (3.0), n=19	5.7±2.1 (6.0), n=15
Disability (after)	3.5±2.2 (4.0), n=16	8.2±1.2 (8.0), n=14
Social activities (before)	5.7±2.6 (6.0), n=26	6.8±1.9 (7.0), n=22
Social activities (after)	5.0±2.5 (5.0), n=22	8.7±1.1 (9.0), n=20

In terms of physical capacity, patients receiving the placebo treatment showed no significant improvement, while patients treated with the Rayocomp bioresonance device showed significant improvements ($p<0.001$) in all parameters (Table 11). The differences (all $p < 0.001$) are summarised in Table 12 and shown in graph form in Figure 7.

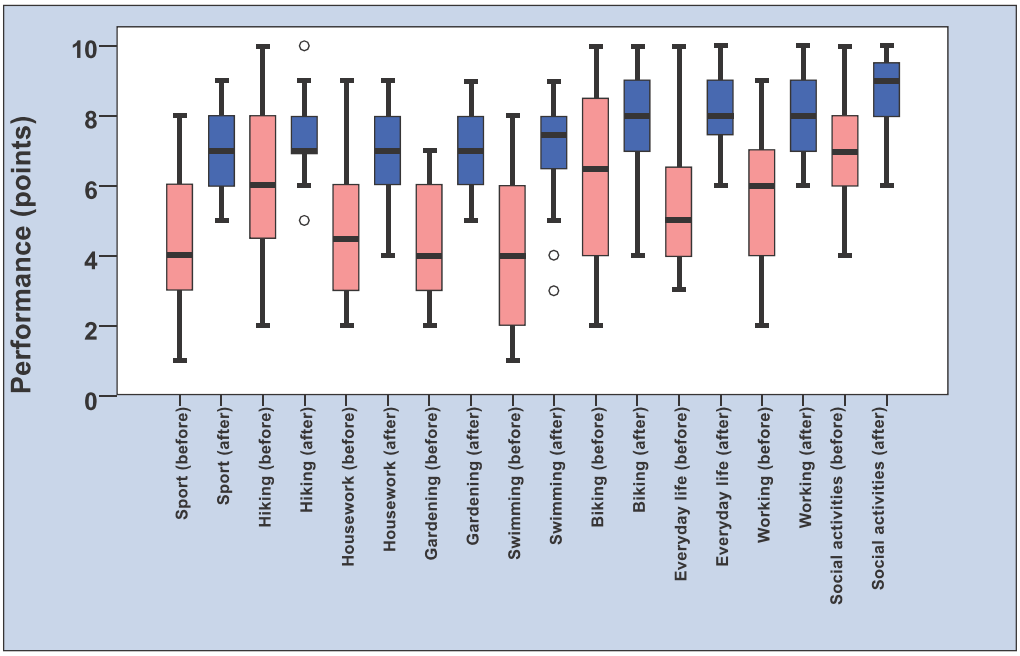


Figure 5 Performance before and after treatment (Rayocomp)

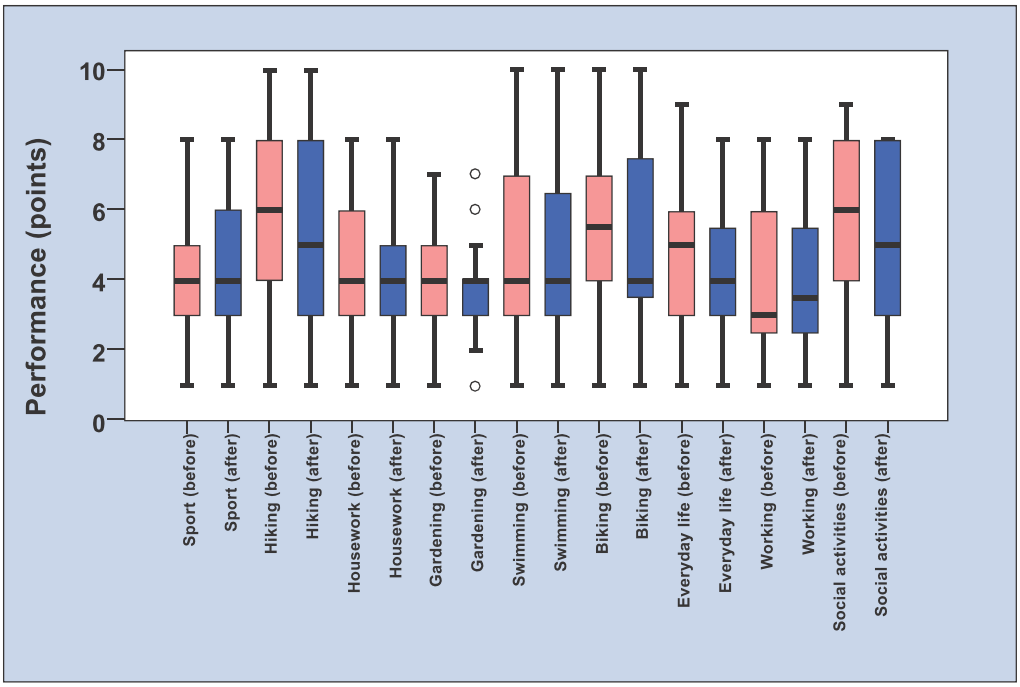


Figure 6 Performance before and after treatment (placebo)

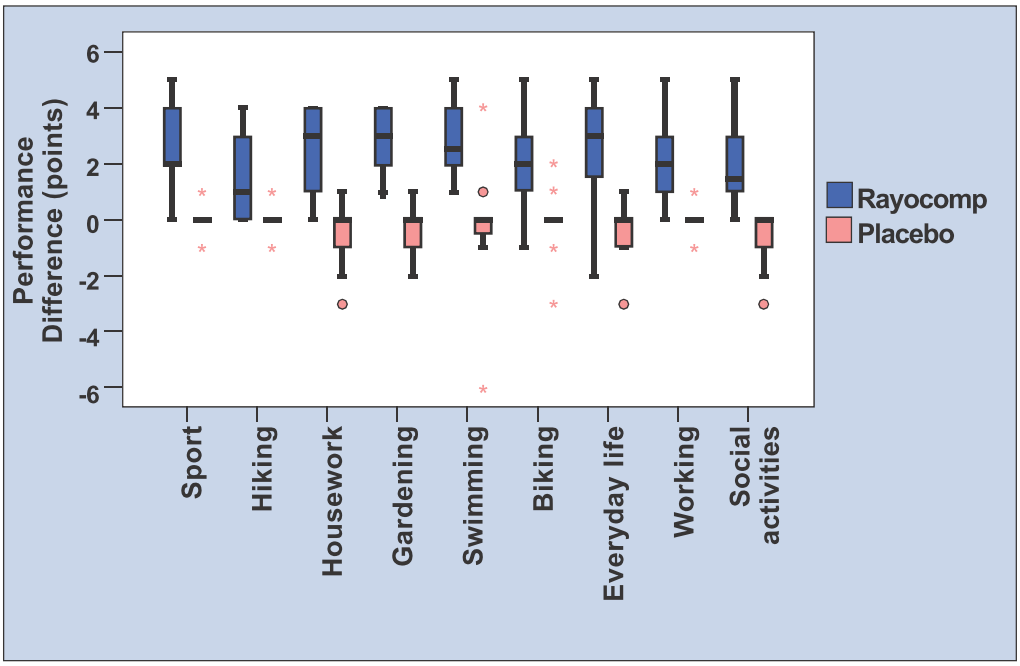


Figure 7 Differences in performance before and after treatment

Table 12 Differences in performance assessment

Performance [MV±SD (Median)]	Placebo	Rayocomp
Sport	-0.1±0.5 (0.0), n=21	1.6±1.4 (1.0), n=21
Hiking	-0.1±0.4 (0.0), n=21	4.5±1.4 (3.0), n=23
Housework	-0.2±1.0 (0.0), n=23	2.9±1.1 (3.0), n=21
Gardening	-0.4±0.8 (0.0), n=21	2.8±1.3 (4.0), n=16
Swimming	-0.2±1.9 (0.0), n=16	1.9±1.5 (2.0), n=21
Biking	0.0±1.1 (0.0), n=16	2.5±1.7 (3.0), n=24
Everyday life	-0.3±1.0 (0.0), n=23	2.4±2.0 (2.0), n=14
Disability	0.0±0.5 (2.0), n=16	1.9±1.4 (1.5), n=20
Social activities	-0.5±0.8 (0.0), n=22	1.6±1.4 (1.0), n=21
Significance	**p < 0.001**	

6.5.1.4 Quality of Life (SF36)

The SF-36 questionnaire is an instrument for measuring the health-related quality of life in patients. It consists of 36 items and measures eight (8) dimensions of subjective health, namely: Physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health. These are the basic dimensions of physical and mental health.

Table 13 SF-36 summary

SF-36 [MV±SD (Median)]	Placebo	Rayocomp
Changes in health (before) Changes in health (after)	3.3±0.4 (3.0), n=27 3.2±0.5 (3.0), n=23	3.0±0.8 (3.0), n=27 1.9±0.7 (2.0), n=24
Physical functioning (before) Physical functioning (after)	73.3±14.7 (75.0), n=27 70.0±16.2 (70.0), n=23	64.3±24.4 (70.0), n=27 83.5±13.1 (85.0), n=24
Physical role functioning (before) Physical role functioning (after)	39.8±36.2 (25.0), n=27 42.4±37.3 (50.0), n=23	34.3±34.8 (25.0), n=27 81.3±33.2 (100.0), n=24
Bodily pain (before) Bodily pain (after)	35.9±11.7 (32.0), n=27 34.8±12.5 (32.0), n=23	33.9±14.3 (31.0), n=27 58.7±16.7 (62.0), n=24
SF-36 [MV±SD (Median)]	**Placebo**	**Rayocomp**

General health perceptions (before) General health perceptions (after)	50.2±21.0 (47.0), n=27 47.6±18.8 (47.0), n=23	51.3±15.0 (55.0), n=27 61.8±13.8 (64.5), n=24
Vitality (before) Vitality (after)	45.7±17.2 (45.0), n=27 44.6±40.0 (40.0), n=23	45.2±12.0 (45.0), n=27 62.7±11.9 (65.0), n=24
Social functioning (before) Social functioning (after)	78.7±18.9 (75.0), n=27 77.2±19.5 (75.0), n=23	78.7±18.3 (75.0), n=27 92.2±15.1 (100.0), n=24
Emotional role functioning (before) Emotional role functioning (after)	76.5±36.8 (100.0), n=27 76.8±39.5 (100.0), n=23	61.7±46.9 (100.0), n=27 86.1±33.9 (100.0), n=24
Mental health (before) Mental health (after)	66.7±17.3 (72.0), n=27 65.5±15.5 (68.0), n=23	64.1±14.1 (68.0), n=27 75.3±11.8 (76.0), n=24
Physical Summary Scale (before) Physical Summary Scale (after)	36.7±6.8 (35.6), n=27 36.1±7.2 (35.2), n=23	35.4±8.4 (34.2), n=27 45.9±5.5 (46.6), n=24
Mental Health Summary (before) Mental Health Summary (after)	49.3±10.4 (50.2), n=27 48.7±9.9 (50.5), n=23	47.8±10.1 (50.8), n=27 52.9±7.4 (55.6), n=24

A complete overview of the individual characteristics of the SF-36 questionnaire can be found in the statistical report in Sections 6 and 7.

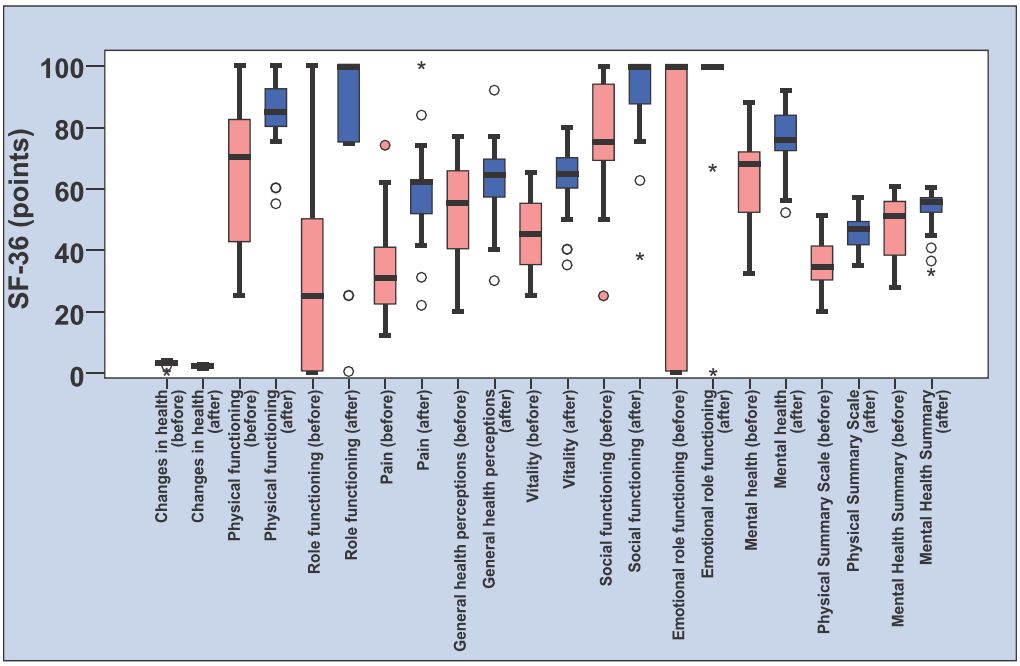


Figure 8 SF-36 before and after treatment (Rayocomp)

The overall result is summarised in Table 14 and in the corresponding figures (Figure 8 and Figure 9)

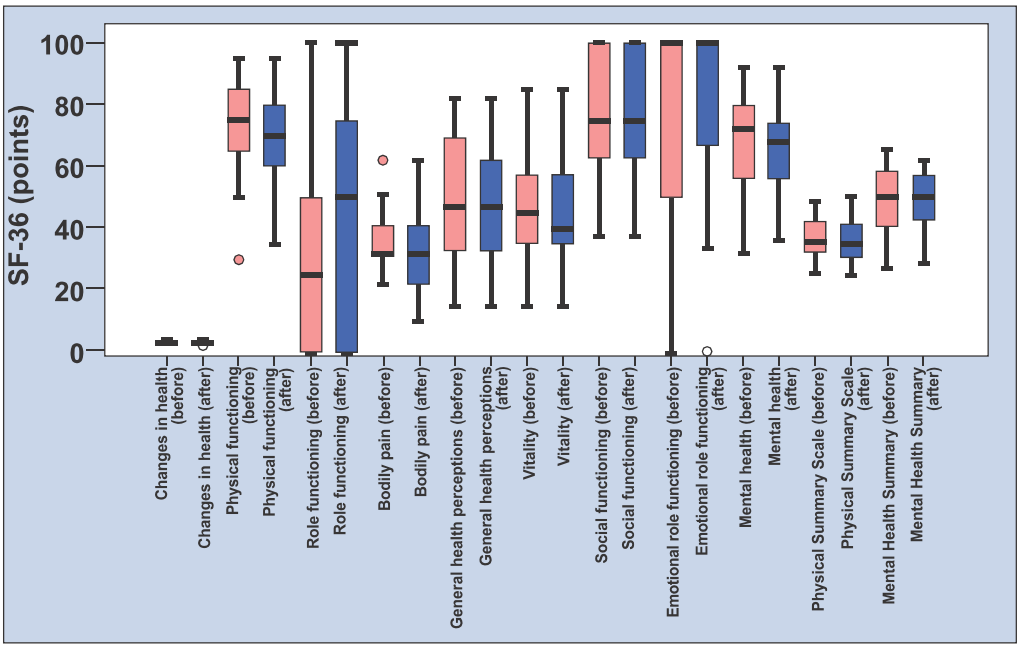


Figure 9 SF-36 before and after treatment (placebo)

The SF-36 parameters of physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health achieved no significant improvement in patients receiving the placebo treatment. Whereas, all of the parameters showed significant improvements ($p<0.001$) in patients receiving treatment with the Rayocomp bioresonance device. The differences (all $p < 0.05$) are summarised in Table 14 and shown in graph form in Figure 10.

Table 14 SF-36 differences after treatment

SF-36 [MV±SD (Median)]	Placebo	Rayocomp
Changes in health	-0.1±0.6 (0.0), n=23	-1.2±0.7(,1.0), n=24
Physical functioning	-3.3±6.1 (0.0), n=23	21.0±17.2 (17.5), n=24
Physical role functioning	0.0±13.1 (0.0), n=23	45.8±38.1 (50.0), n=24
Bodily pain	-1.0±10.6 (0.0), n=23	27.0±17.3 (30.0), n=24
General health perceptions	0.0±3.5 (0.0), n=23	11.0±11.5 (7.0), n=24
Vitality	0.9±0.1 (0.0), n=23	17.3±10.5 (15.0), n=24

SF-36 [MV±SD (Median)]	Placebo	Rayocomp
Social functioning	-0.5±4.6 (0.0), n=23	14.1±12.4 (12.5), n=24
Emotional role functioning	0.0±10.1 (0.0), n=23	23.6±43.4 (0.0), n=24
Mental health	-1.7±5.4 (0.0), n=23	11.7±10.0 (8.0), n=24
Physical Summary Scale	-0.5±6.6 (-0.8), n=23	11.1±7.8 (12.6), n=24
Mental Health Summary	-0.3±3.2 (0.0), n=23	4.9±6.4 (2.8), n=24
Significance	**P < 0.05**	

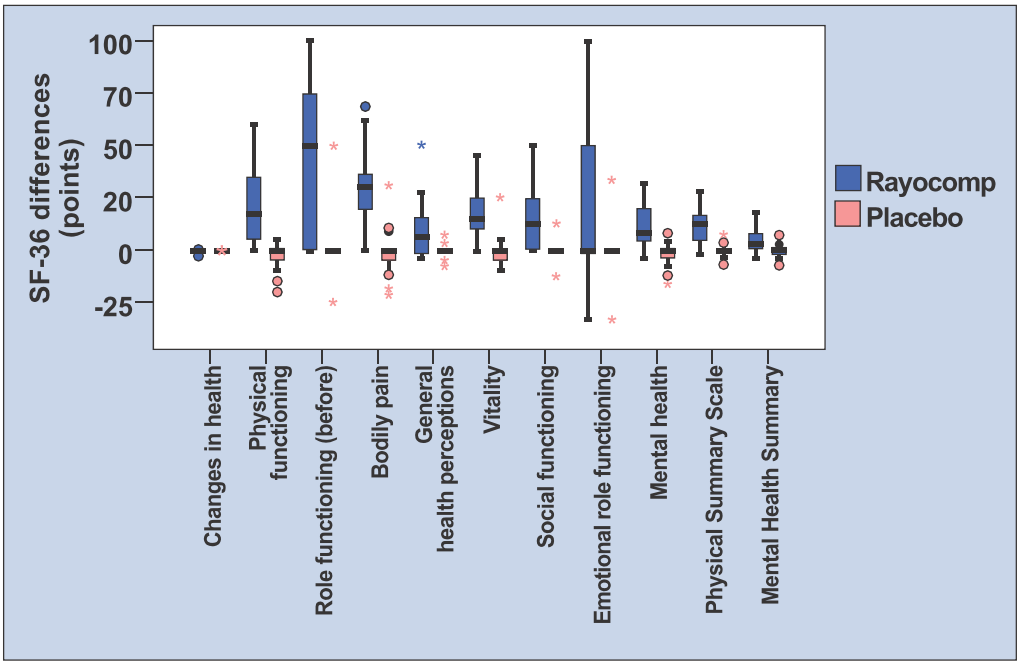


Figure 10 SF-36 differences before and after treatment

6.5.1.5 Satisfaction with the Therapy

Overall, there were significant differences in how patients answered the question of whether they would recommend the treatment to others. All patients in the Rayocomp group said that they would recommend it, while only around a quarter of patients in the placebo group said the same. The results are summarised in Table 15.

Table 15 Therapy recommendation

Assessment of the therapy	Placebo		Rayocomp	
	n	(%)	n	(%)
Therapy recommendation	6	26.1%	24	100.0%
No recommendation of the therapy	17	73.9%	0	0.0%

6.5.1.6 Adverse Events

In total, only three (3) of the 52 patients reported a total of 10 adverse events (AE). The results are summarised in Table 16 below.

Table 16 Adverse events

Patient ID	Visit Nr.	Description of AE	Group
FIW123	2	Tachycardia	Rayocomp
FIW123	3	Slight agitation	Rayocomp
FIW123	4	Palpitation	Rayocomp
PIA518	1	Sensory disturbances in hands, abdominal pain, head pressure, dragging pain in neck	Rayocomp
PIA518	3	Right foot cramp, abdominal pain	Rayocomp
PIA518	4	Stomach rumble	Rayocomp
YXI570	1	Stabbing pain in shoulders and neck, yawn, left eye twitching, pricking in foot "energy flow"	Placebo
YXI570	6	Twitches in shoulders	Placebo
YXI570	7	Heartburn	Placebo
YXI570	9	Crying fit (in pain relief)	Placebo

There were no reported problems with the product and there was no link between the adverse events and the test product. No further action was needed and the patients fully recovered. The degree of severity of all AEs were described as mild. A detailed description can be found in the statistical report in Section 8.

Severe AEs did not occur.

6.5.2 Product Defects

No product defects were reported in the study.

6.5.3 Analyses

The statistical analyses were summarised in a statistical report, which is attached as an annex to this report.

6.5.4 Data Reliability

There were no significant deviations from the Study Protocol. There were no screening failures reported. Slight deviations from scheduled occurred more frequently due to holidays, etc. The effects of these were reduced through an amendment (see Section 6.4). Seven patients did not complete the study. 47 patients concluded the study normally. The sponsor and principal investigator decided to include two more patients in the study due to 7 drop-outs. As a result, 54 patients were recruited in total. All study data was correctly recorded as source data.

The site was regularly monitored. Monitoring visits took place on:

First visit:	22/05/2019
Routine visits (n=5):	10.07.2019, 20.08.2019, 21.08.2019, 22.10.2019, 23.10.2019
Final visit:	18/12/2019

The data was also monitored online.
There were no audits or inspections.

7 Discussion and Conclusions

The worldwide application and acceptance of bioresonance therapy is based on the experience gained by alternative medicine practitioners (20). It is most successful in treating, among other things:

- Allergies and intolerances
- Psychosomatic illness
- Metabolic disorders
- Acute and chronic pain including rheumatic diseases

There have been several clinical trials involving human subjects. However, the explanation of the therapeutic effect of the treatment is solely theoretical. The physical principles put forward have not yet been proven. Controlled studies have not demonstrated a therapeutic effect, which is why the treatment is not recognised in conventional medicine (18, 19, 20).

The Swiss Society for Allergology and Immunology (18) even warns doctors and patients against using this treatment, which has been banned in the USA since 1986 and has not been covered by health insurance funds in Germany since the mid-1990s.

The literature presented in this study (18, 19, 20) does not apply to the bioresonance devices manufactured by Rayonex Biomedical GmbH. The aim of this study was therefore to collect data on the performance and safety of the Rayocomp bioresonance device when used for its intended purpose. The main aim was to assess the effectiveness of the device using the Neck Disability Index (NDI). Adverse events were recorded to assess the safety of the device.

The study population consisted of 52 patients who suffered from at least moderate pain in the cervical spine region.

The primary output measure was a change in NDI after treatment. Based on the results from Table 7, the differences are shown in Table 8 and Figure 1.

	Placebo (n=23)	**Rayocomp[2] (n=24)**
Difference NDI [MV±SD (Median)]	0.6±5.4 (0.0)	24.1±9.9 (21.0)
Significance	**p < 0.001**	

The Mann-Whitney U test showed one statistically significant difference in the primary output measure in support of the bioresonance therapy according to Paul Schmidt.

All secondary aims substantiated this result. Significant differences were observed in the visual analogue scale for pain characterisation, performance and quality of life (SF-36), which supports the bioresonance therapy according to Paul Schmidt.

In total, only three (3) of the 52 patients reported a total of 10 adverse events. There were no reported problems with the product and there was no link between the adverse events and the test product. No further action was needed.

The Rayocomp PS 1000 polar 4.0 bioresonance device achieved significant improvements in all objective and subjective parameters of the study when compared to the placebo device.

This study is particularly important as it adopts a double-blind design involving a placebo device for comparison.

7.1 Safety, Performance and All Other Endpoints

Based on the results of this clinical trial and when used for its intended purpose, no adverse effects were detected that could alter the risk profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. All things considered, the results confirmed the favourable safety profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. The device was shown to be safe when used according to the instructions.

2 Treatment with the Rayocomp PS 1000 polar 4.0

7.2 Risk and Benefit

The Rayocomp PS 1000 polar 4.0 bioresonance device achieved significant improvements in all objective and subjective parameters. This study has confirmed that the Rayocomp PS 1000 polar 4.0 bioresonance device is safe. The risk-benefit balance for the Rayocomp PS 1000 polar 4.0 bioresonance device is generally positive.

7.3 Clinical Relevance and Importance of the Data Compared to Other Available Information

The Rayocomp PS 1000 polar 4.0 bioresonance device is a certified / authorised medical device that is available on the market. This study has confirmed the effectiveness, safety and compatibility of treatment with this device.

The treatment achieved significant improvements in the baseline of both the primary and secondary efficacy variables.

7.4 Impact on Conducting Future Clinical Examinations

Bioresonance therapy is a widely used treatment method in naturopathy. The known treatment effects are largely based on the experience gained by alternative medicine practitioners. This study supports these findings. However, there is still a lack of evidence on the treatment's mode of action. This is one of the limitations of bioresonance therapy.

7.5 Limitation of the Test Assertions

Proof of efficacy was demonstrated through planned primary analysis of the primary output measure. In addition, a double-blind design was implemented using inactivated devices (placebo).

8 Abbreviations and Definitions

CE	*Communautés Européenes*	ICH	*International Council for Harmonisation*
CRO	*Clinical Research Organisation*		
		ISO	*International Standards Organization*
EC	*Ethics committee*		
GCP	*Good Clinical Practise*	MPG	*Medical Devices Act*
CSS	*cervical spine syndrome, Cervical spine syndrome*	NDI	*Neck Disability Index*

Rayocomp	*Rayocomp PS 1000 polar 4.0*	Sham	*Placebo medical device*
		AE	*Adverse Events*
SD	*Standard deviation*	VAS	*Visual Analogue Scale, Visual Analogue Scale*
SF-36	*Health Questionnaire*		

9 Ethical Considerations

The study was conducted in compliance with the following laws, standards and regulations:

- The clinical trial was conducted in accordance with the current version of the Declaration of Helsinki and the standard of "Good Clinical Practices" as outlined in DIN EN ISO 14 155 and ICH-GCP.
- The professional code of conduct of the State Medical Association pertinent to the study site
- The Federal Data Protection Act and the state protection laws that apply to the participating study site
- A written vote on protocol was held before commencing clinical trial. The clinical trial began only after it had received a positive vote from the ethics committees that were responsible for the participating sites.
- The study was conducted in accordance with §23b of the Medical Devices Act (MPG). As a result, no approval was required from the higher federal authority.

10 Administrative Structure of the Test

10.1 Organisation of the Test

The study was initiated and sponsored by Rayonex Biomedical GmbH, Sauerland-Pyramiden 1, 57368 Lennestadt, Germany.

As CRO, CRO Dr. med. Kottmann GmbH & Co. KG was responsible for data management, statistics, project management and monitoring.

CRO Dr. med. Kottmann GmbH & Co. KG was also responsible for regulatory tasks, such as submitting study documents to the ethics committee and the higher federal authority.

10.2 Investigator

The principal investigator was:

Dr. med. Axel Schußmann
Zur Ohe 2
21406 Melbeck, Germany
Telephone: +49 (0) 4134 900-313
Telefax: +49 (0) 4134 900-483

The principal investigator was temporarily substituted by Dr. Jesko Matthes and Ms Frederike Reimann.

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12 Table of Figures

The patient and user information presents the results of a clinical prospective, double-blind, randomised, study of the highest scientific level that aims to provide objective proof of the performance and safety of the Rayocomp bioresonance device in patients with cervical spine syndrome.

The final report concludes that the Rayonex bioresonance devices according to Paul Schmidt are safe and effective to use. The following are citations from Chapter VII of the final report:

"There was no change in the NDI of the placebo group, but a significant improvement in the NDI of the group treated with the Rayocomp bioresonance device ($p<0.001$)."

"The placebo treatment did not achieve significant improvements in neck pain, headaches, back pain, shoulder pain or muscle tension, while treatment with the Rayocomp bioresonance device showed significant improvements ($p<0.001$) in all parameters (Figure 2, Figure 3, Table 10)."

"In terms of physical capacity, patients receiving the placebo treatment showed no significant improvement, while patients treated with the Rayocomp bioresonance device showed significant improvements ($p<0.001$) in all parameters (Table 11). The differences (all $p < 0.001$) are summarised in Table 12 and shown in graph form in Figure 7."

"The SF-36 parameters of physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning and mental health achieved no significant improvement in patients receiving the placebo treatment. Whereas, all of the parameters showed significant improvements ($p<0.001$) in patients receiving treatment with the Rayocomp bioresonance device.The differences (all $p < 0.05$) are summarised in Table 14 and shown in graph form in Figure 10."

"Overall, there were significant differences in how patients answered the question of whether they would recommend the treatment to others. All patients in the Rayocomp group said that they would recommend it, while only around a quarter of patients in the placebo group said the same. The results are summarised in Table 15."

"Furthermore, the study confirms that the Rayocomp PS 1000 polar 4.0 bioresonance device is safe. Based on the results and information provided in the manual, no adverse effects were detected during this clinical trial that could alter the risk profile of the Rayocomp PS 1000 polar 4.0 bioresonance device. The favourable safety profile of the medical device was confirmed. It was shown to be safe when used according to the instructions in the manual."

This scientific study proves to patients and therapists alike that bioresonance therapy according to Paul Schmidt is both safe and effective when applied with the Rayocomp bioresonance devices.

Rayonex Biomedical GmbH
Sauerland - Pyramiden 1 | 57368 Lennestadt (Germany)
Telephone: +49 2721 6006-0 | Telefax: +49 2721 6006-66
E-Mail: info@rayonex.de | www.rayonex.de

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