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Clinical Investigation Report

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Clinical Investigation Report

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TITLE OF THE CLINICAL INVESTIGATION:

'USE OF THE ELECTROPHYSIOLOGICAL BIOFEEDBACK SYSTEM NUCLEUS Biofeedback System IN

- **STRESS DETECTION AND REDUCTION**
- **MUSCULAR REEDUCATION**
- **PAIN TREATMENT**
- **PREGNANCY STABILITY IMBALANCE (DETECTION OF MEDICAL CONDITIONS)'**

CODE OF THE CLINICAL INVESTIGATION:

BFK-01

Monocentric and comparative clinical investigation

Clinical Investigation Plan
BFK-CIP-01

Clinical investigation carried out in accordance with the standard
SR EN ISO 14155:2012
Date: October 20TH, 2022

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[signature and stamp]

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Table of contents

1 SUMMARY

1.1 Title of the clinical investigation

'USE OF THE ELECTROPHYSIOLOGICAL BIOFEEDBACK SYSTEM
NUCLEUS IN

- STRESS DETECTION AND REDUCTION
- MUSCULAR REEDUCATION
- PAIN TREATMENT
- PREGNANCY STABILITY IMBALANCE (DETECTION OF MEDICAL CONDITIONS)'

1.2 Introduction

The purpose of the clinical investigation is to evaluate the performance and tolerance of the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in stress detection and reduction, muscular reeducation, pain treatment, assessed in patients with neuromuscular dystonia and muscle contractures and in detecting the medical conditions (pregnancy stability imbalance).

1.3 Demographic data of the patients

The demographic data of the 57 patients enrolled in this clinical investigation are:

Gender	
Male	11(19,30%)
Female	46(80,70%)
Average age	61,81 years
Residence	
Urban	12(21,05%)
Rural	45(78,95%)
Profession	
Pensioner	41(71,93%)
Worker	3(5,26%)
Home staying	3(5,26%)
Other	10(17,55%)

In order to assess the effectiveness of the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the following parameters were monitored:

- Score of depression, anxiety and stress of the subject (patient)
- Score of neuromuscular dystonia
- Intensity of the pain felt by the subject (patient), in case of dystonia and muscle contracture
- Analysis of the incidence of all adverse events, including the overall impression regarding the success of the treatment

- Analysis of the subject's perception on the extent to which the daily activities and the leisure time activities were restricted.

To assess the tolerance of the Universal Electrophysiological Biofeedback System NUCLEUS, its ease of use was also appreciated.

1.4 Results

The occurrence of the adverse phenomena and / or adverse events was not indicated in any patient, the use of the Universal Electrophysiological Biofeedback System NUCLEUS being safe, without causing the feeling of confusion after the procedure, vasovagal response (dizziness, sweating, etc.) or irritation of the skin, at the site of application of the electrodes.

The ease of use of the Universal Electrophysiological Biofeedback System NUCLEUS was appreciated by the physician investigator as being very good, the product being acceptable from the user's point of view.

Regarding the performance of the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, we found the following:

1. The procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in order to reduce the stress, depression and anxiety are extremely efficient and safe; the benefits for patient being represented on the one hand by the reduction improvement of depression, anxiety and reduction of stress, on the other hand, as a consequence, by the improvement of certain medical disorders, including the pain associated with them.

2. The patients in the group receiving specific procedures carried out with the Biofeedback Universal System NUCLEUS, had a remarkable improvement of the health condition; the average score of dystonia, after making the procedures, decreased by 50%. Regarding the patients in the control group, at the end of the tracking period, the average score of dystonia decreased by 7%.

3. After 6 specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the average pain felt by patients decreased from the value of 6,2 Wong-Baker scale (pronounced pain, which determines the patient's inability to conduct some activities), to a value equal to 1,8 which means, according to the same scale, a pain which can be neglected. Therefore, after 6 procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the patients were able to perform all daily activities, practically, without restrictions. Although the rate of decrease of the pain intensity was higher in the early days in the patients in the control group, later, it stagnated around the value 4 (moderate pain), while in the patients who received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the rate of decrease (although initially a little lower) was maintained; moreover, it widened, the pain decreasing significantly. The major benefits of using the Universal Electrophysiological Biofeedback System NUCLEUS consisted in significant

improvement of the pain felt by the patients with muscular dystonia and / or with muscle contractures, when the procedures are associated with the standard treatment (physiotherapy, kinetic therapy, treatment with medication).

4. In percentages, the medical conditions detected during the scan performed with the Biofeedback Electrophysiological Universal System, represent 33% of those detected by the standard medical investigations. With one exception, all medical conditions detected by scanning the human body were confirmed by the standard medical investigations: we appreciate that the Universal Electrophysiological Biofeedback System NUCLEUS is a very useful tool to guide the patients to the clinics for medical tests, recommending the investigations to be performed by it.

5. There is a significant decrease in the restriction of the daily activities and the leisure time activities in the case of patients in the group which received specific procedures carried out by the Universal Electrophysiological Biofeedback System NUCLEUS, while in the patients in the control group, the largest share is represented by the patients who appreciated a stagnation of the restriction of activities.

6. The Universal Electrophysiological Biofeedback System NUCLEUS is particularly effective in improving the condition of the patients, with positive influences on their quality of life.

1.5 Conclusions

The data collected after conducting the clinical investigation proved a particularly effectiveness of the Universal Electrophysiological Biofeedback System NUCLEUS in:

- Detection and reduction of stress, depression and anxiety
- Muscular re-education (improvement of the neuromuscular dystonia symptoms and of the muscle contractures)
- Pain treatment
- Detection of medical conditions

as well as safety of its use, no patient reported adverse phenomena / adverse events.

Initiation date of the clinical investigation: 22nd April 2015
Date of analysis: 29th May 2015.

2 INTRODUCTION

The Universal Electrophysiological Biofeedback System NUCLEUS is a 2nd class medical device, according to Directive 93/42/CEE, as amended by Directive 2007/47/EC, which fully meets the regulatory requirements, bearing the mark EC1868.

The clinical investigation was initiated in order to assess with a greater accuracy the performance and tolerability of the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in stress detection and reduction, muscular re-education, pain treatment and in detection of the patients' medical conditions.

3. Biofeedback System NUCLEUS DEVICE AND METHODS

3.1 Description of the Universal Electrophysiological Biofeedback System NUCLEUS

The EUDCTOR device is a biofeedback electrophysiological universal system. The device coordinates a complex electro-modal of biofeedback with software for computer in order to obtain bioenergetic information from the patient's subconscious. The information is obtain through electrodes placed on the head, on the wrists and legs, which provide an accurate picture of the patient's general condition. The information is selected and listed by NUCLEUS in the order to the reaction scores and the stress factors are analysed during the session of stress reduction.

The Universal Electrophysiological Biofeedback System NUCLEUS uses low-frequency currents.
Its components are:

- biofields transceiver, NUCLEUS;
- electrodes / harness;
- Cable to connect the device NUCLEUS to computer / LAPTOP;
- a package of programs installed on a computer and a compatibility tester.

The Universal Electrophysiological Biofeedback System NUCLEUS detects the difference between the input and output signals of various frequencies and the associated computer program selects the standards (models) that are closest to the registration of the person. The measurements depend on the quality of the equipment, and the diagnostic's accuracy depends on the compliance with the statistical data (standards).

Principle of operation

Every organ and every cell has its own frequency or 'electromagnetic signature' and by collecting some huge amounts of data from thousands of patients, it could be found the normal frequencies for each organ. The viruses, bacteria and diseases specifically change the frequency of that organ, and thus, the device can diagnose fairly accurately. Also, the viruses, bacteria and pathogens have their own frequency (electromagnetic signature) and their presence in the body can thus be detected by the Universal Electrophysiological Biofeedback System NUCLEUS.

3.2 Clinical Investigation Plan

The main objectives of the clinical investigation conducted for the Universal Electrophysiological Biofeedback System NUCLEUS consist in the evaluation of its performance and tolerability in stress detection and reduction, muscular re-education, pain treatment and in detection of the subject's (patient's) medical conditions.

The clinical investigation was monocentric and comparative, performed on 4 groups of subjects, as follows:

- A control group of 30 subjects with muscular dystonia / muscular contractures, which received the standard treatment;
- A group of 27 subjects with muscular dystonia / muscular contractures, in addition to the standard therapy, received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS;
- A control group of 14 subjects with gluteal muscle contracture (illness associated with muscle dystonia) which received the standard treatment;
- A group of 14 subjects with gluteal muscle contracture (illness associated with muscle dystonia) which, in addition to the standard therapy, received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS.

It was conducted in compliance with ethical considerations and it was obtained the approval of the Ethics Commission attached to the National Institute of Recovery, Physical Medicine and Balneo- climatology of Bucharest.

The assurance of the data quality was carried out by auditing the clinical investigation by the sponsor's representatives, SC BIOFEEDBACK 2014 SRL, as well as by the monitor appointed by it, which verified the manner of storing and using the electrophysiological systems of biofeedback NUCLEUS during the investigation, but also the manner of collecting / registering and archiving the data taken during the evaluation of subjects by the physicians-investigators.

3.2.1 Subjects of the clinical investigation

The criteria for including the subjects in the clinical investigation were:

- The acceptance of the subject by signing the consent form (BFK-ICF-01);
- Age of the subject: between 18 and 75 years;
- Subject with depression, anxiety, stress, muscular dystonia, muscle contracture;
- Gender: male or female;
- The non-inclusion of the subject in one of the exclusion criteria in the clinical investigation.

The criteria for excluding the subjects from the clinical investigation were:

- Refusal of the subject to sign the consent form (BFK-ICF-01);
- Subject belonging to the vulnerable populations;
- Age of subject - less than 18 years;
- Subject with concurrent conditions that could affect the evaluated parameters (listed above):
  - ⇒ Epilepsy;
  - ⇒ Patients with pacemaker;
  - ⇒ Patients with electric hyper-reactivity;
  - ⇒ Patients with skin diseases at the site of application of the electrodes;
- Pregnant women;

- Patients under the influence of drugs and alcohol;
- Patients who received procedures carried out with bio-resonance devices in the last 4 weeks;
- Insufficient cooperation of the subject;
- The occurrence of events excluding the subject from the including criteria in the investigation.

3.2.2. Procedures carried out by subjects during the clinical investigation

During the clinical investigation, the subject were examined at the beginning of registration and during the investigation, concerning:

- Subjects with muscular dystonia:
  - Score of depression, anxiety, stress;
  - Score of muscular dystonia;
  - Duration;
  - Pain felt;
  - Detection of other medical conditions.
- Subjects with muscle contracture:
  - Score of depression, anxiety, stress;
  - Time period with that condition;
  - Localization;
  - Pain felt;
  - Detection of other medical conditions.
- Overall impression regarding the success of the treatment;
- Subject's perception on the extent to which the daily activities and the leisure time activities were restricted.

Later, after signing the informed consent, the patient received, in addition to the standard treatment, 6 specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, except for the patients in the control groups, who received only the standard treatment.

The choice of the type of procedure, depending on the medical condition which justified the inclusion of the subject in the medical investigation (procedure of scanning the body, specific procedures) was performed according to the user manual of the Universal Electrophysiological Biofeedback System NUCLEUS and according to the navigation manual, where it its detailed the operation manner of the device, together with the computer where the software NUCLEUS64 is installed.

After the 6 procedures, the patients were assessed by the registration of the following parameters:

- Subjects with muscular dystonia:
  - Score of depression, anxiety, stress;
  - Score of muscular dystonia;
  - Pain felt;
- Subjects with muscle contracture:

- Score of depression, anxiety, stress;
- Time period with that condition;
- Pain felt;

- Overall impression regarding the success of the treatment;
- Subject's perception on the extent to which the daily activities and the leisure time activities were restricted.

3.2.2 Treatment / simultaneous medication

The subjects included in this clinical investigation received the following treatments:

Subjects in the control group:

TREATMENT / SIMULTANEOUS MEDICATION PATIENTS IN THE CONTROL GROUP		**TREATMENT / SIMULTANEOUS MEDICATION PATIENTS IN THE GROUP RECEIVING SPECIFIC PROCEDURES CARRIED OUT WITH THE DEVICE NUCLEUS**	
Nr. subject / initials	**Treatment / medication**	**Nr. subject / initials**	**Treatment / medication**
1. GS	US, KT	1. SM	US, KT
2. PT	US, KT	2. DN	IF,US
3. PD	US, KT, Massage	3. SAG	US, Parafin
4. SA	US, KT, Massage	4. MG	US, Magnetotherapy
5. MM	US, Massage	5. MV	US, Magnetotherapy
6. AG	TENS, Augmentin	6. NM	US, Magnetotherapy
7. CP	US, KT, Massage, US, Magnetotherapy	7. NG	US, Lasertherapy, Magnetotherapy
8. CM	Massage, Paraffin	8. IA	US, Parafin
9. AE	US, KT, Massage	9. SE	US, Parafin
10. BE	KT, US, Magnetotherapy	10. GT	US, Parafin
11. IS	US, KT, Massage, Paraffin	11. MM	US, Magnetotherapy
12. GS	US, KT, Massage, Paraffin	12. IC	US, KT
13. TB	US, KT, Massage, Paraffin	13. BF	US, Massage, Paraffin
14. MG	US, KT, Massage	14. VE	US, Lasertherapy,
15. AE	US, Lasertherapy, Paraffin	15. PV	US, Magnetotherapy
16. DM	US, KT, Massage	16. VA	US, TENS, Magnetotherapy
17. MR	KT, US, Magnetotherapy	17. MDD	US, KT
18. IA	US, KT, Massage, Paraffin	18. VT	US, KT, Lasertherapy

TREATMENT / SIMULTANEOUS MEDICATION PATIENTS IN THE CONTROL GROUP		**TREATMENT / SIMULTANEOUS MEDICATION PATIENTS IN THE GROUP RECEIVING SPECIFIC PROCEDURES CARRIED OUT WITH THE DEVICE NUCLEUS**	
Nr. subject / initials	**Treatment / medication**	**Nr. subject / initials**	**Treatment / medication**
19. DE	Lasertherapy, Massage	19. NI	US, Magnetotherapy
20. GE	US, Paraffin, US, Magnetotherapy	20. ME	US, Lasertherapy,
21. DF	US, KT, Massage, Paraffin	21. PG	US, Massage, Paraffin
22. DR	US, Massage, Lasertherapy	22.BE	TENS, Paraffin, Lasertherapy
23. IR	US, Parafin	23. PEG	US, Lasertherapy,
24. IF	US, Massage, Paraffin	24. SG	US, Lasertherapy,
25. BT	US, Massage	25. VA1	US, Massage, Paraffin
26. VV	Massage, Paraffin	26. OS	US, Massage
27. SM	US, Massage	27. MP	US, KT
28. GS	US, KT, Massage		
29. BG	US, KT, Massage		
30. BM	US, KT, Massage, Paraffin		

3.2.4. Duration of the subjects' evaluation

The subjects were evaluated for 2 weeks or until the performance of the 6 specific procedures, using the Universal Electrophysiological Biofeedback System NUCLEUS

3.2.5. Statistical analysis

Several null assumptions H_{01}, H_{02}... were taken into account, therefore:

H_{01} – depression, anxiety and stress of the subject after 6 specific procedures carried out with the device NUCLEUS; H_{01} = score equal to the one of the subjects in the control group, with the limit permissible error r_1 = severe;

H_{02} – dystonia of the subject after 6 specific procedures carried out with the device NUCLEUS; H_{02} = score equal to the one of the subjects in the control group, with the limit permissible error r_2 = severe;

H_{03} – pain felt by the subject before carrying out each specific procedure with the device NUCLEUS; H_{03} = severe pain, with the limit permissible error r_3 = moderate;

H_{04} – overall impression regarding the success of the treatment, after 6 specific procedures carried out with the device NUCLEUS; H_{04} = 7, with the limit permissible error: r_4 = 6;

H_{05} – extent to which the daily activities of the subject (patient) and his / her leisure time activities were restricted after 6 specific procedures carried out with the device NUCLEUS; H_{05} = 4, with the limit permissible error: r_5 = 3;

H_{06} – ease of using the device NUCLEUS; H_{06} = hard; with the limit permissible error r_6 = relatively easy.

The alternative assumptions were the following:

H_{11} – the depression, anxiety and stress of the subject after 6 specific procedures carried out with NUCLEUS device, with the materiality limit α_1 = moderate;

H_{12} – the dystonia of the subject after 6 specific procedures carried out with NUCLEUS device, with the materiality limit α_2 = moderate;

H_{13} – the pain felt by the subject before carrying out each specific procedure with NUCLEUS device, with the materiality limit α_1 = moderate;

H_{14} – the general impression regarding the success of the treatment, after 6 specific procedures carried out with NUCLEUS device, with the materiality limit α_4 =3;

H_{15} – the extent to which the daily activities of the subject (patient) and this /her leisure time activities were restricted, after 6 specific procedures carried out with NUCLEUS device, with the materiality limit α_5 =2;

H_{16} – ease of using NUCLEUS device, with the materiality limit α_6 = easy.

The calculation was carried out on 57 patients.

3.2.5.1 Score of depression, anxiety, stress;

The data regarding the scores related to depression, anxiety and stress were summarized in a table, the average score for each group was calculated, and subsequently and the results were compared. It was also calculated the statistical power p.

The scores of depression, anxiety and stress were determined according to the scale (*Depression, Anxiety and Stress Scale*) below:

Depression Anxiety and Stress Scale

Scores

Scores of depression, anxiety and stress are calculated by summing the relevant results.

The questions related to the depression are: 3,5,10,13,16,17,21,24,26,31,34,37,38,42

The questions related to the anxiety are: 2,4,7,9,15,19,20,23,25,28,30,36,40,41

The questions related to the stress are: 1,6,8,11,12,14,18,22,27,29,32,33,35,39

The severity is assessed according to the table below:

	Depression	**Anxiety**	**Stress**
Normal	0 – 9	0 – 7	0 – 14
Poor	10 – 13	8 – 9	15 – 18
Moderate	14 – 20	10 – 14	19 -25
Severe	21 – 27	15 – 19	26 – 33
Extremely severe	28+	20+	34+

Reference : Lovibond, S.H. & Lovibond, P.f. (1995). Manual for the Depression anxiety Stress Scales. (2nd Ed) Sydney: Psychology Foundation.

Please reach each question and circle one of the numbers 0, 1. 2 or 3, which best indicates your situation in the last week. There are no right or wrong answers. Do not spend too much time to any question.

The numbers have the following meanings:
0 – Not applicable in my case
1 – It applies in my case, to some extent or some of the time
2 – It applies in my case, to some considerable extent or a good part of the t*i*me
3 – It applies in my case, to a large extent or most times

1	I woke up upset because of things quite banal	0	1	2	3
2	I found that I have dry mouth	0	1	2	3
3	I could not find any positive feeling, regardless of the situation.	0	1	2	3
4	I experienced breathing difficulties (for example, excessively rapid or difficult, in the absence of physical exertion)	0	1	2	3
5	I could not leave the house	0	1	2	3
6	I had the tendency to overreact to ordinary situations	0	1	2	3
7	I experienced a tremor condition (for example, feeling of weak legs)	0	1	2	3
8	It was difficult to relax	0	1	2	3
9	I was placed in situations where I felt anxiety; I felt relieved when it ended	0	1	2	3
10	I felt I had no expectation	0	1	2	3
11	I was angry quite easily.	0	1	2	3
12	I felt that I have consumed a lot of angry energy	0	1	2	3
13	I felt sad and depressed	0	1	2	3
14	I was anxious when I was late for various reasons (for example, elevator, semaphore, etc.)	0	1	2	3

15	I was senselessness	0	1	2	3
16	I felt that I lost interests almost for everything	0	1	2	3
17	I felt that I was not valued, as a person	0	1	2	3
18	I was quite sensitive	0	1	2	3
19	I sweat visibly (for example, hands), in the absence of high temperature or effort	0	1	2	3
20	I felt scared for no reason	0	1	2	3
21	I felt that the life is not worth living	0	1	2	3
22	I found it hard to get up	0	1	2	3
23	I had difficulties when swallowing	0	1	2	3
24	I could not feel any joy as result of the things I have done	0	1	2	3
25	I was aware of the state of my heart, in the absence of the physical exertion (for example, the feeling of increased pulse rate or the absence of heartbeat)	0	1	2	3
26	I felt discouraged	0	1	2	3
27	I found that I was very irritable	0	1	2	3
28	I felt that I was close to panic	0	1	2	3
29	It was hard for me to calm down, after I got angry	0	1	2	3
30	I feared I would not be able to fulfil unknown tasks	0	1	2	3
31	I was not existed under any circumstances	0	1	2	3
32	It was difficult for me to tolerate the interruption of the work I was performing	0	1	2	3
33	I was in a tautness state	0	1	2	3
34	I felt that I was quite worthless	0	1	2	3
35	I could not tolerate any situation that prevented me to obtain the thing I was doing	0	1	2	3
36	I felt terrified	0	1	2	3
37	I could not see anything good in the future so that I be optimistic	0	1	2	3
38	I felt that the life was meaningless	0	1	2	3
39	I felt restless	0	1	2	3
40	I was concerned about situations where I might panic and to make a fool of myself	0	1	2	3
41	I experienced trembling (for example, hands)	0	1	2	3
42	It was hard for me to carry out my activity and to take initiatives	0	1	2	3

3.2.5.2 Neuromuscular dystonia

The data concerning the scores related to the neuromuscular dystonia were summarized in a table. The average score was calculated and the results obtained for each group were compared (control group and patients receiving the specific procedures carried out by the device NUCLEUS). It was also calculated the statistical power p.

The neuromuscular dystonia was analysed according to *Unified Dystonia Rating Scale – UDRS*, according to the template below:

Unified Dystonia Rating Scale – UDRS	
Factor (area)	**Criterion**
Length	
0	Absent
0.5	Infrequent (<25% of the time); predominantly submaximal
1.0	Infrequent (<25% of the time); predominantly maximal
1.5	Intermittent (25-50% of the time); predominantly submaximal
2.0	Intermittent (25-50% of the time); predominantly maximal
2.5	Common (50-75% of the time); predominantly submaximal
3.0	Common (50-75% of the time); predominantly maximal
3.5	Constant(>75% of the time); predominantly submaximal
4.0	Constant(>75% of the time); predominantly maximal
Motor severity	
Eyes and upper face	
0	Absent
1	Light: it increased intermittently, light wrinkles on the forehead (≤25% of the maximum intensity)
2	Moderate: closing the eyes, without forcing or pronounced wrinkles on the forehead (>25% but ≤50% of the maximum intensity)
3	Severe: closing the eyes, with force , able to open the eyes in 10 seconds or prominent wrinkles on the forehead (>50% but ≤75% of the maximum intensity)
4	Extreme: closing the eyes, with force, able to open the eyes in 10 seconds or intense wrinkles on the forehead (>75% of the maximum intensity)
Lower face	
0	Absent
1	Light: grimaces, with minimal distortions of the mouth (≤25% of the maximum intensity)
2	Moderate: grimaces, with moderate distortions of the mouth (>25% but ≤50% of the maximum intensity)
3	Severe: obvious grimaces, with severe distortions of the mouth (>50% but ≤75% of the maximum intensity)
4	Extreme: intense grimaces, with extreme distortions of the mouth (>75% of the maximum intensity)
Jaw and tongue	
0	Absent
1	Light: grimaces, with minimal distortions of the mouth (≤25% of the maximum intensity)
2	Moderate: opening the jaw or tongue protrusion (>25% but ≤50% of the possible range) or jaw clenching with light bruxism
3	Severe: opening the jaw or tongue protrusion (>50% but ≤75% of the possible range) or jaw clenching with pronounced bruxism

Unified Dystonia Rating Scale – UDRS	
Factor (area)	**Criterion**
4	Extreme: opening the jaw or tongue protrusion (>70% of the possible range) or jaw clenching with the impossibility of opening the mouth
Larynx 0 1 2 3 4	 Absent Light: barely detectable hoarseness or drowned voice or occasional voice breaks Moderate: clear hoarseness or clearly drowned voice or frequent voice breaks Severe: marked hoarseness or markedly drowned voice or continuous voice breaks Extreme: unable to speak
Throat 0 1 2 3 4	 Absent Light: head movement from the neutral position ≤25% of the normally possible limits Moderate: head movement from the neutral position >25% but ≤50% of the normally possible limits Severe: head movement from the neutral position >50% but ≤75% of the normally possible limits Extreme: head movement from the neutral position >75% of the normally possible limits
Shoulder and upper arm (left and right) 0 1 2 3 4	 Absent Light: shoulder and arm movement ≤25% of the normally possible limits Moderate: shoulder and arm movement >25% but ≤50% of the normally possible limits Severe: shoulder and arm movement >50% but ≤75% of the normally possible limits Extreme: shoulder and arm movement ≤75% of the normally possible limits
Lower arm, including the elbow (left and right) 0 1 2 3 4	 Absent Light: arm and hand movement ≤25% of the normally possible limits Moderate: arm and hand movement >25% but ≤50% of the normally possible limits Severe: arm and hand movement >50% but ≤75% of the normally possible limits Extreme: arm and hand movement ≤75% of the normally possible limits
Pelvis and upper leg (left and right) 0 1 2	 Absent Light: tilting the pelvis or leg or hip movement ≤25% of the normally possible limits Moderate: tilting the pelvis or leg or hip movement >25% but ≤50% of the normally possible limits

Unified Dystonia Rating Scale – UDRS	
Factor (area)	**Criterion**
3 4	Severe: tilting the pelvis or leg or hip movement >50% but ≤75% of the normally possible limits Extreme: tilting the pelvis or leg or hip movement >75% of the normally possible limits
Lower leg, including the knee (left and right) 0 1 2 3 4	 Absent Light: leg or foot movement ≤25% of the normally possible limits Moderate: leg or foot movement >25% but ≤50% of the normally possible limits Severe: leg or foot movement >50% but ≤75% of the normally possible limits Extreme: leg or foot movement >75% of the normally possible limits
Torso 0 1 2 3 4	 Absent Light: torso bending ≤25% of the normally possible limits Moderate: torso bending >25% but ≤50% of the normally possible limits Severe: torso bending >50% but ≤75% of the normally possible limits Extreme: torso bending >75% of the normally possible limits

3.2.5.3 Pain felt by the patient

The intensity level of the pin felt by subjects, assessed according to Wong-Baker scale (0 - 10 numerical scale, combination with facial symbols) was centralized in a table. The average pain was calculated before the first procedure, namely at the enrolment of the subject, and also before carrying out the procedure, namely at the moment of consultation (in the case of the control group). The data were represented in a chart comprising the intensity levels of the pain felt by the subjects of the two groups.

3.2.5.4 Overall impression regarding the success of the treatment

The overall impression regarding the success of the treatment was appreciated by the patients (both in the control group and in the group receiving specific procedures carried out with the device NUCLEUS), according to the scale below:

Overall impression regarding the success of the treatment	☐ 1 – Very much improved condition ☐ 2 – Much improved condition ☐ 3 – Slightly improved condition ☐ 4 – Unchanged condition

	☐ 5 – Slightly worse condition ☐ 6 – Much worse condition ☐ 7 – Very much worse condition

The data were registered in a table, the number of subjects / each score registered were determined in percentages for each group of subjects.

3.2.5.5 The extent to which the daily activities and the leisure time activities were restricted

The extent to which the daily activities and the leisure time activities were restricted was appreciated by the patients (both in the control group and in the group receiving specific procedures carried out with the device NUCLEUS) before the first procedure with the device NUCLEUS (at the enrolment time) and after carrying out the 6 procedures / namely at the enrolment time and after the last follow-up, according to the scale below, the data being registered in a table:

The extent to which the daily activities and the leisure time activities were restricted	☐ 0 – Without restrictions ☐ 1 – Light restrictions ☐ 2 – Moderate restrictions ☐ 3 – Substantial restrictions ☐ 4 – Extreme restrictions

The number of subjects / each score registered were determined in percentages for each group of subjects.

3.2.5.6. Detection of the medical conditions of the subject (patient)

The medical conditions detected by scanning the body of the subject (patient), were registered in a table, being calculated the percentage of the medical conditions detected by scanning the human body using the device NUCLEUS, conditions confirmed by the standard medical analysis / investigations.

3.2.5.7 The occurrence of the local and / or systemic undesirable phenomena; ease of use of the Electrophysiological Biofeedback System, NUCLEUS

The data relating to: the occurrence of the local / systemic undesirable phenomena, as well as the ease of use of the devices NUCLEUS were centralized in a table, in the case of subjects which received the specific procedures.

The calculation of the statistical power in case of determinations

As n1 30 (number of subjects receiving the procedures carried out with the device NUCLEUS) and n2 < 30 (number of subjects in the control group), the t test was applied.

Regarding the differentiation between the independent and dependent tests, it is made depending on the nature of the standard included in the experiment.

As the two standards are randomly selected based on their natural situation, the independent tests are used.

The independent t calculation.

$$t = \frac{M_1 - M_2}{EE_{M_1 - M_2}}$$

Where: M1 and M2 represent the averages of the two standards; EE_{M1-M2} represent the standard error of the difference between the two averages

$$EE_{M_1 - M_2} = \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$$

Where: s_1^2 represent the dispersion of the first group; s_2^2 represent the dispersion of the second group; n1 - number of subjects in the first group = 30; n2 - number of subjects in the second group = n1.
After calculating the independent t, the value obtain must be compared to the value given to t in the table:

a. Setting the degrees of freedom (in order to know the value of t in the table, which will be compared with the value obtained). The calculation of the degrees of freedom for the independent t test is made as follows: *df* = (n1 + n2) - 2.
b. The second intermediate step is choosing the type of situation of t, between unilateral t and bilateral t. The average of the comparative standard is less than the average of the population to which the standard belongs, therefore, we will use the values of the unilateral test t in the table.
c. Setting the value of t according to the materiality limit chosen. The statistical practice considers to be necessary the establishment of the confidence level of maximum 0,05 (.05).

Turning to the issue given, we will refer to the t table in order to compare the value obtained with the value presented in the table for *df* (degree of freedom) for unilateral t to a materiality limit of p = 0.05

If the module of the value obtained is greater than the value in the table: the null assumption is rejected, therefore the results obtained cannot be considered entirely such a chance, so there is a significant difference statistically in terms of the difference between the two averages. The result obtained is mathematically denoted as follows:
t(*df*)=a, p < .05.

If the result obtained is higher than the values in the table of t for p = 0.2; p = .01; p = .005 or p = .001, we can present the result obtained as being significant also to the latter value (there is 1 to 1000 changes that the result obtained to be due to the change). In this case, we denote: t(*df*) = a, p<.001 unilateral test.

4 RESULTS

Initiation date of the clinical investigation: 22nd April 2015.
Date of analysis: 29th May 2015.

4.1. Arrangement of the subjects and the devices NUCLEUS Biofeedback System

No. of subjects selected	57
No. of subjects who abandoned the investigation	0
No. of subjects with muscular dystonia	55
No. of subjects with muscle contracture*	28

* *also includes the muscle contractures subjects, having as etiology the muscular dystonia*

4.1.1 Demographic data of the subjects

Gender	
Male	11(19,30%)
Female	46(80,70%)
Average age	61,81 years
Residence	
Urban	12(21,05%)
Rural	45(78,95%)
Profession:	
Pensioner	41(71,93%)
Worker	3(5,26%)
Home staying	3(5,26%)
Other	10(17,55%)

4.1.2 Medical history of the subjects

MEDICAL HISTORY	
Hearth	21(36,84%)
Diabetes	9(15,79%)
Smokers	5(8,77%)
Other	**21(36,84%)**
AVC	1(1,75%)
HTA	1(1,75%)
Cholecystectomy	2(3,50%)
Liver fibrosis	1(1,75%)
Intervention lumbar spine	2(3,50%)

Intervention herniated disc	3(5,25%)
Osteoporosis	1(1,75%)
Coxarthrosis	2(3,50%)
Gallbladder	2(3,50%)
Compression of thoracic vertebrae	1(1,75%)
Rheumatism	2(3,50%)
Spondylosis	3(5,25%)

4.1.3 Blood group

Blood group	
A	26(45,64%)
B	3(5,22%)
AB	2(3,50%)
0	26(45,64%)

4.1.4 Compliance with the Clinical Investigation Plan, BFK-CIP-01

All 57 subjects met the criteria for inclusion in the clinical investigation.

4.2 Analysis of the performances provided in the Clinical Investigation Plan, BFK-CIP-01

4.2.1 Data about depression, anxiety and stress, muscular re-education, pain treatment and detection of the medical conditions

The stress represents the adaptation syndrome that the individual performs after the environment aggressions; the assembly comprising intention, tension, coercion, force, stress, mobbing.
Starting from the concept of stress, we note that the term belongs to Hans Hugo Bruno Selye who considers that the stress is connected to the adaptation syndrome. Hans Selye defines the stress as an assembly of reactions of the human body to the external action of some causative agents (physical, chemical, biological and psychological), consisting in morphological and functional changes, most often endocrine changes. If the stressor agent has a long lasting action, we are talking about the general syndrome of adaptation that involves a stage development.

The basic principles of neuromuscular physiology are applied clinically in the treatment of the muscular paresis. The physiological principles involves both the muscular system and the nervous system, but especially the latter; strictly speaking, the muscle reeducation is an inappropriate term, because only the nervous system is able to be educated.

The muscle contraction (shrinkage strength of a particular muscle) is determined by the following factors: anatomical and physiological status of the muscle fibres at the contraction time; number of contracted fibres; number and frequency of the nerve impulses that reach the muscle fibres; functional

status of the neuromuscular junctions and structural and functional status of the tissues around the muscle fibres, such as blood vessels and connective tissue.

The ATP deficiency is associated with chronic pain. The ATP supplies energy to the sodium pump, the transport mechanism which removes from the inside of cells the waste resulting from the metabolic processes and by which it is ensured the intake n = with nutrients from the bloodstream into the cell.

In a study conducted on 50 patients complaining, in particular, sore throat, Steven R. Doyle, Steven W. Baker used the device Tens-O-Matic, an electric stimulator, manufactured by Monad Corp, at a frequency of 0,6 Hz for all cases, the micro-amperage ranging from 300 - 600 mA, the treatment lasting between 3 and 15 minutes. In nine of the 50 patients, it was found a discomfort during the treatment.

After conducting the study, the authors found that the device Tens-O-Matic is safe and effective, either used solely or in combination with other therapies.

36 women and 24 men were treated with the above device, the maximum number of sessions being 27.

The sick body has vibration frequencies which differ from those of the healthy body. The transition from one frequency pattern to another, therefore the transition from the status of health to the status of disease and reverse occurs by quantum leaps.

The identification of the medical conditions is difficult because a minor cause, such as the exposure of the body to a toxin for a long period of time, affects the body until it, as system, malfunctions.

The non-classical systems, like the human body, are non-linear, which means that a cause that seems insignificant, determines its sudden and dramatic change.

Every activity of a living tissue is correlated with a change in the electric power. The flow of the electric power generates a magnetic field in the surrounding space; the electricity in the human body also creates an electromagnetic field that surrounds it. The electromagnetic field varies according to the activities of the body and its health condition.

4.2.2 Depression, anxiety and stress of the subjects

Score of depression, anxiety and stress of the subjects													
The subjects receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS							**Subjects in the control group**						
No. subject / initials	Depression		Anxiety		Stress		No. subject / initials	Depression		Anxiety		Stress	
	Initially	After 6 procedures	Initially	After 6 procedures	Initially	After 6 procedures		Initially	After 6 follow-ups	Initially	After 6 follow-ups	Initially	After 6 follow-ups
1. SM	4	1	4	3	5	3	1.GS	21	19	13	10	21	18
2. DN	6	5	6	4	9	6	2.PT	4	4	13	11	9	9
3. SAG	6	5	4	1	15	5	3.PD	17	12	21	17	17	18
4. MG	0	0	4	1	1	1	4.SA	4	2	9	7	14	11
5. MV	0	0	6	2	1	0	5. MM	0	0	7	6	3	3
6. NM	1	1	3	2	5	3	6.AG	8	5	8	4	16	16
7. NG	0	0	2	2	1	0	7.CPS	7	9	6	6	10	9
8. IA	1	1	7	2	4	2	8.CM	3	4	16	15	15	13
9. SE	0	0	2	1	2	1	9.AE	17	16	32	27	28	25
10. GT	11	7	10	10	20	11	10.BE	18	15	18	17	14	15
11. MM	3	1	10	5	9	7	11. IS	2	2	8	6	2	1
12. IC	4	2	5	2	10	6	12.GS	8	6	21	17	19	16
13. BF	3	1	6	2	3	3	13.TB	14	13	17	17	23	19
14. VE	25	16	24	15	32	22	14. MG	3	6	13	13	14	12
15. PV	0	0	3	1	1	0	15.AE	1	2	17	17	19	14
16. VA	7	2	6	5	12	8	16.DM	5	6	8	7	15	14
17. MDD	6	2	13	5	10	2	17.MR	5	11	8	13	18	13
18. VT	0	0	0	0	0	0	18.IA	7	6	8	8	8	7
19. NI	6	2	14	5	4	2	19.DE	21	13	9	9	8	9
20. ME	1	1	11	7	9	7	20.GE	11	13	13	15	9	10
21. PG	5	3	15	7	10	8	21. DF	11	19	10	14	19	23
22.BE	4	3	2	1	11	6	22. DR	19	19	29	27	25	23
23. PEG	9	3	7	5	11	6	23.RM	10	10	24	21	18	17
24. SG	14	10	22	14	16	11	24.IF	10	9	8	7	12	13
25. VA1	0	0	1	1	1	0	25.BT	0	1	11	12	12	11
26. OS	7	3	16	9	9	8	26.VV	6	8	9	7	8	10
27. MP	4	2	7	2	11	9	27.SM	6	7	8	7	9	10
28.							28.GS	0	2	4	6	1	4
29.							29.BGS	0	0	0	0	0	0
30.							30.BM	0	0	4	3	3	2
Average score	**4.7**	**2.6**	**7.8**	**4.2**	**8.2**	**5.1**		**7.9**	**8.0**	**12.4**	**11.5**	**13.0**	**12.2**
%	**100**	**55.0**	**100**	**53.8**	**100**	**62.2**		**100**	**101**	**100**	**93.0**	**100**	**94.0**

	Depression	**Anxiety**	**Stress**
Normal	0 – 9	0 – 7	0 – 14
Poor	10 – 13	8 – 9	15 – 18
Moderate	14 – 20	10 – 14	19 -25

Severe	21 – 27	15 – 19	26 – 33
Extremely severe	28+	20+	34+

It is found that the depression of the patients who received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS is within the normal limits (average score = 4,7 before starting the procedures; average score = 2,6 after completing the procedures), but, at the end of the 6 procedures, the average score in relation to depression dropped to 55% of the initial score.

The depression of the patients in the control group is also within the normal limits (average score = 7,9 at registration; average score = 8,0 after performing the controls. It is found that, unlike the patients in the group that received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the depression decreased with 45% in the case of patients in the control group, it increased by 1%.

The data regarding the score related to anxiety reveal that the patients in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS are poorly anxious (average score at enrolment - 7,8). After the completion of the 6 specific procedures carried out with the device NUCLEUS, the average score regarding the anxiety dropper to 4,2; practically, reduced to 53,8% of the initial one, the patients presenting anxiety within the normal limits.

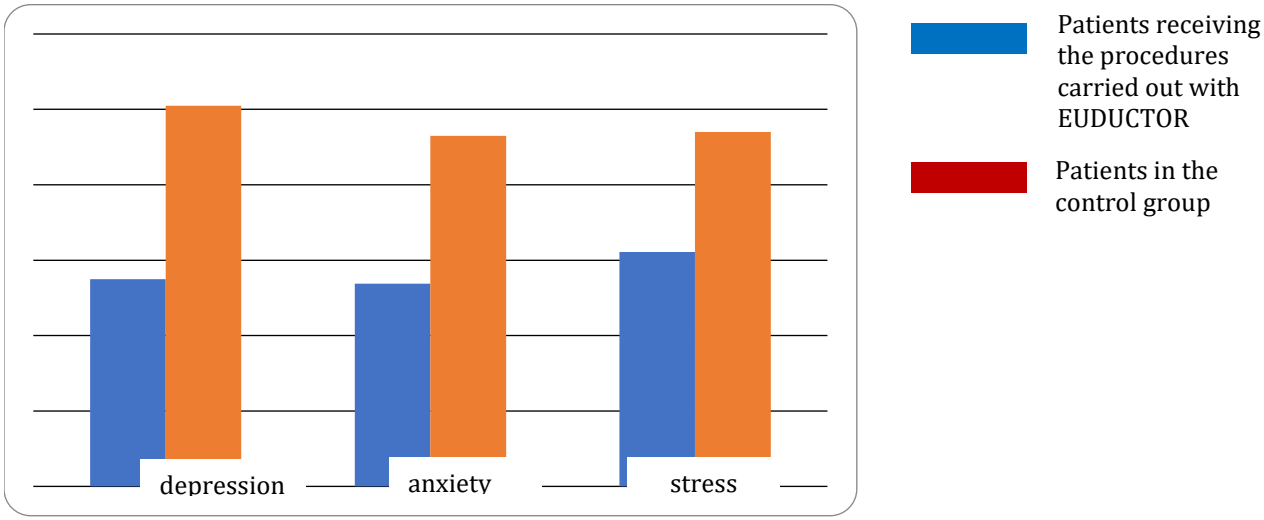
The patients in the control group are moderately anxious (average score at enrolment = 12,4); at the end of the follow-up period, the score regarding the anxiety being 11,5 reduced to 93% of the initial one; the patients presenting also a moderate anxiety. It is found that the anxiety was reduced insignificantly (with only 7%) in the case of the control group, unlike the patients in the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the anxiety decreased by 46,2%.

Regarding the stress, the condition of the patients in the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS is normal, its average score at enrolment being 8,2. Upon the completion of the 6 specific procedures, the average score related to the stress dropped to 5,1 - namely 62,1% of the initial score.

The patients in the control group presented at enrolment a stress that fit, as in the case of the patients in the group receiving the specific procedures carried out with the device NUCLEUS, within the normal limits, the average score at enrolment being 13,0. AT the end of the follow-up period, the average score related to the stress dropped to 12,2 - namely 94% of the initial score. It is found that the stress was reduced insignificantly (with only 6%) in the case of the control group, unlike the patients in the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the stress decreased by 37,8%.

The statistical power in the case of the three determinations (depression, anxiety, stress) is $p < .0005$.

Graphically, the comparative situation of the depression, anxiety and stress is shown below:



The above data demonstrates that the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in order to reduce the stress, depression and anxiety are extremely efficient and safe; the benefits for patient being represented on the one hand by the reduction improvement of depression, anxiety and reduction of stress, on the other hand, as a consequence, by the improvement of certain medical disorders, including the pain associated with them, as we will show further below.

4.2.3 Muscular dystonia

Characteristics of muscular dystonia;

ETIOLOGY	
Primary (idiopathic)	3(5,45%)
Dystonia plus	0(0,00%)
Hereditary degenerative dystonia	0(0,00%)
Secondary	48(87,27%)
Paroxysmal	4(7,28%)
Age of onset	
Early (≤ 20 – 30 years)	3(5,45%)
Late	52(94,55%)
ANATOMICAL DISTRIBUTION	
Focal (one region of the body)	4(7,28%)
Segmental (anatomical regions in contiguity)	30(54,54%)

Multifocal (anatomical regions in non-contiguity)	19(34,54%)
Generalized (both lower limbs and at least another area of the body	0(0,00%)
Hemidystonia (half of the body)	2(3,64%)

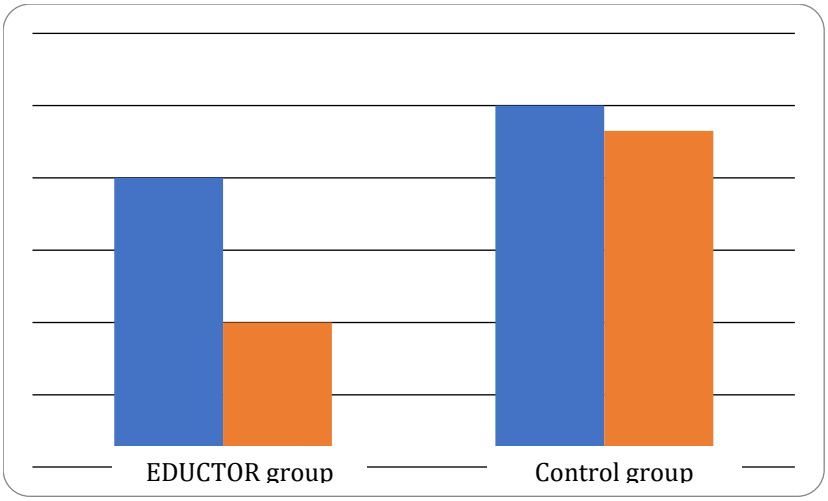
The data relating to the scores associated to the muscular dystonia are summarized in the table below:

Score of muscular dystonia					
The subjects receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS			**Subjects in the control group**		
Nr. subject / initials	Initially	After 6 procedures	Nr. subject / initials	Initially	After 6 follow-ups
1. SM	6.5	3.5	1.GS	10.5	9.5
2. DN	5.5	3.5	2.PT	8.0	7.5
3. SAG	8.5	3.5	3.PD	9.5	9.0
4. MG	7.5	4.0	4.SA	7.5	7.5
5. MV	5.5	3.5	5. MM	8.5	8.5
6. NM	4.5	2.5	6.AG	21.5	18.5
7. NG	6.5	3.5	7.CPS	7.5	6.5
8. IA	6.5	4.0	8.AE	14.0	13.5
9. SE	5.5	3.0	9.BE	7.5	7.5
10. GT	8.0	3.5	10. IS	5.5	5.5
11. MM	5.5	3.0	11.GS	9.5	8.5
12. IC	7.5	4.0	12. MG	8.5	7.5
13. BF	5.5	3.5	13.AE	8.0	8.5
14. VE	9.5	4.5	14.DM	5.5	4.5
15. PV	8.5	3.5	15.MR	5.5	6.5
16. VA	9.0	3.5	16.IA	6.5	6.5
17. MDD	10.5	4.0	17.DE	8.0	3.5
18. VT	10.5	5.5	18.GE	10.5	10.5
19. NI	6.5	3.0	19. DF	9.0	11.0
20. ME	9.5	5.0	20.DR	9.5	10.5
21. PG	12.5	4.0	21.RM	10.0	11.0
22. BE	7.5	3.5	22.IF	12.0	10.5
23. PEG	17.5	10.5	23.BT	10.0	10.5
24. SG	7.5	4.0	24.VV	11.0	10.5
25. VA1	8.5	4.5	25.SM	8.0	8.0
26. OS	8.5	4.0	26.GS	11.0	10.0
27. MP	6.5	2.5	27.BGS	12.5	10.5
28.			28.BM	21.0	18.5
Average score	**8.0**	**4.0**		**10.0**	**9.3**
%	**100**	**50**		**100**	**93**

The data regarding the score of the muscular dystonia reveals that the patients in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS had a remarkable improvement of the health; the average score of dystonia after conducting the procedures being equal with 4, as compared to the initial score, at enrolment, which was 8. Basically, after conducting the procedures, the dystonia score decreased by 50%.
Regarding the patients in the control group, at the end of the follow-up period, the average score of dytonia was equal to 9,3; at enrolment it was equal to 10,0; the decrease of the average score being equal to 7%.

The statistical power in the case of determinations is p< .0005.

Graphically, the comparative situation of the average score related to the muscular dystonia is shown below:



4.2.4 Muscle contracture

Characteristics of muscle contracture:

ETIOLOGY Neuromuscular dystonia Enthesopathy of hips laterally	 26(92,86 %) 2(7,14%)
DURATION	Approximately: 5, 6 months
LOCALIZATION Lower torso / pelvis Upper torso	 27(96,43%) 1(3,57%)
CLASSIFICATION Type C2 Type B	 9 (32,14%) 19 (67,86%)

The data regarding the perception of the subjects on the extent to which the daily activities and the leisure time activities were restricted, as well as the data related to the success of the treatment (appreciated by subjects) are shown below:

4.2.5 Intensity of the pain felt by the subjects

The intensity of the pain felt y the patient at enrolment in this clinical investigation was considered to be 100%; the subsequent intensities of the pain, depending on the number of the control, namely the day of treatment were calculated in percentages, related to the initial average value of 100%.
The evolution of the pain felt by the subjects is presented in the tables below:

THE INTENSITY OF THE PAIN FELT BY THE SUBJECT IN MOVEMENT - Group of subjects receiving procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS							
No. subject / initials	**No. follow-up**						
	Before the first procedure	**1**	**2**	**3**	**4**	**5**	**6**
1.SM	7	7	5	4	2	3	2
2.DN	6	6	5	4	2	2	-
3.SAG	5	5	4	2	2	1	-
4.MG	6	6	5	3	3	2	-
5.MV	6	6	5	3	3	2	-
6.NM	7	7	5	4	3	2	-
7.NG	6	6	4	3	2	2	-
8.IA	6	6	4	4	2	2	-
9.SE	6	6	4	4	3	1	-
10.GT	7	7	6	4	4	3	2
11.MM	6	6	5	3	3	2	-
12.IC	7	7	6	4	4	2	-
13.BF	6	6	5	3	2	2	-
14.VE	7	7	6	4	3	3	2
15.PV	7	7	5	3	2	-	-
16 VA	6	6	4	3	3	-	-
17.MDD	6	6	4	3	2	-	-
18.VT	6	6	5	3	3	-	-

THE INTENSITY OF THE PAIN FELT BY THE SUBJECT IN MOVEMENT - Group of subjects receiving procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS							
No. subject / initials	**No. follow-up**						
	Before the first procedure	**1**	**2**	**3**	**4**	**5**	**6**
19.NI	6	6	5	3	-	-	-
20.ME	6	4	3	2	3	2	1
21.PG	4	4	4	3	2	-	-
22.BE	6	6	5	4	2	2	2
23.PEG	6	6	5	3	2	2	-
24.SG	6	6	5	3	3	2	-
25.VA1	7	7	6	4	4	3	2
26.OS	7	7	6	4	3	3	-
27.MP	6	6	4	3	2	2	-
Average intensity of the pain	**6.2**	**6.1**	**4.8**	**3.3**	**2.7**	**2.1**	**1.8**
	100%	**98.39%**	**77.42%**	**53.22%**	**43.55%**	**33.88%**	**29.00%**

No. subject / initials	**No. follow-up**						
	At enrolment	**1**	**2**	**3**	**4**	**5**	**6**
1. GS	8	7	6	5	5	4	-
2. PT	6	5	3	4	4	3	-
3. PD	7	6	4	5	4	5	-
4. SA	7	6	4	4	4	3	3
5. MM	6	4	3	4	3	3	-
6. AG	7	7	6	6	5	5	4
7. CPS	7	5	4	4	5	4	-
8. CM	4	3	3	3	-	-	-
9. AE	7	6	5	3	3	-	-
10. BE	6	4	3	4	4	3	-

No. subject / initials	**No. follow-up**						
	At enrolment	**1**	**2**	**3**	**4**	**5**	**6**
11. IS	5	5	3	4	4	3	3
12.GS	6	4	4	3	4	3	-
13.TB	6	4	3	3	4	3	-
14. MG	7	6	4	5	4	4	-
15.AE	7	5	4	4	3	3	-
16.DM	5	3	3	2	3	3	-
17.MR	6	5	4	3	4	3	-
18.IA	6	4	4	3	4	3	-
19.DE	7	7	5	4	4	5	4
20.GE	7	5	4	4	4	4	3
21. DF	8	7	6	4	4	5	4
22. DR	7	6	5	3	3	4	3
23.RM	8	6	5	5	4	4	-
24.IF	7	6	4	3	3	4	3
25.BT	7	5	4	5	5	4	-
26.VV	8	6	6	7	6	5	-
27.SM	7	5	6	5	5	4	-
28.GS	6	4	4	5	4	4	-
29.BGS	7	5	3	4	4	4	4
30.BM	6	4	4	3	4	4	-
Average intensity of the pain	**6.6**	**5.2**	**4.2**	**4.0**	**4.0**	**3.8**	**3.4**
	100%	**78.79%**	**63.64%**	**60.61%**	**60.61%**	**57.58%**	**51.52%**

The statistical power in the case of determinations is p< .005.

In order to view the evolution of the pain intensity felt by the patients, depending on the day of treatment, in the day / days the patient did not come to follow-up and did not receive the specific procedure carried out with the Universal Electrophysiological Biofeedback System NUCLEUS (namely, the patients in the control group were not evaluated), it was calculated the increase / decrease of the pain intensity based on the intensities determined on the previous follow-up, namely subsequently, complying with the rate of decline / growth and for the subsequent days, the data related to the pain evolution for 14 days of follow-up, being shown in the tables below.

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Clinical Investigation Report

No. subject / initials	No. day													
	Before the first procedure	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1.SM	**7.0**	7.0	5.0	4.8	4.5	4.3	4.0	2.0	3.0	2.0	1.8	1.6	1.4	1.2	1.0
2.DN	**6.0**	6.0	5.9	5.7	5.6	5.4	5.3	5.0	4.0	3.6	3.2	2.8	2.4	2.0	1.6
3.SAG	**5.0**	5.0	4.7	4.4	4.0	3.5	3.0	2.5	2.0	2.0	1.5	1.0	0.5	0.0	0.0
4.MG	**6.0**	6.0	5.5	5.0	4.0	3.0	3.0	3.0	2.5	2.0	1.5	1.0	0.5	0.0	0.0
5.MV	**6.0**	6.0	5.0	4.0	3.0	3.0	3.0	3.0	2.5	2.0	1.5	1.0	0.5	0.0	0.0
6.NM	**7.0**	7.0	5.0	4.0	3.0	2.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7.NG	**6.0**	6.0	5.5	5.0	4.5	4.0	3.5	3.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
8.IA	**6.0**	6.0	5.5	5.0	4.5	4.0	4.0	3.7	3.4	3.1	2.9	2.6	2.3	2.0	1.7
9.SE	**6.0**	6.0	5.5	5.0	4.5	4.0	4.0	3.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0
10.GT	**7.0**	7.0	6.8	6.5	6.3	6.0	5.0	4.0	4.0	3.7	3.3	3.0	2.7	2.4	2.1
11.MM	**6.0**	6.0	5.0	3.0	3.0	2.8	2.5	2.3	2.0	1.8	1.5	1.3	1.0	0.8	0.5
12.IC	**7.0**	7.0	6.5	6.0	4.0	4.0	4.0	4.0	4.0	3.0	2.0	1.0	0.0	0.0	0.0
13.BF	**6.0**	6.0	5.8	5.6	5.4	5.2	5.0	4.0	3.0	2.8	2.6	2.4	2.2	2.0	1.8
14.VE	**7.0**	7.0	6.7	6.4	6.0	5.0	4.0	3.8	3.6	3.4	3.2	3.0	3.0	2.0	1.0
15.PV	**7.0**	7.0	5.0	3.0	2.5	2.0	1.5	1.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
16 VA	**6.0**	6.0	4.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
17.MDD	**6.0**	6.0	4.0	3.0	2.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
18.VT	**6.0**	6.0	5.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0

19.NI	**6.0**	6.0	5.0	4.0	3.0	2.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
20.ME	**6.0**	5.0	4.0	3.0	2.0	2.2	2.4	2.6	2.8	3.0	2.8	2.6	2.4	2.2	2.0
21.PG	**4.0**	4.0	4.0	4.0	3.0	2.8	2.6	2.4	2.2	2.0	1.8	1.6	1.4	1.2	1.0
22.BE	**6.0**	6.0	5.5	5.0	4.5	4.0	3.4	2.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0
23.PEG	**6.0**	6.0	5.5	5.0	4.4	3.8	3.0	2.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0
24.SG	**6.0**	6.0	5.0	4.0	3.0	3.0	2.7	2.4	2.0	1.7	1.4	1.1	0.8	0.5	0.2
25.VA1	**7.0**	7.0	6.0	5.5	5.0	4.5	4.0	4.0	3.0	2.8	2.5	2.3	2.0	1.0	2.0
26.OS	**7.0**	7.0	6.5	6.0	5.5	5.0	4.5	4.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
27.MP	**6.0**	6.0	4.0	3.0	2.5	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Average intensity of the pain	**6.2**	**6.1**	**5.3**	**4.5**	**3.9**	**3.5**	**3.1**	**2.7**	**2.3**	**2.1**	**1.9**	**1.7**	**1.5**	**1.3**	**1.2**
	100%	**98.39 %**	**85.48%**	**72.58%**	**62.90%**	**56.45%**	**50.00%**	**43.55%**	**37.10%**	**33.87%**	**30.61%**	**27.42%**	**24.19%**	**20.97%**	**19.36%**

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Clinical Investigation Report

No. subject / initials	No. day														
	At enrolment	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. GS	**8.0**	7.5	7.0	6.8	6.6	6.4	6.2	6.0	5.0	5.0	5.0	5.0	5.0	4.5	4.0
2. PT	**6.0**	5.5	5.0	4.5	4.0	3.5	3.0	3.5	4.0	4.0	4.0	4.0	4.0	3.5	3.0
3. PD	**7.0**	6.5	6.0	5.6	5.2	4.8	4.4	4.0	5.0	4.8	4.6	4.4	4.2	4.0	3.8
4. SA	**7.0**	6.5	6.0	5.6	5.2	4.8	4.4	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
5. MM	**6.0**	5.6	5.2	4.8	4.4	4.0	3.7	3.4	3.0	2.2	3.5	3.7	4.0	3.5	3.0
6. AG	**7.0**	7.0	7.0	6.7	6.4	6.0	6.0	6.0	6.0	5.8	5.5	5.2	5.0	5.0	5.0
7. CPS	**7.0**	6.0	5.0	5.0	5.0	4.5	4.0	4.0	4.0	4.2	4.4	4.6	4.8	5.0	5.2
8. CM	**4.0**	3.5	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
9. AE	**7.0**	6.5	6.0	5.8	5.5	5.3	5.0	4.4	3.7	3.0	2.4	1.8	1.2	0.6	0.0
10. BE	**6.0**	5.0	4.0	3.8	3.6	3.4	3.2	3.0	3.5	4.0	4.0	4.0	4.0	4.0	4.0
11. IS	**5.0**	5.0	5.0	4.6	4.2	3.8	3.4	3.0	3.5	4.0	4.0	4.0	4.0	4.0	4.0
12.GS	**6.0**	5.6	5.2	4.8	4.4	4.0	4.0	4.0	3.9	3.7	3.6	3.4	3.3	3.0	2.9
13.TB	**6.0**	4.0	3.8	3.5	3.3	3.0	3.0	3.1	3.2	3.4	3.5	3.6	3.8	4.0	3.0
14. MG	**7.0**	6.8	6.5	6.3	6.0	5.0	4.0	4.1	4.3	4.4	4.5	4.7	5.0	4.0	3.0
15.AE	**7.0**	6.6	6.2	5.8	5.4	5.0	4.8	4.6	4.4	4.2	4.0	4.0	4.0	3.5	3.0
16.DM	**5.0**	4.5	4.0	3.5	3.0	3.0	3.0	2.8	2.6	2.4	2.2	2.0	2.5	3.0	3.0
17.MR	**6.0**	5.8	5.5	5.3	5.0	4.5	4.0	3.8	3.5	3.3	3.0	3.2	3.5	3.7	4.0
18.IA	**6.0**	5.4	4.7	4.0	4.0	4.0	3.0	3.2	3.4	3.6	3.8	4.0	3.7	3.4	3.0

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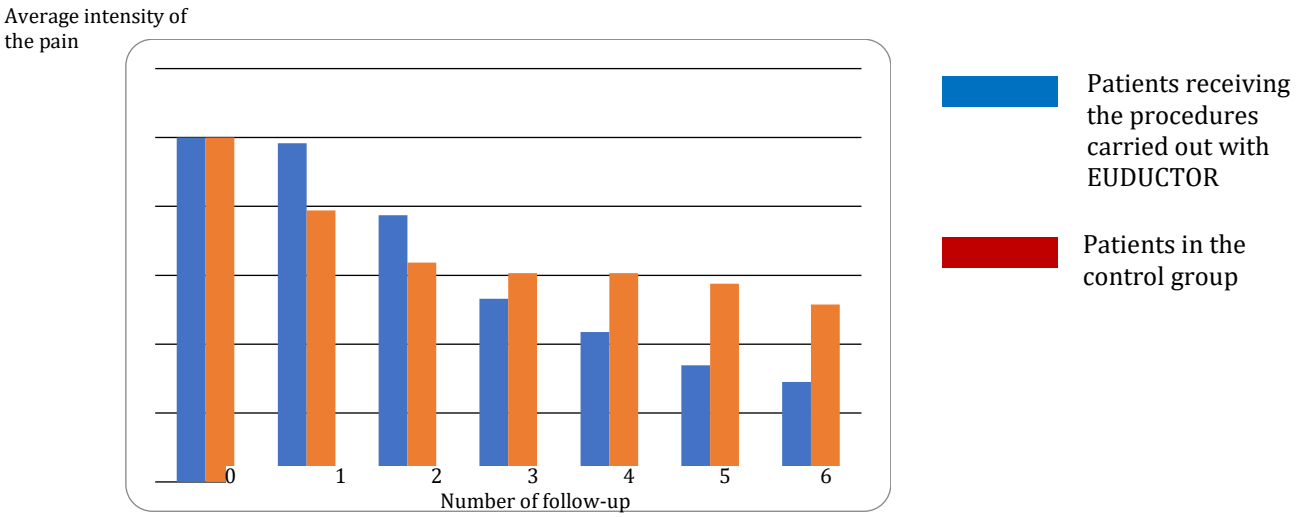
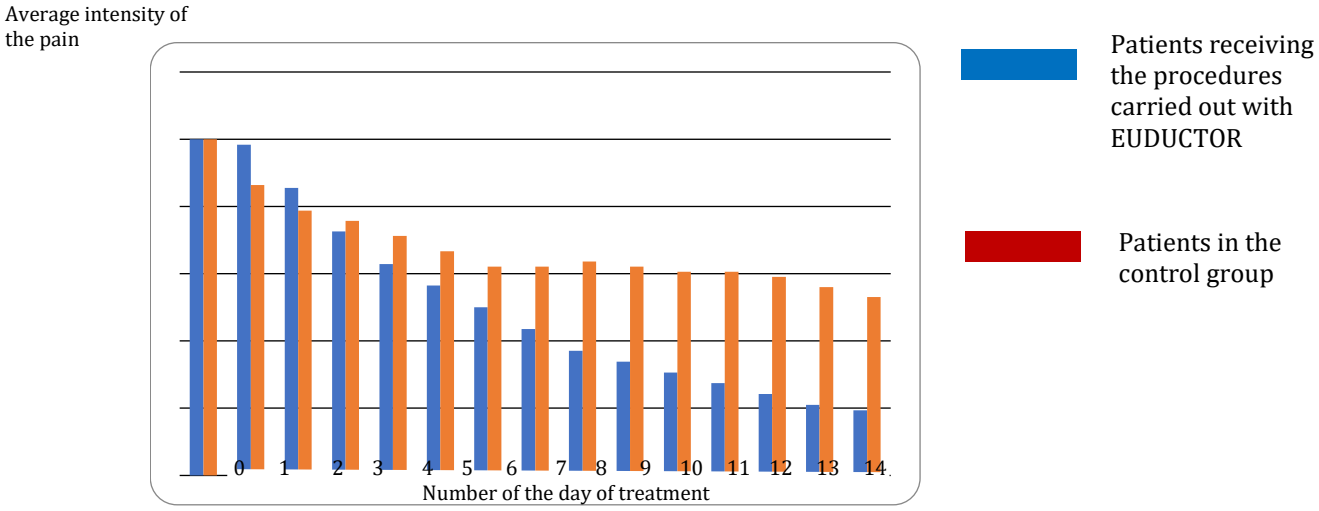
Clinical Investigation Report

19.DE	**7.0**	7.0	7.0	7.0	6.4	5.7	5.0	4.8	4.5	4.3	4.0	4.0	4.0	4.0	4.0
20.GE	**7.0**	6.4	5.7	5.0	4.8	4.6	4.4	4.2	4.0	4.0	4.0	4.0	4.0	4.0	4.0
21. DF	**8.0**	7.0	6.0	5.5	5.0	4.5	4.0	4.0	4.0	4.5	5.0	4.8	4.5	4.3	4.0
22. DR	**7.0**	6.0	5.0	4.5	4.0	3.5	3.0	3.0	3.0	3.5	4.0	3.7	3.3	3.0	2.7
23.RM	**8.0**	6.0	5.0	5.0	5.0	5.0	5.0	5.0	4.5	4.0	4.0	4.0	4.0	4.0	4.0
24.IF	**7.0**	6.0	4.0	3.8	3.5	3.3	3.0	3.0	3.5	4.0	3.8	3.5	3.3	3.0	2.7
25.BT	**7.0**	5.0	4.0	4.2	4.4	4.6	4.8	5.0	5.0	5.0	4.0	3.0	2.0	1.0	0.0
26.VV	**8.0**	6.0	6.0	6.1	6.2	6.4	6.5	6.6	6.8	7.0	6.0	5.8	5.5	5.3	5.0
27.SM	**7.0**	5.0	5.2	5.5	5.7	6.0	5.5	5.0	5.0	5.0	5.0	5.0	5.0	4.5	4.0
28.GS	**6.0**	5.6	5.2	4.8	4.4	4.0	4.0	4.0	4.1	4.2	4.4	4.5	4.6	4.8	5.0
29.BGS	**7.0**	5.0	4.5	4.0	3.5	3.0	3.5	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
30.BM	**6.0**	4.0	4.0	4.0	4.0	4.0	3.5	3.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Average intensity of the pain	**6.6**	**5.7**	**5.2**	**5.0**	**4.7**	**4.4**	**4.1**	**4.1**	**4.2**	**4.1**	**4.0**	**4.0**	**3.9**	**3.7**	**3.5**
	100%	**86.36%**	**78.79**	**75.76**	**71.21**	**66.67**	**62.12**	**62.12**	**63.64**	**62.12**	**60.61**	**60.61**	**59.09**	**56.06**	**53.03**

Graphically, the evolution of the pain intensity felt by the patients, depending on the number of the procedure carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, namely the number of the follow-up, in case of the patients in the control group, but also depending on the day of treatment, has the following configurations:





After 6 specific procedures carried out by means of the Universal Electrophysiological Biofeedback System NUCLEUS, is has been concluded that the average pain felt by patients decreased from the value of 6,2 Wong-Baker scale (pronounced pain, which determines the patient's inability to conduct some activities), to a value equal to 1,8 which means, according to the same scale, a pain which can be neglected. Therefore, after 6 procedures carried out with the

Universal Electrophysiological Biofeedback System NUCLEUS, the patients were able to perform all daily activities, practically, without restrictions.

Regarding the patients in the control group, after 6 evaluations, the average pain felt by patients decreased from the value of 6,4 Wong-Baker scale (pronounced pain, which determines the patient's inability to conduct some activities), to a value equal to 3,4 which means, according to the same scale, a moderate pain, which determines discomfort. Although the rate of decrease of the pain intensity was higher in the early days in the patients in the control group, later, it stagnated around the value 4 (moderate pain), while in the patients who received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the rate of decrease (although initially a little lower) was maintained; moreover, it widened, the pain decreasing significantly.

Regarding the evolution of the pain felt by the patients depending on the day of treatment, it is found that it has an evident decreasing trend in the case of the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, unlike the control group, for which the pain intensity has a random evolution; however, at levels much higher than the intensity related to the group NUCLEUS.

The major benefits of using the Universal Electrophysiological Biofeedback System NUCLEUS consisted in significant improvement of the pain felt by the patients with muscular dystonia and / or with muscle contractures, when the procedures are associated with the standard treatment (physiotherapy, kinetic therapy, treatment with medication).

The fact that the patients benefit from significant improvements of the pain associated with the neuromuscular dystonia and with the muscle contracture has a particularly positive effect on their quality of life, especially if it is taken into account that, in addition to the increase of the comfort degree, by decreasing the pain under the limits that makes the patient in able, he / she regain his / her mobility, being able to carry out their current daily activities

4.2.6 Detection of the medical conditions of the patients

The detection of the medical conditions adjacent to the muscular dystonia / muscle contracture in the case of 5 patients receiving the specific procedure of scanning the human body carried out with the Universal Electrophysiological Biofeedback System NUCLEUS and who were willing to carry out additional medical investigations is shown in the table below:

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Clinical Investigation Report

No. subject / initials	Medical conditions detected by scanning the human body	
	Medical condition detected by scanning with the Universal Electrophysiological Biofeedback System NUCLEUS	**Confirmation / Infirmation medical condition, by medical tests / medical investigations (YES / NO)**
6. NM	Lumbar discopathy; BAVP; Neuromuscular dystonia	HTAE Lumbar discopathy BAVP Gonarthrosis Neuromuscular dystonia
8. IA	Obsesity; Cervical spondylosis; Neuromuscular dystonia	CDL Spondylolysis DVL IV BAVP BCI Anxious - depressive syndrome - minor current episode Obesity I degree Neuromuscular dystonia
13. BF	Cholecystectomy; Hyperglycemia; Neuromuscular dystonia	Cholecystectomy HTA Neuromuscular dystonia Secondary gonarthrosis Arthrosis BCI Spondylolysis with multiple localizations IVC Diabetes mellitus Hyperglycemia
17. MDD	HDL increased; Neuromuscular dystonia	Basedow Graves disease Hyperthyroidism - diffuse goiter approx. 2013 HDL5-S1 operated (2002-2009) C6 bilateral and vertebrogenic radiculopathy, trenant algoparesthesic form Operated L5 and S1 radiculopathy (2001 - 2009) Cephalalgic syndrome Neuromuscular dystonia
27. MP	Uterine fibroid; Ovarian cyst; Neuromuscular dystonia	HTA Uterine fibroid Ovarian cyst Hemorrhoids Gonarthrosis BAVP Cervical spine spondylosis Hyperuricemia Neuromuscular dystonia

It is found that only in the case of the patient MDD, when scanning his body with the Biofeedback Electrophysiological Universal System, it was detected an increased HDL, not

confirmed by the medical tests; in all other causes, the medical conditions detected using the device NUCLEUS, being confirmed by additional medical investigations.

In percentages, the medical conditions detected during the scan performed with the Biofeedback Electrophysiological Universal System, represent 33% of those detected by the standard medical investigations.

Taking into account, with one exception, (case of the patient MDD), all medical conditions detected by scanning the human body were confirmed by the standard medical investigations: we appreciate that the is a very useful tool to guide the patients to the clinics for medical tests, recommending the investigations to be performed by it.
Also, the Universal Electrophysiological Biofeedback System NUCLEUS is very useful for the physician to inform the patient about the possible medical conditions in order to either perform additional medical investigations or to adopt a healthy lifestyle.

4.2.7 Subjects' perception on the extent to which the daily activities and the leisure time activities were restricted

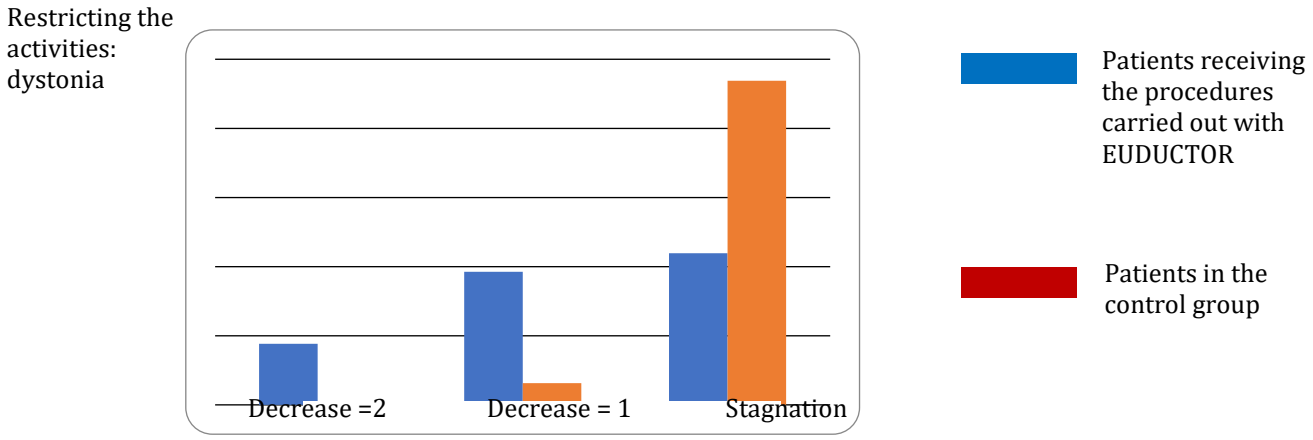
The perception of the subject with muscular dystonia or muscle contracture on the extent to which the daily activities and the leisure time activities were restricted have been appreciated by him / her before carrying out the first procedure with Universal Electrophysiological Biofeedback System NUCLEUS or at enrolment (in case of the patients in the control group) and after carrying out the 6 procedures / respectively follow-ups, the data being shown in the tables below:

Subject's perception with neuromuscular dystonia on the extent to which the daily activities and the leisure time activities were restricted.					
The subjects receiving the specific procedures carried out with the device Biofeedback System NUCLEUS			**Subjects in the control group**		
Nr. subject / initials	Initially	After 6 procedures	Nr. subject / initials	Initially	After 6 follow-ups
1. SM	2	1	1.GS	2	2
2. DN	1	1	4.SA	1	1
3. SAG	2	1	5. MM	1	1
4. MG	1	1	6.AG	3	3
5. MV	1	1	7.CPS	2	2
6. NM	2	1	10.BE	1	1
7. NG	1	1	11. IS	1	1
8. IA	2	1	12. GS	1	1
9. SE	1	1	14. MG	2	2
10. GT	3	1	15.AE	2	2
11. MM	1	1	16.DM	1	1
12. IC	2	1	17.MR	1	1
13. BF	1	1	18. IA	1	1
			19.DE	2	1
			26.VV	2	2
			27.SM	2	2

The above data shows the following:

- The subjects in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS:
  - ❖ The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with 2 units = 17,69%
  - ❖ The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with one unit = 38,46%
  - ❖ The number of the patients who appreciated a stagnation of the restriction of the daily activities and the leisure time activities (the same score) = 43,85%
  - ❖ The number of the patients who appreciated an increase of the restriction of the daily activities and the leisure time activities, with one or more units = 0,00%
- Patients in the control group:
  - ❖ The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with 2 units = 0,00%
  - ❖ The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with one unit = 6,25%
  - ❖ The number of the patients who appreciated a stagnation of the restriction of the daily activities and the leisure time activities (the same score) = 93,75%
  - ❖ The number of the patients who appreciated an increase of the restriction of the daily activities and the leisure time activities, with one or more units = 0,00%

Graphically, the results are shown below:



The patients receiving the specific procedures carried out with the device NUCLEUS appreciated a decrease of the restriction of the daily activities and the leisure time activities, as follows:

- From substantial restrictions, to light restrictions = 17,69%
- From substantial restrictions, to moderate restrictions = 0,00%
- From moderate restrictions, to light restrictions = 48,97%
- Stagnation of restrictions = 33,34%

The patients in the control group appreciated a decrease of the restriction of the daily activities and the leisure time activities, as follows:

- From substantial restrictions, to light restrictions = 0,00%
- From substantial restrictions, to moderate restrictions = 0,00%
- From moderate restrictions, to light restrictions = 6,25%
- Stagnation of restrictions = 93,75%

The data related to the patients with neuromuscular dystonia and muscle contractures, as shown below:

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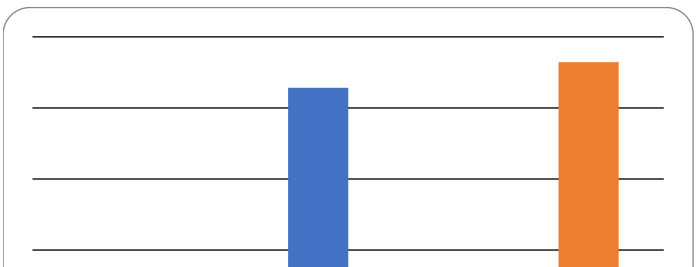
Clinical Investigation Report

Subject's perception with neuromuscular dystonia and muscle contracture on the extent to which the daily activities and the leisure time activities were restricted.					
The subjects receiving the specific procedures carried out with the device Biofeedback System NUCLEUS			**Subjects in the control group**		
Nr. subject / initials	Initially	After 6 procedures	Nr. subject / initials	Initially	After 6 follow-ups
14. VE	2	1	2. PT	1	1
15. PV	2	1	3. PD	2	2
16. VA	1	1	8. CM	3	2
17. MDD	2	1	9. AE	2	2
18. VT	2	1	13. TB	2	2
19. NI	1	1	20. GE	1	1
20. ME	2	1	21. DF	2	2
21. PG	2	1	22.DR	2	2
22. BE	2	1	23. RM	2	2
23. PEG	3	2	24.IF	2	1
24. SG	2	1	25. BT	2	2
25. VA1	2	1	28. GS	2	2
26. OS	2	1	29. BGS	2	2
27. MP	2	1	30.BM	2	2

The above data shows the following:

- The subjects in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS:
  - The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with 2 units = 0,00%
  - The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with one unit = 85,71%
  - The number of the patients who appreciated a stagnation of the restriction of the daily activities and the leisure time activities (the same score) = 14,29%
  - The number of the patients who appreciated an increase of the restriction of the daily activities and the leisure time activities, with one or more units = 00,00%
- Patients in the control group:
  - The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with 2 units = 0,00%
  - The number of the patients who appreciated a decrease of the restriction of the daily activities and the leisure time activities, with one unit = 7,14%
  - The number of the patients who appreciated a stagnation of the restriction of the daily activities and the leisure time activities (the same score) = 92,86%
  - The number of the patients who appreciated an increase of the restriction of the daily activities and the leisure time activities, with one or more units = 0,00%

Graphically, the results are shown below:



Decrease =2 Decrease = 1 Stagnation

The patients receiving the specific procedures carried out with the device NUCLEUS appreciated a decrease of the restriction of the daily activities and the leisure time activities, as follows:

- From substantial restrictions, to light restrictions = 0,00%
- From substantial restrictions, to moderate restrictions = 7,14%
- From moderate restrictions, to light restrictions = 78,57%
- Stagnation of restrictions = 14,20%

The patients in the control group appreciated a decrease of the restriction of the daily activities and the leisure time activities, as follows:

- From substantial restrictions, to light restrictions = 0,00%
- From substantial restrictions, to moderate restrictions = 7,14%
- From moderate restrictions, to light restrictions = 0,00%
- Stagnation of restrictions = 92,86%

There is a significant decrease in the restriction of the daily activities and the leisure time activities in the case of patients in the group which received specific procedures carried out by the Universal Electrophysiological Biofeedback System NUCLEUS, while in the patients in the control group, the largest share is represented by the patients who appreciated a stagnation of the restriction of activities.

The above data demonstrate the particular effectiveness of the Universal Electrophysiological Biofeedback System NUCLEUS in the treatment of the neuromuscular dystonia, musles contracture, pain treatment, as well as depression, anxiety and stress treatment.

4.2.8 The success of the treatment appreciated by patients

The success of the treatment appreciated by subjects (patients) was assessed at the end of the clinical investigation when they answered the corresponding questionnaire, the data being shown in the tables below:

The subjects receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS		**Subjects in the control group**	
Nr. subject / initials	After 6 procedures	Nr. subject / initials	After 6 follow-ups
1. SM	2	1.GS	3
2. DN	1	4.SA	3
3. SAG	1	5. MM	4
4. MG	2	6.AG	3
5. MV	2	7.CPS	4
6. NM	2	10.BE	3
7. NG	2	11. IS	4
8. IA	2	12. GS	3
9. SE	2	14. MG	4
10. GT	1	15.AE	3
11. MM	2	16.DM	4
12. IC	2	17.MR	4
13. BF	2	18. IA	3
		19.DE	2
		26.VV	4
		27.SM	3

The patients in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS appreciated the success of the treatment as follows:

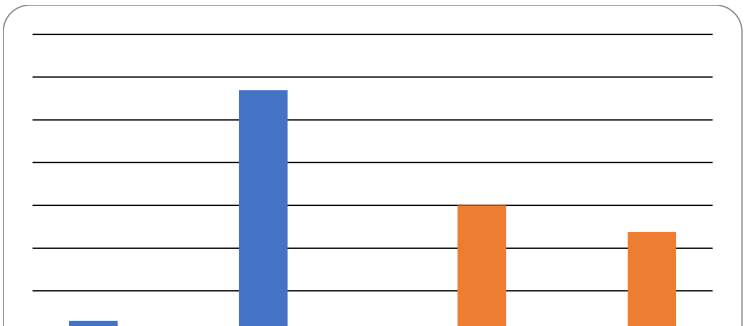
- Very much improved condition (score 1) = 23,01%
- Much improved condition (score 2) = 76,99 %
- Slightly improved condition (score 3) = 0,00%
- Unchanged condition (score 4) = 0,00%

The patients in the control group appreciated the success of the treatment as follows:

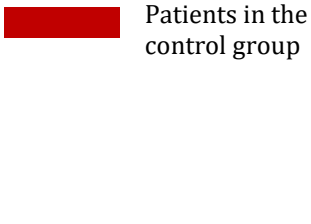
- Very much improved condition (score 1) = 0,00%
- Much improved condition (score 2) = 6,25%
- Slightly improved condition (score 3) = 50,00%
- Unchanged condition (score 4) = 43,75%

Graphically, the above situation takes the following form:

Success of the treatment: dystonia



Patients receiving the procedures carried out with EUDUCTOR



1 – very much improved condition; 2 – much improved condition; 3 – slightly improved condition; 4 – unchanged condition

It is found that the patients with neuromuscular dystonia who, in addition to the standard treatment, received procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS appreciated in a proportion of 23% that their condition has greatly improved, while no patient in the control group appreciated an improvement of their condition.

Also, the patients in the group NUCLEUS appreciated in proportion of 77% that their condition has improved a lot, compared to 6,25% of the patients in the control group appreciated an improvement of their condition.

Regarding the slightly improved condition and the stagnation of the patients' condition, no patient in the group NUCLEUS had such appreciations, while the patients in the control group appreciated in a proportion of 50% that their condition improved slightly and in proportion of 43,75% that their condition did not changed.

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Clinical Investigation Report

The success of the treatment appreciated by the patients with neuromuscular dystonia and muscle contracture			
The subjects receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS		**Subjects in the control group**	
Nr. subject / initials	After 6 procedures	Nr. subject / initials	After 6 follow-ups
14. VE	1	2. PT	3
15. PV	2	3. PD	3
16. VA	2	8. CM	3
17. MDD	2	9. AE	4
18. VT	2	13. TB	4
19. NI	1	20. GE	3
20. ME	1	21. DF	3
21. PG	1	22.DR	5
22. BE	1	23. RM	4
23. PEG	1	24.IF	3
24. SG	2	25. BT	3
25. VA1	1	28. GS	4
26. OS	2	29. BGS	3
27. MP	2	30.BM	3

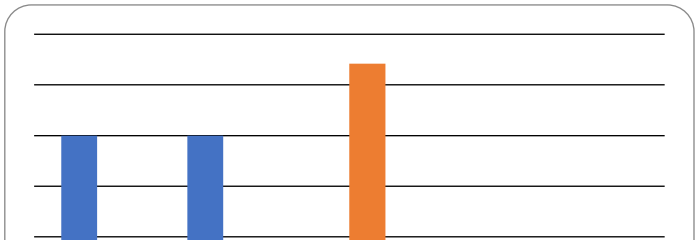
The patients with neuromuscular dystonia and muscle contractures in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS appreciated the success of the treatment as follows:

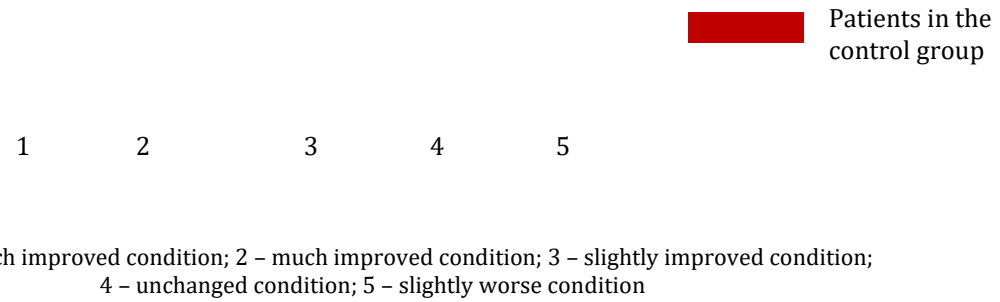
- Very much improved condition (score 1) = 50,00%
- Much improved condition (score 2) = 50,00 %
- Slightly improved condition (score 3) = 0,00%
- Unchanged condition (score 4) = 0,00%

The patients in the control group appreciated the success of the treatment as follows:

- Very much improved condition (score 1) = 0,00%
- Much improved condition (score 2) = 0,00%
- Slightly improved condition (score 3) = 64,29%
- Unchanged condition (score 4) = 28,57%
- Slightly worse condition (score 5) = 7,14%

Graphically, the above situation is shaped under the following form:





1 – very much improved condition; 2 – much improved condition; 3 – slightly improved condition;
4 – unchanged condition; 5 – slightly worse condition

It is found that the patients with neuromuscular dystonia and muscle contractures, who, in addition to the standard treatment, received procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS appreciated in a proportion of 50% that their condition has greatly improved, while no patient in the control group appreciated an improvement of their condition.

Also, the patients in the group NUCLEUS appreciated in proportion of 50% that their condition has improved a lot, compared to 0% of the patients in the control group appreciated an improvement of their condition.

Regarding the slightly improved condition and the stagnation of the patients' condition, no patient in the group NUCLEUS had such appreciations, while the patients in the control group appreciated in a proportion of 64.29% that their condition improved slightly, in proportion of 28,57% that their condition did not changed and in proportion of 7,14% that their condition slightly got worse.

According to the above interpretations, it is found the particular effectiveness of the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in improving the patients' condition, with positive influences on their life quality.

4.2.9 Tolerance and acceptability of the Universal Electrophysiological Biofeedback System NUCLEUS

According to the data from the patients' files, no side effects and no unwanted events were reported using the Universal Electrophysiological Biofeedback System NUCLEUS. Also, in all cases, the physician investigator appreciated the use of the device NUCLEUS as being very easy.

After conducting this clinical investigation, we appreciate that the Universal Electrophysiological Biofeedback System NUCLEUS has a high degree of acceptability from the point of view of the user; also, the tolerance of NUCLEUS, based on the incidence of the adverse events and adverse effects, absent during this investigation, is very good.

4.3 Summary of the adverse events and the adverse effects

According to the above and in accordance with the data, no adverse events / effects were reported with the occasion or after performing the procedures with the Universal Electrophysiological Biofeedback System NUCLEUS.

4.4 Deficiencies of the Universal Electrophysiological Biofeedback System NUCLEUS

There were no deficiencies of the Universal Electrophysiological Biofeedback System NUCLEUS found, neither in terms of the integrity / functioning of the device and harness, nor in terms of the functioning of the related software, which is installed in the computer of the physician investigator.

4.5 Manner of treating the lost data, irregularities, including regarding the subjects

During this clinical investigation, it was not lost the data of any subject (patient); also, no subject manifested the express desire to back up from this clinical investigation.

5 DISCUSSION AND CONCLUSIONS

5.1 Results in terms of safety and performance

According to the data shown above, there was no unwanted adverse effect / phenomenon caused by the use of the Universal Electrophysiological Biofeedback System NUCLEUS, which confirms the safety of using it.

Regarding the performance of the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, we found the following:

7. The procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS in order to reduce the stress, depression and anxiety are extremely efficient and safe; the benefits for patient being represented on the one hand by the reduction improvement of depression, anxiety and reduction of stress, on the other hand, as a consequence, by the improvement of certain medical disorders, including the pain associated with them, as we will show further below.
    - ❖ Unlike the patients in the group that received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the depression decreased with 45% in the case of patients in the control group, it increased by 1%.
    - ❖ The anxiety was reduced insignificantly (with only 7%) in the case of the control group, unlike the patients in the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the anxiety decreased by 46,2%.
    - ❖ The stress was reduced insignificantly (with only 6%) in the case of the control group, unlike the patients in the group receiving specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, for which the stress decreased by 37,8%.

8. The patients in the group receiving the specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS had a remarkable improvement of the health; the average score of dystonia after conducting the procedures being equal with 4, as compared to the initial score, at enrolment, which was 8. Basically, after conducting the procedures, the dystonia score decreased by 50%. Regarding the patients in the control group, at the end of the follow-up period, the average score of dytonia was equal to 9,3; at enrolment it was equal to 10,0; the decrease of the average score being equal to 7%.

9. After 6 specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the average pain felt by patients decreased from the value of 6,2 Wong-Baker scale (pronounced pain, which determines the patient's inability to

conduct some activities), to a value equal to 1,8 which means, according to the same scale, a pain which can be neglected. Therefore, after 6 procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the patients were able to perform all daily activities, practically, without restrictions. Although the rate of decrease of the pain intensity was higher in the early days in the patients in the control group, later, it stagnated around the value 4 (moderate pain), while in the patients who received specific procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS, the rate of decrease (although initially a little lower) was maintained; moreover, it widened, the pain decreasing significantly. The major benefits of using the Universal Electrophysiological Biofeedback System NUCLEUS consisted in significant improvement of the pain felt by the patients with muscular dystonia and / or with muscle contractures, when the procedures are associated with the standard treatment (physiotherapy, kinetic therapy, treatment with medication).

10. In percentages, the medical conditions detected during the scan performed with the Biofeedback Electrophysiological Universal System, represent 33% of those detected by the standard medical investigations. With one exception, all medical conditions detected by scanning the human body were confirmed by the standard medical investigations: we appreciate that the Universal Electrophysiological Biofeedback System NUCLEUS is a very useful tool to guide the patients to the clinics for medical tests, recommending the investigations to be performed by it.

11. There is a significant decrease in the restriction of the daily activities and the leisure time activities in the case of patients in the group which received specific procedures carried out by the Universal Electrophysiological Biofeedback System NUCLEUS, while in the patients in the control group, the largest share is represented by the patients who appreciated a stagnation of the restriction of activities.

12. The Universal Electrophysiological Biofeedback System NUCLEUS is particularly effective in improving the condition of the patients, with positive influences on their quality of life.

13. The Universal Electrophysiological Biofeedback System NUCLEUS has a high degree of acceptability from the point of view of the user; also, the tolerance of NUCLEUS, based on the incidence of the adverse events and adverse effects, absent during this investigation, is very good.

5.2 Risks - assessment and benefits

According to this clinical investigation, no risks related to the use of the Universal Electrophysiological Biofeedback System NUCLEUS have been reported, in addition to those analyzed in the risk analysis report, contained by the Clinical Investigation Plan, BFK-CIP-01.

5.2 Clinical relevance of data and results

The alternative and complementary medicine has a rich and long history in relation to the assessment of body in terms on energy. The Chinese traditional medicine and Indian Ayurvedic medicine have explored for a long time the energies of the human body.
The acupuncture and homoeopathy are widely practised in Asia and Europe (for example, in Great Britain are at least four hospitals exclusively based on homoeopathic medicine) and gains ground in the United States.

It is found an increase of the interest for these unconventional techniques of treatment, because the recent findings show that the chemistry, although it explains many mechanisms of the body, it cannot explain by itself the integrative way of functioning of the human body.

The modern science recognizes the fact that the human body contains all types of energy, including electromagnetic energy. For example, the brain produces different electromagnetic waves (eg. alpha, beta, delta, theta), used in encephalography (EEG) and in determining the state of health of the heart (electrocardiography).

One of the most interesting methods of appreciating the energetic state of the body is the bioresonance method. Paul Schmidt was the German researcher who established the sound scientific of the method in 1976. He started from the theory that the objects with identical oscillatory abilities resonate with each other. The body's cells and all their components are resonators of electromagnetic energy, emitting and absorbing very high frequency energy.

A large number of people are suffering from stress associated with daily activities, existing a close correlation between stress and mental health, also, the physiological stress (associated with emotions such as anger, anxiety and depression) may influence the physical health. When the brain is subjected to stressors, it initiates an answer resulting in a series of chemical reactions, representing a defence mechanism that involves the release of hormones with numerous biochemical and physiological effects.

The hormonal answer determined by prolonged stress increases the risk of occurrence of different actions, such as heart disease, stroke and angina; hormones that weaken the immune system and increase the vulnerability to infections. At the same time, the hormones released from the stress determine the increase of the blood pressure, heart rate and breathing and increases the risk of stroke, and myocardial infarction (Noback et al., 1986).

The answer to the stressors can be measured and evaluated by assessing the patient's behaviour, perception and physiological answers.

As an alternative medicine, the biofeedback is used, by which the heart rate, blood pressure, skin resistance, temperature, etc. are monitored. The biofeedback is widely used in the treatment of

psychiatric disorders, such as anxiety and depression and psychosomatic disorders, such as migraine (Sadock B.J. & Sadock V.A. 2004).

The low-intensity electric currents are biocompatible and have effect beyond the simply blocking of the pain perception, it turned out that they are also responsible for tissue regeneration. In general, the currents with intensity between 20 mA - 120 mA are applied in order to block the neuronal transmission of the pain signals and to stimulate the release of endorphins and other neurotransmitters that are involved in relieving the acute or chronic pain.

The neuromuscular dystonia is a disorder characterized by the involuntary muscle contraction, which causes repetitive movements or abnormal postures. The movements can be painful, some people affected by dystonia may present tremor. Dystonia may affect different parties of the body.

The cause of neuromuscular dystonia is unknown - naturally, the brain sends chemical messengers to keep under control the muscle movements; one of these messengers is acetylcholine. In cervical dystonia, it is assumed that too much acetylcholine is produced, which can lead to muscle tension of over-activity. Some patients with cervical dystonia present history of injuries of the head or neck, but it is not yet clear if these are related to the dystonia they suffer, further investigation is needed. As for other diseases, it is very likely that the disease is caused by a combination of genetic and environmental factors.

The neuromuscular dystonia is the third most common movement disorder after the essential tremor and Parkinson's disease.

The muscle contracture is scientifically defined as a muscular hypertrophy. Specifically, the muscle no longer relaxes, the tone and the intramuscular tension being both high, generating an acute and persistent pain. A muscle contracture can occur as a result of the physical effort without an warming-up in accordance with the exercises to be performed. Also, the contractures can be generated by performing some sudden movements or by transporting heavy loads. Sometimes, the contractures are also caused by joint problems or muscle imbalances.

The permanent intramuscular tension is pressing on the intramuscular capillaries and vessels determining an intramuscular circulatory deficiency, which causes muscular hypoxia (low oxygenation of the muscle). The accumulation of carbon dioxide in muscle causes pain.

In view of the above, it is particularly to improve the neuromuscular dystonia associated or not with contractures, as long as their cause remain unknown.

Although there is no remedy, the symptoms associated with dystonia can be controlled by the oral administration of drugs, additional therapies and / or therapy by injection of botulinic toxin; or, by performing specific procedures to the Universal Electrophysiological Biofeedback

System NUCLEUS, along with the medication and alternative therapies (physiotherapy, kinetic therapy, etc.) has obtained a remarkable improvement in the health of patients, of course associated with the manifest improvement of symptoms.

5.4 Benefits specific to or precautions necessary to the patients or some subgroups

This clinical investigation ..... that the biofeedback protocols of reducing the stress, pain, etc. are effective and safe. The benefits for heath include:

- Reduction of the patient's stress and improvement of certain associated conditions (anxiety, depression);
- NUCLEUS device measures a wide spectrum of electrical and electromagnetic reactions of the body, being extremely sensitive even to the smallest incipient signs of the functional disturbance of body and, therefore of the disease. It is a complex program that combines bio-resonance and biofeedback with the simplicity of IT technology in order to produce the most advanced system of evaluation and analysis of the human body and for energetic treatment;
- The assessment of the health, namely the biofeedback therapy, are non-invasive, with no adverse and / or secondary effects.

However, the user should not use the Universal Electrophysiological Biofeedback System NUCLEUS:

- For children aged less than 3 years;
- It shall be used with caution in the patients with psychiatric disorders;
- It shall not be used in patients with epilepsy or for which there was performed electroshocks or in patients who have a pacemaker.

Also, it cannot be said that certain subgroups [related to gender, blood group, profession, etc.] would have additional benefits over other subgroups of patients, but neither additional risks.

5.5 Implications on the future clinical investigations

The results of this clinical investigation are useful in any performance evaluation of the biofeedback protocols on large groups of patients (hundreds, thousands), but also in assessing the performance in shortening the healing time or in improving the symptoms of other medical condition, including in associating this type of procedures with the standard treatment of the acute wounds (such as burns) or chronic wounds (such as bedsores, peripheral venous ulcer, diabetic ulcers).

5.6 Limitations of the clinical investigation

This clinical investigation did not aimed to analyse the performance of the procedures carried out with Universal Electrophysiological Biofeedback System NUCLEUS, compared to certain subgroups of subjects (patients).

Also, another limitation is the non-differentiation between the aetiology of the neuromuscular dystonia and muscle contracture, but also the non-assessment of the improvement of symptoms after completing the procedures carried out with the Universal Electrophysiological Biofeedback System NUCLEUS (follow-up).

The aspects pointed out above are to be assessed on the occasion of performing future clinical investigations.

6 ABBREVIATIONS; TERMS AND DEFINITIONS

HTA – arterial hypertension
HTA – essential arterial hypertension
DVL – lumbar vertebral discopathy
HDL – lumbar disc herniation
BCI – ischemic coronary disease
IVC – chronic venous insufficiency
US – ultrasound therapy
KT – kinetic therapy

The terms and definitions used in the documentation of the clinical investigation [Manual of the Investigator, Clinical Investigation Plan] are in accordance with SR EN ISO 14155, SR EN ISO 13485 and SR EN ISO 14971.

7 ETHICS

The Clinical Investigation Plan was reviewed by the Ethics Committee of the National Institute of Recovery, Physical Medicine and Balneoclimatology of Bucharest.

All ethical issues mentioned in the investigation documentation, BFK-01 and in the Clinical Investigation Plan, BFK-CIP-01 were complied with throughout the clinical investigation.

8 INVESTIGATORS AND ADMINISTRATIVE STRUCTURE OF THE CLINICAL INVESTIGATION

8.1 Summary of the clinical investigation organization

The clinical investigation took place at the National Institute of Recovery, Physical Medicine and Balneoclimatology of Bucharest, until the enrolment of the number of subjects, provided in the Clinical Investigation Plan BFK-CIP-01.

8.2 List of investigations

Dr. Dima Augustin, Primary Care Physician in Physical Recovery and Balneophysiotherapy

8.3 Name and address of sponsor

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9. SIGNATURES PAGE

Dr. Dima Augustin, Primary Care Physician in Physical Recovery and Balneophysiotherapy

I, Laura Maria IANCU, hereby certify that I translated the attached document from Romanian into English and that, to the best of my knowledge and belief, it is a true, accurate and correct translation.

I further certify that I am competent in both Romanian and English to render and certify such translation.

Full legal name: *Laura Maria IANCU*

Sign: _____

Date: _____

*Translator's note:
Each page of this document contains the seal reading: Romania – Health Ministry – Physical and balneo-climatology Medicine – The National Recovery Institute – THE MANAGER