ANF Academy

Clinical Investigation

Post-Market Clinical Investigation of the ANF Therapy® Device

Version 2 June 2021

Investigator: Irina A. Heinisuo Berná

Investigational medical device: ANF Therapy® Device.

Medical Device Class I

Availability in the market since 2013

Investigation center: ANF Academy, Amino Frequency Corporation SL, Calle de las Adelfas 5, 29660 Marbella. Spain

Clinical development stage: Post-Market Stage

Period: March 2021 to June 2021

Type of clinical investigation design: Observational Clinical Investigation

Descriptors of clinical investigation: Registry. An organized electronic system that uses observational methods to collect data under normal conditions of use relevant during standard clinical practice.

Burden to subjects: Non-interventional clinical investigation. The subjects of the study have not been assigned to intervention groups.

Usage Method: ANF Therapy® Method.

Subject population: Patients worldwide that suffer an injury or disease who have visited one of our worldwide certified ANF Therapists, ANF Practitioners, or students of ANF Therapy®.

Investigational devices: ANF Therapy® Devices.

Sponsor: Amino Frequency Corporation SL, Calle de las Adelfas 5, 29660 Marbella. Spain. Email: hello@anftherapy.com.

Coordinating investigator and other relevant parties:

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- Coordinating investigator: Sanne Kiilerich, sanne@anftherapy.com. Founder and Director of Amino Frequency Corporation SL.
- Mabel de Carranza, AFC Técnico de Salud, mabel@anftherapy.com.
- Investigation site: ANF Academy, Amino Frequency Corporation SL, Calle de las Adelfas 5, Nueva Andalucía, 29660 Marbella. Spain.

Statement: This Clinical Investigation follows Good Clinical Practice principles (DS/ISO 14155:2020).

Date of report: 14th June 2021

Authors of report: Irina A. Heinisuo Berná

Post-Market Clinical Investigation of the ANF Therapy® Device

Abstract

The ANF Therapy® Device, available in the market since 2013, has shown promising practical evidence in reducing pain and inflammation among patients treated by ANF Therapists. This study aims to evaluate the clinical performance, effectiveness, and safety of ANF Therapy® Devices following the ANF Therapy® Method.

Based on the findings, it can be concluded that a combination of ANF Therapy® Devices is effective in injury and disease alleviation, with a notable improvement in pain reduction, swelling/edema reduction, range of motion, and overall quality of life-related to health. These positive effects highlight the potential of ANF Therapy® in managing various conditions. Furthermore, using ANF Therapy® Devices demonstrated a good safety profile, with only minor risks reported. This conclusion is based on a post-market clinical investigation that has examined the impact of ANF Therapy® on patient outcomes.

To further expand the knowledge on ANF Therapy®, future research should focus on exploring the potential benefits of ANF Therapy® Devices in other medical fields, particularly in more severe pathologies. Investigating the effects of ANF Therapy® in a broader range of conditions will provide valuable insights into its efficacy and applications.

Additionally, there is a need for further investigation into the use of ANF Therapy® Devices among specific populations, such as premature infants, babies, toddlers, and pregnant women. Understanding the safety and efficacy of ANF Therapy® in these vulnerable groups will help determine its potential benefits and risks in specialized healthcare settings.

In summary, the combined use of ANF Therapy® Devices demonstrates effectiveness in treating injuries and diseases, with potential applications in various medical fields. Continued research and exploration of ANF Therapy's effects in different populations will contribute to the advancement of this promising therapeutic approach.

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1. EXECUTIVE SUMMARY

Introduction

This Post-Market Clinical Investigation focuses on the ANF Therapy® Device and aims to analyze its clinical safety and performance in pain reduction. The report has considered data from various sources, such as clinical data generated by the manufacturer and scientific literature on related concepts, to provide a comprehensive assessment.

The context

The ANF Therapy® Device (ANF Device) has been available on the market since 2013, and numerous therapists and patients have reported positive outcomes from its use. Amino Frequency Corporation SL, the device manufacturer, has actively engaged with healthcare professionals through educational platforms, forums, direct communication, and training sessions. Since 2017, a structured electronic registry system has been in place to collect clinical data and ensure safety and performance monitoring.

The intended medical indications for the ANF Device include musculoskeletal, nervous, cardiovascular, lymphatic, and digestive disorders. The ANF Device aims to address pain, abnormal swelling/edema, lack of range of motion, and impaired health-related quality of life.

Benefit/Risk profile in the intended target groups

Benefits of the ANF Device have been observed across various patient groups. It has demonstrated effectiveness in reducing pain, improving range of motion and mobility, reducing swelling, and enhancing overall health-related quality of life. The positive effects of the device can be long-lasting and significant. Pain relief has been reported in cases of chronic pain, acute pain, nerve problems, low back pain, and injuries to muscles, ligaments, and tendons. Chronic conditions have observed improved range of motion, mobility, and health-related quality of life.

The ANF Device shows potential in addressing other conditions and complaints, such as improving sleep, vision, energy levels, sore throat, and intestinal function, and reducing stomach pain and anxiety. It may also aid in regaining strength after a stroke, improving stability, facilitating return to work and sports activities, enhancing mood, and providing a sense of safety during physical activities.

While there are potential benefits, using ANF Devices can result in detoxification (detox) symptoms in approximately 28% of cases. However, the detox symptoms typically occur only once, with mild intensity and lasting less than 24 hours. The incidence of detox symptoms may be slightly higher in patients with other health issues and significantly higher when applying many devices per session (more than 10). Notably, age does not appear to be a determining factor for detox incident rates, indicating the device's safety for all ages, from infants to older people.

Although rare, there is a small risk of skin incision or other unexpected adverse incidents if the ANF Therapy® Method is not followed correctly. The risk evaluation suggests that the overall risks associated with the device are mostly tolerable when used as intended. In cases where the device is not applied on clean skin, the risk level may increase to a moderate level.

Risk Evaluation

Based on the risk evaluation data, the ANF Device has shown favorable clinical safety and performance in pain reduction and improving the health-related quality of life in patients with musculoskeletal, nervous system, cardiovascular, lymphatic, and digestive disorders. The device's benefits outweigh its risks, making it an acceptable option for healthcare professionals seeking noninvasive and drug-free alternatives in pain management. The recommended control measure in all cases is to remove the patch if discomfort persists beyond 24 hours.

Acceptability based on state of the art in the medical fields

Based on the current scientific literature, there is no solid scientific evidence to recommend a specific solution for pain management. Consequently, this Post-

Market Clinical Investigation Report sheds light on a noninvasive, drug-free medical device that has demonstrated high effectiveness in injury alleviation and potentially in addressing various diseases. Further research and exploration of the device's potential applications are warranted.

2. INTRODUCTION

The ANF Device has been available in the market since 2013. Based on practical evidence from hundreds of ANF therapists and thousands of patients worldwide, ANF Devices can decrease pain and inflammation within minutes, although there is a lack of scientific evidence.

Since these years, the device has proven to be safe and only causes minor risks for the patient and with a very low frequency.

The purpose of this investigation is to draw inferences about the possible effects of an intervention with ANF Devices on patients and intends to answer specific questions relating to clinical performance, effectiveness, and safety of the ANF Device when used in accordance or not with ANF Therapy® Method.

Hypothesis: The ANF Device is effective in injury and disease alleviation and is safe to use by ANF Therapists worldwide.

Target population: patients worldwide that suffer an injury or disease and complain of pain, swelling, range of motion limitation, or impaired health-related quality of life.

Treatment: Application of 1 or more ANF Devices following an ANF Protocol designed by an ANF Therapist.

Follow-up duration: decided by the ANF Therapist, as a healthcare professional.

3. CLINICAL BACKGROUND, CURRENT KNOWLEDGE, STATE OF THE ART.

3.1. Pain

An unpleasant sensation induced by noxious stimuli which are detected by nerve endings of nociceptive neurons.

3.2. Pain evaluation scales:

Visual analog scales (VAS): A subjective psychometric response scale used to measure distinct behavioral or physiological phenomena based on linear numerical gradient or yes/no alternatives.

3.3. Current therapies and unmet needs:

Web-based search engines: Cochrane

3.3.1. Patient Education for neck pain. (1)

- Sound methods: Lack scientific validity for demonstration.
- Safety: There appeared to be no harmful effects of patient education.
- Benefit/risk: Inconclusive.
- Performance: no strong evidence of the effectiveness of educational interventions in various neck disorders.
- Undesirable side-effects: No adverse events were reported in the trials.

3.3.2. Patient Education for acute/subacute low back pain. (2)

- Sound methods: lack scientific validity for demonstration.
- Safety: There appeared to be no harmful effects of patient education.
- Benefit/risk: Inconclusive.
- Performance: For patients with acute or subacute low back pain, intensive patient education seems to be effective.
- Undesirable side-effects: No adverse events were reported in the trials.

3.3.3. Patient Education for chronic low back pain. (2)

- Sound methods: Lack scientific validity for demonstration.
- Safety: There appeared to be no harmful effects of patient education.
- Benefit/risk: Inconclusive.
- Performance: For patients with chronic low back pain, the effectiveness of individual education is still unclear.
- Undesirable side-effects: No adverse events were reported in the trials.

3.3.4. Patellar taping (3)

- Sound methods: Lack scientific validity for demonstration. Evidence is low.
- Safety: Non-mentioned.
- Benefit/risk: Inconclusive.
- Performance: Low quality and insufficient to draw conclusions on the effects of taping.
- Undesirable side-effects: Non-mentioned.

3.3.5. TENS (4–7)

- Sound methods: Lack scientific validity for demonstration.
- Safety: Unable to conclude that TENS is harmful in people with chronic pain.
- Benefit/risk: Inconclusive.
- Performance: Unable to conclude that TENS is beneficial for pain control, disability, health-related quality of life, use of pain-relieving medications, or global impression of change in people with chronic pain. Conflicting evidence regarding the benefits of TENS for chronic LBP, does not support the use of TENS in the routine management of chronic LBP.

- Undesirable side-effects: Unable to draw any conclusion on TENS-associated harms or side-effects. Minor skin irritation occurred at the site of electrode placement (intervention and placebo groups). One case of severe dermatitis.

3.3.6. Flexibility exercise training: (8)

- Sound methods: Lack scientific validity for demonstration. The certainty of the evidence is very low.
- Safety: Evidence on adverse events was scarce; therefore, its safety is uncertain.
- Benefit/risk: Unclear.
- Performance: The evidence does not show that flexibility exercise significantly improves health-related quality of life, pain, fatigue, or physical function.
- Undesirable side-effects. No clear information on harm. One case of swelling (tendinitis) of an ankle tendon (Achilles).

3.3.7. Whole body vibration (9)

- Sound methods: Lack scientific validity for demonstration. Evidence is very low.
- Safety: Studies were few and very small, which prevented meaningful estimates of harms and definitive conclusions about WBV safety.
- Benefit/risk: Inconclusive.
- Performance: Unclear.
- Undesirable side-effects: Acute pain in legs, mild anxiety attack.

3.3.8. Placebo interventions: (10)

- Sound methods: Lack scientific validity for demonstration.
- Safety: Inconclusive.

- Benefit/risk: Unclear.
- Performance: Placebo interventions have no important clinical effects in general.
- Undesirable side-effects: Not mentioned.

3.3.9. Acupuncture: (11,12)

- Sound methods: Lack scientific validity for demonstration. Evidence is very low to moderate.
- Safety: Unclear.
- Benefit/risk: Inconclusive.
- Performance: Compared with usual care, acupuncture did not appear to reduce pain significantly clinically.
- Undesirable side-effects: Adverse effects related to acupuncture were considered minor or moderate. The most common adverse events were pain at insertion points, hematoma, bleeding, worsening of LBP, and pain other than LBP (pain in leg and shoulder).

3.3.10. Chiropractic intervention: (13)

- Sound methods: Unclear.
- Safety: Unclear.
- Benefit/risk: Inconclusive.
- Performance: Any demonstrated differences in effects are minor and not clinically relevant compared to other treatments. Any benefits do not appear to be long-lasting.
- Undesirable side-effects: Minor, transient exacerbations of symptoms.

3.3.11. Yoga treatment: (14)

- Sound methods: Evidence 'moderate', 'low', or 'very low'.

- Safety: Yoga was not associated with a risk of serious adverse events.
- Benefit/risk: Inconclusive.
- Performance: There was little information on clinical improvement, health-related quality of life, and depression, and no evidence of work-related disability.
- Undesirable side-effects: There was moderate-certainty evidence that the risk of harm was higher in yoga than in non-exercise. Increased back pain.

4. INVESTIGATIONAL DEVICE AND METHODS

Description of the device:

Wearable non transdermal adhesive patches made of a carbonized metal embedded with a specific frequency, a PET layer, and a Skin-friendly 3M adhesive layer.

Intended purpose: Injury and disease alleviation.

Clinical performance: Pain relief, swelling reduction, range of motion improvement, quality of life-related to health improvement.

Conditions for treatment: Musculoskeletal disorders, nervous system disorders, cardiovascular disorders, lymphatic disorders, and digestive disorders.

Necessary training and experience required to apply the ANF Device: Used in accordance with ANF Therapy® Method. Only ANF Therapists can use the ANF Devices on patients after attending an ANF Education created by ANF Academy. An ANF Therapist is a healthcare professional who has joined and successfully completed at least ANF course level 1.

5. CLINICAL INVESTIGATION PLAN

5.1. Clinical investigation objective

The purpose of this investigation is to draw inferences about the possible effects of an intervention with ANF Devices on patients and intended to answer specific questions relating to clinical performance, effectiveness, and safety of the ANF Therapy® Device.

5.2. Clinical investigation design

5.2.1. *Type of clinical investigation*

5.2.1.1. Observational Clinical Investigation.

5.2.2. *Justification*

5.2.2.1. Observational:

The design of this clinical investigation is important for monitoring the usage of ANF Devices by ANF Therapists worldwide.

5.2.2.2. Non-interventional:

The design has been chosen to avoid altering the standard clinical practice of our worldwide ANF therapists/practitioners' clinics.

5.2.2.3. Registry:

The webform which collects the data about the subjects and cases is made based on the regular intake of information that a healthcare professional and ANF therapist will gather in their everyday clinical practice.

5.2.3. Objectives

5.2.3.1. Primary objectives: Investigate the clinical performance, effectiveness, and safety of using ANF Devices on patients suffering an injury and/or disease by ANF Therapists worldwide.

- Verify that ANF Devices help alleviate pain within minutes.
- Verify that ANF Devices help alleviate pain.

- Verify that ANF Devices help alleviate pain during daily activities.
- Verify that ANF Devices help alleviate the swelling.
- Verify that ANF Devices help improve the range of motion.
- Verify that ANF Devices help improve quality of life.
- Verify that ANF Devices are safe to use.
- Verify that ANF Devices are safe to use on vulnerable populations.
- Verify that ANF Devices are linked to known adverse reactions.
- Verify that ANF Devices provide a positive Benefit / Risk ratio.

5.2.3.2. Secondary objectives: Investigate other possible negative or positive effects of using ANF Devices on patients suffering injury and/or disease.

- Verify that the benefits of applying ANF Devices are durable.
- Verify that the benefits of applying ANF Devices are multiple.
- Verify that the benefit of applying ANF Devices are significantly relevant.
- Verify that patients are satisfied after the application of ANF Devices.
- Verify that therapists are satisfied with the results of applying ANF Devices to their patients.

5.2.4. Clinical investigation endpoints

5.2.4.1. Primary endpoints Clinical performance and effectiveness.

5.2.4.2. Pain

- Pain before ANF: bar rating scale 0-100.
- Pain after ANF (5-60 minutes): bar rating scale 0-100.

- Pain improvement during daily activities: Scoring categories.
- Duration of pain improvement.
- Pain after 1 or more ANF applications (end of treatment): bar rating scale 0-100.

5.2.4.3. ROM/Mobility

- Improvement in ROM/Mobility: Scoring categories.
- Duration of ROM/Mobility improvement.

5.2.4.4. Swelling

- Improvement in swelling: Scoring categories.
- Duration of swelling improvement.

5.2.4.5. Quality of life (QoL)

- Improvement in QoL: Scoring categories
- Duration of QoL improvement.

5.2.4.6. Primary endpoints Safety.

5.2.4.7. Known Adverse effects: Any detox symptoms? None, Headache, Dry mouth, Dizziness, Light flu symptoms, Shivers, Fatigue, General discomfort, Runny nose, Hives, Itching, Nausea, or Vomiting.

- Detox intensity: None, Mild (little bit), Medium (moderate), Strong (a lot).
- Detox duration: None, minutes, hours, days, weeks.
- Detox frequency: None, only once, not very often, very often, every time the Devices are applied.

5.2.4.8. Risk of use incidents: No incidents, Skin incision (cut from edge of Device), Skin lesion (Devices removed too fast), Spray glue issue (extra adhesive application), Excessive hair extraction (remove Devices and hair comes off), Skin burns (using external heating device or sunburn).

- Incident duration: None, minutes, hours, days, weeks.

- Incident frequency: None, only once, not very often, very often, every time the Devices are applied.

5.2.4.9. Severe adverse reaction: None, Life-threatening illness or injury, Permanent impairment of body structure or body function, Hospitalization, Medical or surgical intervention (not planned).

5.2.4.10. Secondary endpoints

- Any unexpected benefit? Yes, No. If yes, specify.
- Other unexpected negative incidents? Yes, No. If yes, specify.
- Therapist satisfaction: Bar rating scale 0-100.
- Patient satisfaction: Bar rating scale 0-100.

5.2.5. Control group

The control group is absent due to the nature of the study.

5.3. Ethical considerations

5.3.1. This post-market study follows the ethical principles of the Declaration of Helsinki.

5.3.2. All ANF Therapists are healthcare professionals holding a degree from competent Universities in their own countries. This study does not collect this information, but the manufacturer has these documents within the therapist´s profile.

5.3.3. Ethics Committee (Denmark) has confirmed that this type of clinical investigation does not have an obligation to inform to Ethics Committee to perform the study.

5.4. Data quality assurance

The ANF Therapist is asked to confirm that he/she has fulfilled the form with truthful and correct information to the best ability as Healthcare Professional and ANF Therapist.

5.5. Subject population criteria

5.5.1. *Inclusion criteria.*

ANF Pain Entry Cases uploaded by ANF Therapists. Subject population: Patients worldwide who suffer an injury or disease and visit one of our worldwide ANF Therapists or Practitioners.

5.5.2. *Exclusion criteria:*

When ANF Devices have not been used.

5.5.3. *Sample size:*

The number of subject cases depends on the willingness of ANF Therapists to upload cases into the Pain Entry Cases study webform. Deadline date: May 2021 for version 1 June 2021.

5.5.4. *Treatment and treatment allocation schedule*:

Location of ANF Therapists worldwide: www.findanf.com

5.5.5. Concomitant medications/treatments:

These aspects are not covered in this post-market surveillance.

5.5.6. Durations of follow-up:

Each ANF Therapist follows up with the patient as standard clinical practice and can communicate directly with the Investigator in case of abnormal events. A minimum of 3 days and the maximum follow-up period depends on each ANF Therapist according to their everyday clinical practice.

5.6. Statistical design, analysis, and justification

5.6.1. *Hypothesis*

5.6.1.1. The ANF Device is effective in alleviation of injury and disease and is safe to use by ANF Therapists worldwide.

5.6.2. Statistical analysis methods

5.6.2.1. Descriptive statistics. Measures of frequency (count, percent, frequency).

5.6.2.2. The chosen statistical methods have been used based on the need of listing and describing the safety and performance requirements of the medical device.

5.6.2.3. The statistics measures are based and relevant to standard clinical practice.

5.6.3. Measures of frequency

5.6.3.1. Count

- How many Devices have been used in each single session?
- How many types of Devices have been used in the study?
- How many visits have the subject attended for ANF Therapy®?
- How much pain does the pain have before ANF application?
- How much pain does the pain have after ANF application?

5.6.3.2. Percent:

- Which percentage of subjects experienced any detox symptoms?
- Which percentage of subjects experienced any negative incidents?
- Which percentage of subjects experienced any severe adverse reaction?
- Which percentage of subjects experienced any pain relief?
- Which percentage of subjects experienced any swelling reduction?
- Which percentage of subjects experienced any ROM improvement?
- Which percentage of subjects experienced any health-related quality-of-life improvement?

5.6.3.3. Frequency:

- How often has the subject experienced any detox symptoms?
- How often has the subject experienced any negative incidents?

5.6.4. Sample size

The number of subjects cases depend on the willingness of ANF therapists to upload cases into the Pain Entry Cases study webform.

5.6.5. Pass/fail criteria

Cases are not included in the study, if they are duplicated, out of scope, made by a therapist with insufficient course level, show unrealistic result, no Confirmation of Truthful case, or no Consent to Share.

6. STATEMENT OF COMPLIANCE

6.1. This post-market study follows the ethical principles of Declaration of Helsinki.

6.2. All ANF Therapists are healthcare professionals holding a degree from competent Universities in their own countries. This study does not collect this information, but the manufacturer has these documents within the profile of the therapist.

6.3. The Ethics committee has confirmed that this type of clinical investigation does not have the obligation to inform to Ethics Committee to perform the study.

6.4. Each ANF Therapist has their own professional liability insurance according to their regular clinical practice and based on their professional background and their country requirements. This study does not collect this information.

6.5. Informed consent process: Due to the nature of this investigation, informed consent will not be collected. Although each ANF Therapist, being a healthcare professional, is asked to collect informed consent for each patient seen in their clinic, with their own form, content, management and saving procedures.

7. DATA MANAGEMENT

7.1. Methods for data entry and collection: Podio electronic clinical data system webform, through student's online educational platform.

7.2. Data tracking: Each ANF therapist has a unique identification number, and this number is associated with each uploaded case.

7.3. If needed, the rectification of errors done together with the ANF Therapist who has uploaded the case by sharing the item with "read-only" mode was entered in the comments side.

7.4. Data review was made by the ANF Investigator.

7.5. Data collection was converted into Excel document format.

7.6. The online educational platform, where the webform is located to fill in a case, is secured with personal identifications and passwords.

7.7. The electronic clinical data system, where all cases are located, is secured by personal identifications and passcodes.

7.8. Only personnel involved in the Clinical investigation have access to the data.

7.9. Every change made to the original case has been registered in the comments area.

7.10. Subject privacy is protected since no personal information is asked within the webform. The ANF therapist can identify the cases by adding the patient's initials or the patient´s journal number.

7.11. The database is protected by an electronic security system within the Podio system.

7.12. The data is stored and used periodically for future investigations, with the goal to increase the number of cases for better results.

8. RESULTS

8.1. Initiation date

March 2021.

8.2. Completion/suspension date

24th May 2021 for Clinical Investigation Version 1 June 2021.

8.3. Disposition of subjects

8.3.1. ***Number of Pain Cases screened***: 113.

8.3.2. ***Number of Pain Cases allowed to share data***: 111.

8.3.3. ***Number of Pain Cases accepted in the clinical investigation***: 109.

8.3.4. ***Number of ANF Therapists involved in the clinical investigation***: 19.

ANF Therapist	Cases
Igor Kochekovich	24
Helen Slama	19
Ciprian Cozmuleasa	13
Renata Von Kouh-Wright	10
Kim Demuth	8
Gemma Guilford	6
Serena Semaan	5
Rok Kajzer	5
Claire Dunkley	5
Cristian Chihaia	2

Sam Leslie	2
Caren Lieberman	2
Aire Pärtel Araújo	2
Hafsa Sliman	1
Ohood Hujooj	1
Marcus Benitez	1
Sue Phillips	1
Ciro Espindola	1
Batul Adil	1
Total general	**109**

8.3.5. Number of Cases per level of education:

Therapist course level	Cases	%
ANFC8Holistic	38	34,9%
ANFC4	37	33,9%
ANFC7	21	19,3%

ANF3O	5	4,6%
ANF2O	3	2,8%
ANFC1-2	2	1,8%
ANF4PT	1	0,9%
ANFC5-6	1	0,9%
ANFC3Pain	1	0,9%
Total general	109	100,0%

8.3.6. Date of uploading cases:

Created on	Cases
2021-03-02 14:19	1
2021-03-03 8:11	1
2021-03-04 7:46	1
2021-03-06 6:57	1
2021-03-06 7:58	1
2021-03-06 8:06	1
2021-03-06 8:15	1
2021-03-06 8:26	1
2021-03-06 8:34	1
2021-03-06 8:41	1
2021-03-06 8:48	1
2021-03-06 8:56	1
2021-03-06 9:04	1
2021-03-06 9:11	1
2021-03-09 2:20	1
2021-03-10 2:52	1
2021-03-10 5:56	1
2021-03-10 7:32	1
2021-03-10 9:31	1
2021-03-10 10:52	1
2021-03-10 17:46	1
2021-03-10 18:11	1
2021-03-10 22:59	1
2021-03-10 23:15	1
2021-03-11 8:02	1
2021-03-11 8:15	1
2021-03-11 14:15	1
2021-03-11 19:54	1
2021-03-11 20:09	1
2021-03-11 20:42	1
2021-03-11 21:11	1
2021-03-11 21:43	1
2021-03-12 2:49	1
2021-03-12 3:59	1
2021-03-12 4:27	1
2021-03-12 6:37	1
2021-03-13 8:54	1
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2021-03-13 9:40	1
2021-03-13 9:51	1
2021-03-13 13:47	1
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2021-03-18 11:57	1
2021-03-18 17:16	1
2021-03-19 1:35	1
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2021-03-19 2:15	1
2021-03-21 13:08	1
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2021-03-23 14:07	1
2021-03-23 17:56	1
2021-03-24 10:09	1
2021-03-24 17:03	1
2021-03-26 19:55	1

2021-03-26 21:28	1	2021-04-07 1:58	1	2021-04-17 19:19	1	2021-05-21 10:39	1
2021-03-27 0:56	1	2021-04-07 2:25	1	2021-04-17 19:47	1	2021-05-21 10:53	1
2021-03-27 1:20	1	2021-04-07 2:55	1	2021-05-10 14:39	1	2021-05-21 11:14	1
2021-03-31 18:53	1	2021-04-07 5:14	1	2021-05-10 14:50	1	2021-05-21 11:40	1
2021-03-31 18:57	1	2021-04-07 5:34	1	2021-05-10 16:12	1	2021-05-21 12:22	1
2021-03-31 20:50	1	2021-04-17 8:09	1	2021-05-10 17:24	1	Total general	109
2021-04-07 1:45	1	2021-04-17 18:43	1	2021-05-10 17:51	1		

8.4. **Disposition of the investigational device**

8.4.1. ***Number of device types***: 97.

8.4.2. Device types:

Devices used

Total	97	NX2	19	VC2	7	P211	5
P-9	79	M2	17	VD1	7	HA2	5
P200	74	P-1	17	HD3	7	E-1	5
ACA	56	NX3	16	P620	7	E+8	5
AGL	54	MCT	16	P400	7	SC10	4
MC	49	E+6	16	CR2	6	VK1	4
P130	42	P300	14	BF3	6	CR1	4
ACAS	40	HD4	12	LV3	6	PH3	4
MCS	31	P-17	12	PH17	6	PH10	4
HD2	28	HXH	12	P411	6	P460	4
P311	26	P580	10	SC6	5	LYC3	4
P217	25	VC1	9	LV4	5	KY	4
P271	24	P-5	9	NR2	5	SPL2	4
P-15	22	P280	9	P500	5	MT	4
BF2	21	E-6	8	E+10	5	P218	4
AGLS	20	P350	8	LV	5	P150	4
AS	19	P240	8	HA3	5	P140	4

P590	3	NR3	3	VK2	2	NX4	2
BF4	3	TYGAG	3	NX	2	VA1	2
SC4	3	E-10	3	EST2	2	E+1	2
WXC5	3	SK2	3	VD2	2	SB3	2
PH4	3	EDM	3	SC3	2	WXC3	2
VB12	3	WXC	3	PTX1	2	PH9	2
LV2	3	PTX6	2	HPT1	2		
WXC4	3	SC7	2	DP2	2		

8.4.3. ***Combination of ANF Devices***: each case has a different combination of ANF Devices. Table 2 or Link here

8.4.4. Average Devices used in a single visit

Devices used in each application	Cases	%
5 - 10	30	27,5%
11 - 15	21	19,3%
less than 5	16	14,7%
16 - 20	16	14,7%
21 - 25	9	8,3%
26 - 30	8	7,3%
31 - 35	6	5,5%
more than 40	3	2,8%
Total general	109	100,0%

8.4.5. How many total ANF applications

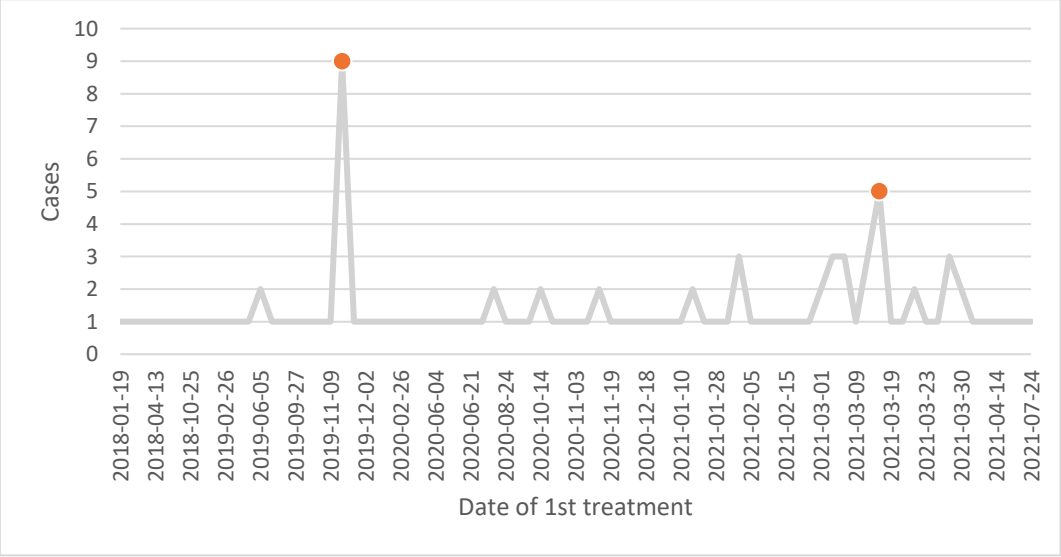
Total ANF applications	Cases	%
1	49	45,0%
2	16	14,7%

4	15	13,8%
3	10	9,2%
6	6	5,5%
7	5	4,6%
5	5	4,6%
8	2	1,8%
10 or more	1	0,9%
Total general	109	100,0%

8.4.6. Consecutive applications

Were those applications consecutive?	Cases	%
not relevant, only one application	48	44,0%
yes	32	29,4%
no	29	26,6%
Total general	109	100,0%

8.4.7. Date of first treatment



8.5. Compliance

8.5.1. *Hydration*

At least 17% of patients were not compliant with drinking water during the treatment.

Patient was hydrated	Cases	%
yes	88	80,7%
no	19	17,4%
I dont know	2	1,8%
Total general	109	100,0%

8.5.2. Devices placed on clean skin

At least 5% of cases were not compliant with applying the Devices on clean skin.

Devices placed on clean skin	Cases	%
yes	104	95,4%
no	4	3,7%
I dont know	1	0,9%
Total general	109	100,0%

8.5.3. Protocol applied as intended

Protocols were applied as intended in 109 cases (100%).

8.5.4. Truthful and correct information

Therapists confirm that they have fulfilled the form with truthful and correct information to their best ability as Healthcare Professionals and ANF Therapist in 109 cases (100% of cases).

8.5.5. ANF Education guidelines compliance according to Investigator

ANF Edu Guideline Compliance	Cases	%
Very Good	57	52,3%
Good	29	26,6%
Non Compliant	17	15,6%

Excellent	6	5,5%
Total general	109	100,0%

8.6. Subject demographics

8.6.1. *Country of patients involved in the clinical investigation*: 21.

Country	Cases	%
United States	24	22,0%
Indonesia	16	14,7%
France	13	11,9%
Australia	8	7,3%
Singapore	8	7,3%
Denmark	8	7,3%
Slovenia	5	4,6%
New Zealand	5	4,6%
Brazil	4	3,7%
United Kingdom	3	2,8%
Romania	2	1,8%
UAE	2	1,8%
Portugal	2	1,8%
Italy	2	1,8%
Turkey	1	0,9%
Lebanon	1	0,9%
Canada	1	0,9%
Sweden	1	0,9%
Jordan	1	0,9%
Switzerland	1	0,9%
Pakistan	1	0,9%
Total general	109	100,0%

8.7. Baseline characteristics

8.7.1. Patient overall health

Patient overall health is different among subjects. Table 1 or Link here

8.7.2. Gender

Gender	Cases	%
Female	63	57,8%
Male	46	42,2%
Total general	109	100,0%

8.7.3. *Age group*

Age Group	Cases	%
Middle-aged adult	53	48,6%
Young adult	28	25,7%
Senior adult	19	17,4%
Old adult	5	4,6%
Child	3	2,8%
Teenager	1	0,9%
Total general	109	100,0%

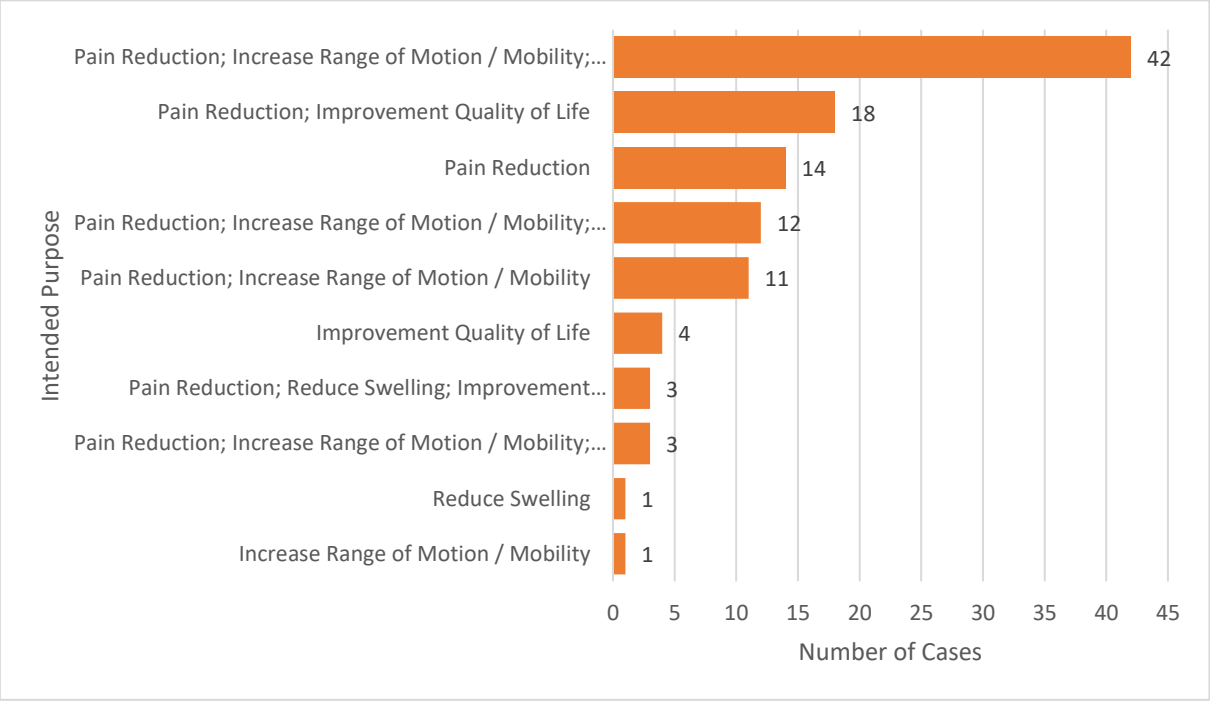
8.7.4. *Main complaint*

Main Complaint	Cases	%
Lower Back/Lumbar	24	22,0%
Knee	10	9,2%
Neck	9	8,3%
Shoulder	9	8,3%
Hip	8	7,3%
Head	7	6,4%
Hand / Fingers	5	4,6%
Foot / Toes	4	3,7%
Lower Leg	4	3,7%
Elbow	4	3,7%
Abdomen	4	3,7%
Chest	3	2,8%
Ankle	3	2,8%
Lower arm	3	2,8%
Face	2	1,8%
Sacrum	2	1,8%
Upper Leg	2	1,8%
Pelvis	2	1,8%
Middle Back/Thorax	2	1,8%
Wrist	1	0,9%
Upper Back/Scapular	1	0,9%
Total general	109	100,0%

8.7.5. Duration of complaint

For how long time?	Cases	%
1 - 6 months	25	23,4%
1 - 5 years	23	21,5%
Few days to 1 month	19	17,8%
6 months to 1 year	13	12,1%
Just happened	10	9,3%
5 - 10 years	10	9,3%
10 - 15 years	4	3,7%
15 - 20 years	3	2,8%
Total general	107	100,0%
(Missing data)	2	

8.8. Intended purpose



Intended Purpose	Cases	%
Pain Reduction; Increase Range of Motion / Mobility; Improvement Quality of Life	42	38,5%
Pain Reduction; Improvement Quality of Life	18	16,5%
Pain Reduction	14	12,8%
Pain Reduction; Increase Range of Motion / Mobility; Reduce Swelling; Improvement Quality of Life	12	11,0%
Pain Reduction; Increase Range of Motion / Mobility	11	10,1%
Improvement Quality of Life	4	3,7%
Pain Reduction; Reduce Swelling; Improvement Quality of Life	3	2,8%
Pain Reduction; Increase Range of Motion / Mobility; Reduce Swelling	3	2,8%
Reduce Swelling	1	0,9%
Increase Range of Motion / Mobility	1	0,9%
Total general	109	100,0%

8.8.1. ***Body part treated***: link here

Body parts treated with ANF Devices are different among cases.

8.8.2. Side of the body

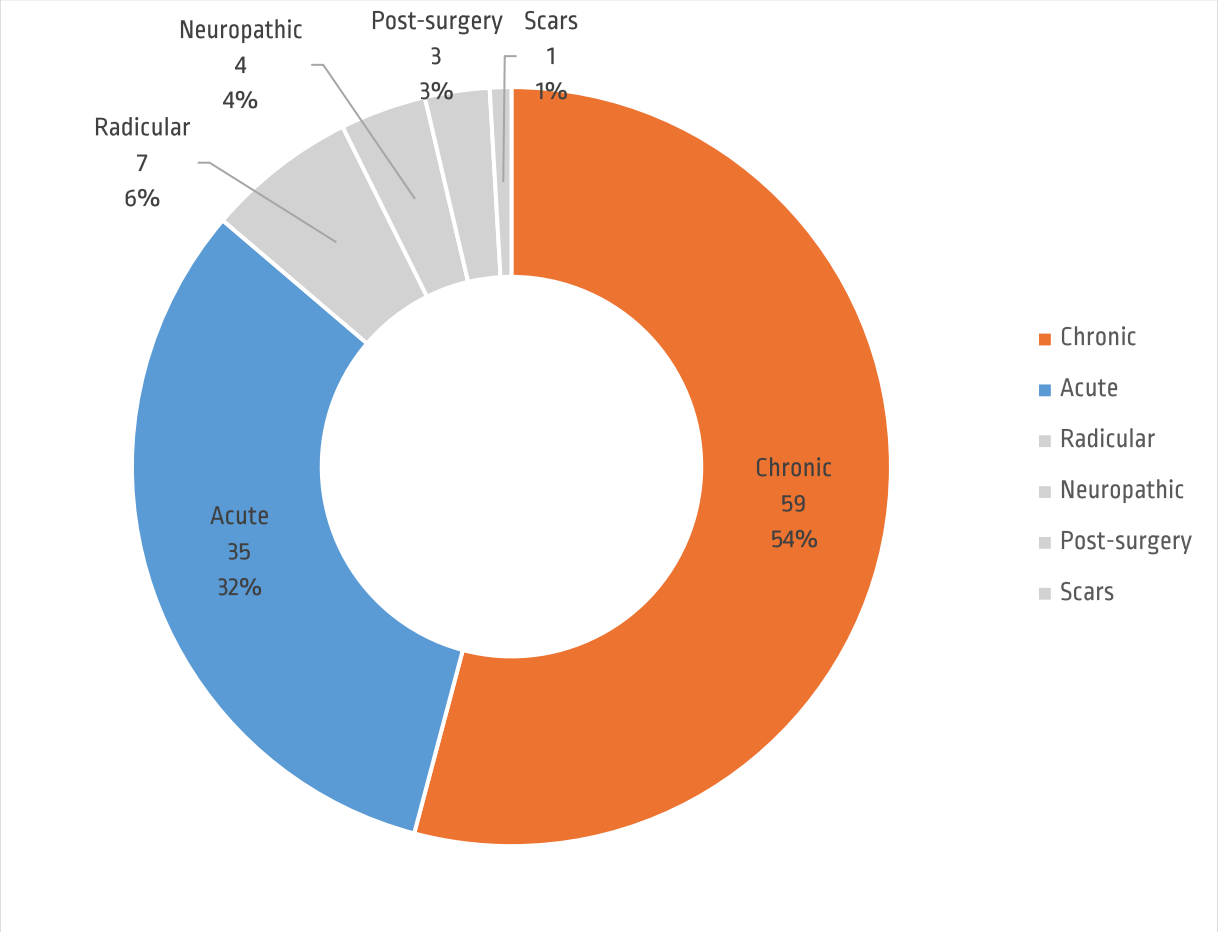
Side of the body	Cases	%
Right	34	31,19%
Bilateral	33	30,28%
Left	27	24,77%
Center	15	13,76%
Total general	109	100,00%

8.8.3. *Case issue*

Case issues are different among subjects. Link here

8.8.4. *Type of issue*

54% of the cases were chronic issues, and 32% acute issues.



8.8.5. *Pain before*

Pain before	Cases	%
100	6	5,5%
99	1	0,9%
90	10	9,2%
89	1	0,9%
87	1	0,9%
85	5	4,6%
81	3	2,8%
80	22	20,2%
79	1	0,9%

78	2	1,8%
75	4	3,7%
71	3	2,8%
70	13	11,9%
68	1	0,9%
65	2	1,8%
60	11	10,1%
50	11	10,1%
45	1	0,9%
40	3	2,8%
30	2	1,8%
25	1	0,9%
20	2	1,8%
0	3	2,8%
Total general	109	100,0%

8.9. CIP compliance:

The study has followed the Clinical Investigation Plan March 2021, version 1.

8.10. Analysis

8.10.1. Clinical performance, effectiveness, and safety analysis

8.10.2. Clinical performance - Pain reduction

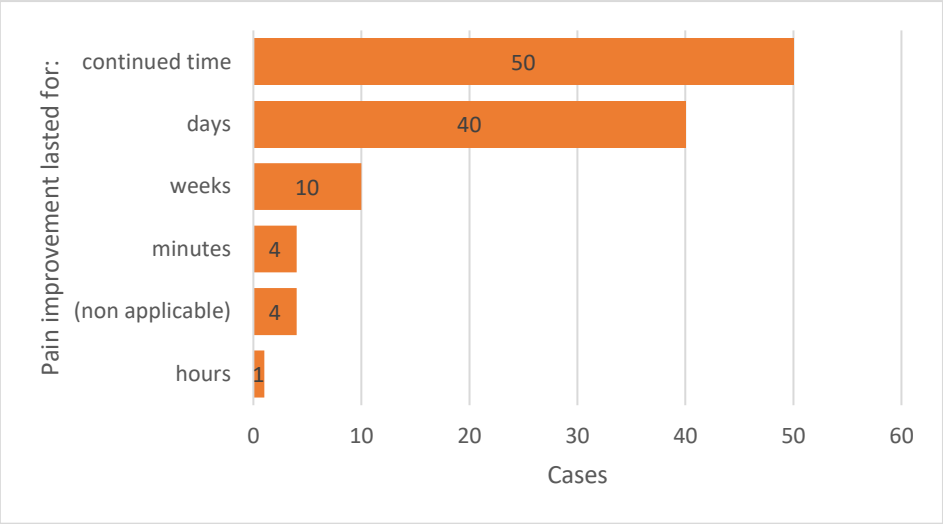
ANF Devices can help decrease pain. The effects and improvement can be long-lasting and considerably high. The pain level can decrease an average of 76% (85% if the treatment consists of more than 1 visit). In 50% of the cases the pain improvement can last for days.

- Pain sensation improvement after 5-60 minutes after applying ANF Devices:

Pain Sensation Improvement	
Media / Mean	-75,96330275
Error típico / Standard error	2,180790888
Mediana / Median	-80
Moda / Mode	-90
Desviación estándar / Standard deviation	22,7681253

Varianza de la muestra / Variance	518,3875297
Curtosis / Kurtosis	2,316122586
Coeficiente de asimetría	1,440390447
Rango / Range	100
Mínimo / Minimum	-100
Máximo / Maximum	0
Suma / Sum	-8280
Cases	109

- Improvement duration:



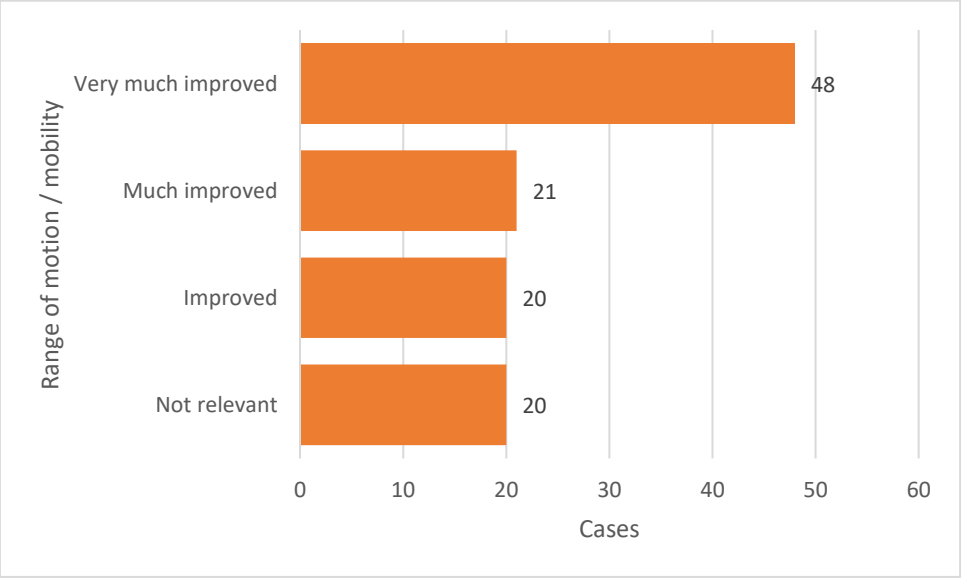
Pain improvement lasted for	Cases	%
continued time	50	45,87%
days	40	36,70%
weeks	10	9,17%
minutes	4	3,67%
(non applicable)	4	3,67%
hours	1	0,92%
Total general	109	100,00%

- Total pain reduction after all visits:

Total pain reduction	
Media / Mean	-85,3027523
Error típico / Standard error	2,02123053
Mediana / Median	-92
Moda / Mode	-100
Desviación estándar / Standard deviation	21,1022662
Varianza de la muestra / Variance	445,305641
Curtosis / Kurtosis	6,27837672
Coeficiente de asimetría	2,35854139
Rango / Range	100
Mínimo / Minimum	-100
Máximo / Maximum	0
Suma / Sum	-9298
Cases	109

8.10.3. Clinical performance - ROM improvement

ANF Devices can help improve the range of motion/mobility. The effects and improvement can be long-lasting and considerably high.



Improvement in ROM/Mobility	Cases	%
Very much improved	48	44,037%
Much improved	21	19,266%
Improved	20	18,349%
Not relevant	20	18,349%
Total general	109	100,000%

- Duration of ROM improvement:

ROM/Mobility improvement lasted for	Cases	%
continued time	54	49,54%
days	24	22,02%
(non applicable)	22	20,18%
weeks	8	7,34%
minutes	1	0,92%
Total general	109	100,00%

8.10.4. Clinical performance - Swelling improvement

ANF Devices can help reduce swelling. The effects and improvement can be long-lasting and considerably high.

Improvement in Swelling	Cases	%
Not relevant	76	69,72%
Very much improved	13	11,93%
Much improved	11	10,09%
Improved	8	7,34%
No change	1	0,92%
Total general	109	100,00%

- Duration of Swelling improvement:

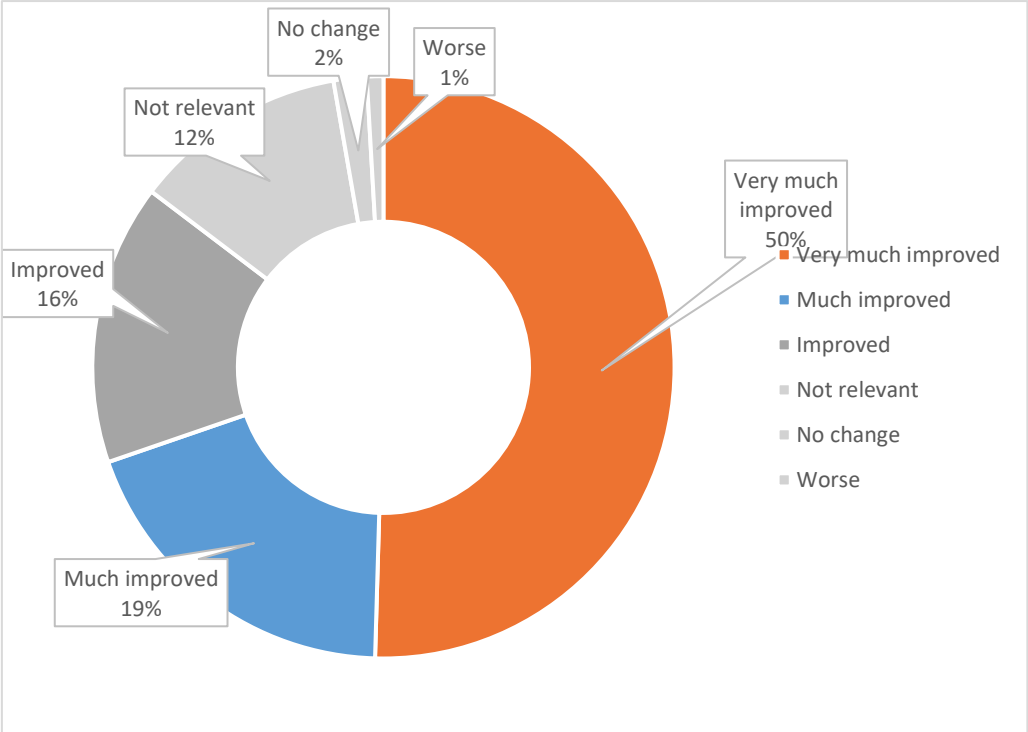
Swelling improvement lasted for	Cases	%
(non applicable)	77	70,64%
continued time	16	14,68%
days	14	12,84%
weeks	1	0,92%
hours	1	0,92%
Total general	109	100,00%

8.10.5. Clinical performance - Daily activity improvement

ANF Devices can help improve health related quality of life. The effects and improvement can be long-lasting and considerably high.

Pain improvement during daily activities	Cases	%
Very much improved	46	42,20%
Much improved	34	31,19%
Improved	27	24,77%
Same	2	1,83%
Total general	109	100,00%

- Improvement in Health-Related Quality of Life.



Improvement in Quality of Life	Cases	%
Very much improved	55	50,46%
Much improved	21	19,27%
Improved	17	15,60%
Not relevant	13	11,93%
No change	2	1,83%
Worse	1	0,92%
Total general	109	100,00%

- Duration on Improvement in Quality of Life:

Quality of Life improvement lasted for	Cases	%
continued time	57	52,29%
days	23	21,10%

(non applicable)	17	15,60%
weeks	9	8,26%
hours	2	1,83%
minutes	1	0,92%
Total general	109	100,00%

8.10.6. Clinical performance - Any unexpected benefit?

Any unexpected benefit?	Cases	%
no	71	65,14%
yes	38	34,86%
Total general	109	100,00%

- Specify unexpected benefit:

Unexpected benefits were different among subjects and cases. Link here

ANF Devices can help:

- improve sleep, vision, energy levels, sore throat, intestinal function.
- reduce medication, stomach pain, anxiety feeling.
- gain strength after stroke, stability.
- return to work, play sports.
- feeling with better mood, happier, relaxed.
- feeling safer to walk, run, jump.

8.10.7. Clinical performance – Efficacy

Results based on Intended purpose:

- Intended purpose – Pain reduction:

In 100% of the cases where the intended purpose was “Pain reduction”, the patient experienced pain reduction (103 cases).

Pain improvement during daily activities	Cases	%
Very much improved	43	41,75%
Much improved	34	33,01%
Improved	26	25,24%
Total general	103	100,00%

- Intended purpose – Swelling reduction:

In 84.21% of the cases where the intended purpose was "Swelling reduction", the patient experienced swelling reduction (of a total of 19 cases).

Improvement in Swelling	Cases	%
Very much improved	8	42,11%
Much improved	6	31,58%
Not relevant	3	15,79%
Improved	2	10,53%
Total general	19	100,00%

- Intended purpose – ROM improvement:

In 97.1% of the cases where the intended purpose was "ROM/mobility improvement", the patient experienced ROM improvement (of a total of 69 cases).

Improvement in ROM/Mobility	Cases	%
Very much improved	37	53,62%
Much improved	20	28,99%
Improved	10	14,49%
Not relevant	2	2,90%
Total general	69	100,00%

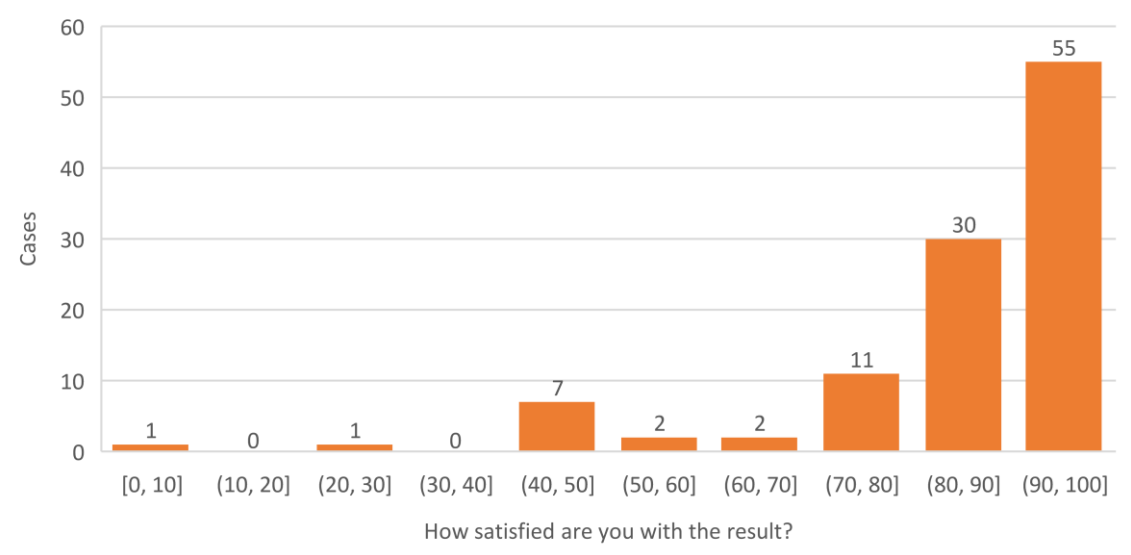
- Intended purpose – Quality of Life improvement:

In 96.19% of the cases where the intended purpose was "Quality of Life improvement", the patient experienced QoL improvement (of a total of 79 cases).

Improvement in Quality of Life	Cases	%
Very much improved	49	62,03%
Much improved	18	22,78%
Improved	9	11,39%
Worse	1	1,27%
Not relevant	1	1,27%
No change	1	1,27%
Total general	79	100,00%

8.10.8. Clinical performance - ANF Therapists satisfaction

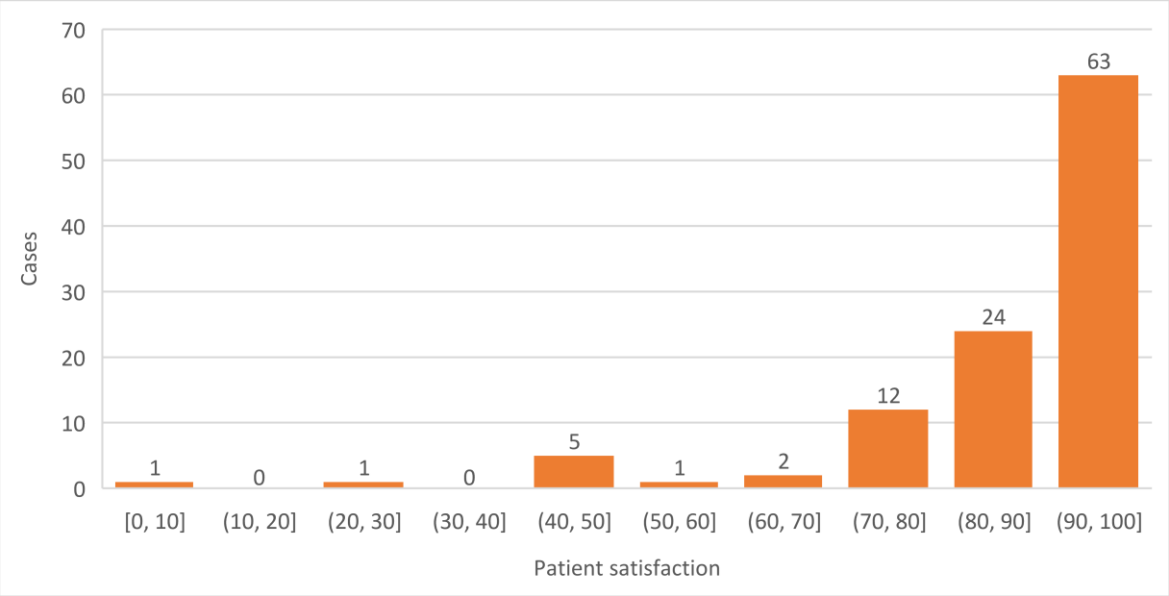
ANF Therapists that use ANF Devices to help their patients are very satisfied with the effects of the device.



Therapist satisfaction	
Media / Mean	88,5412844
Error típico / Standard error	1,63831814
Mediana / Median	92
Moda / Mode	100
Desviación estándar / Standard deviation	17,1045435
Varianza de la muestra / Variance	292,565409
Curtosis / Kurtosis	7,34777161
Coeficiente de asimetría	-2,44210263
Rango / Range	100
Mínimo / Minimum	0
Máximo / Maximum	100
Suma / Sum	9651
Cases	109

8.10.9. Clinical performance - Patient satisfaction

Patients that use ANF Devices are very satisfied with the effects of the combination of ANF Devices.



Patient satisfaction	
Media / Mean	90,6944444
Error típico / Standard error	1,54909605
Mediana / Median	100
Moda / Mode	100
Desviación estándar / Standard deviation	16,0986784
Varianza de la muestra / Variance	259,167445
Curtosis / Kurtosis	10,8815263
Coeficiente de asimetría	-2,91251747
Rango / Range	100
Mínimo / Minimum	0
Máximo / Maximum	100
Suma / Sum	9795
Cases	108

8.10.10. Clinical Safety – Detox symptoms

In 27.52% of cases the application of ANF Devices can lead to detox symptoms. Detox usually occurs once, with a mild intensity and lasts for less than 24 hours.

In 0.92% of cases, the intensity of the detox symptoms was strong. The longer duration of detox symptoms (days) occurred in 5.5% of cases. The higher frequency of detox symptoms (every time the Devices are applied) occurred in 4.59% of cases.

Detox incident rate in cases where the patient suffers other health issues was higher, with 29,31% of cases.

The detox incident rate in cases where there was a high number of Devices applied per session (more than 10 Devices) was higher, with a 33.3% of cases experiencing detox symptoms.

Any detox symptoms?	Cases	%
NONE	79	72,48%
Headache	3	2,75%
Fatigue	3	2,75%
Itching	3	2,75%
Dry mouth; General discomfort	2	1,83%
Headache; Dry mouth; Fatigue	2	1,83%
Headache; General discomfort; Hives	1	0,92%
Dry mouth	1	0,92%
Fatigue; General discomfort	1	0,92%
Headache; Dry mouth; Light flu symptoms; Fatigue	1	0,92%
General discomfort	1	0,92%
Headache; Dry mouth; Light flu symptoms; Fatigue; Nausea	1	0,92%
Headache; Fatigue	1	0,92%
Hives; Itching	1	0,92%
Headache; Shivers	1	0,92%
Light flu symptoms	1	0,92%
Dry mouth; Fatigue; General discomfort	1	0,92%
Headache; Dry mouth; Fatigue; General discomfort	1	0,92%
Nausea	1	0,92%
Headache; Dry mouth; Fatigue; Nausea	1	0,92%
Shivers	1	0,92%
Headache; Dry mouth; Itching	1	0,92%
Headache; Dry mouth; Light flu symptoms	1	0,92%
Total general	109	100,00%

- Detox intensity:

Detox intensity	Cases	%
NONE	80	73,39%
Mild (little bit)	21	19,27%
Medium (moderate)	7	6,42%
Strong (a lot)	1	0,92%
Total general	109	100,00%

- Detox duration

Detox duration	Cases	%
NONE	80	73,39%
hours	18	16,51%
days	6	5,50%
minutes	5	4,59%
Total general	109	100,00%

- Detox frequency:

Detox frequency	Cases	%
NONE	80	73,39%
only once	17	15,60%
not very often	7	6,42%
every time the discs are applied	5	4,59%
Total general	109	100,00%

8.10.11. Clinical Safety – Risk of use incidents

In 0.92% of cases, the application of ANF Devices can lead to skin incision. This incident does not occur frequently and lasts for less than a week.

Risk of use incidents	Cases	%
No incidents	108	99,08%
Skin incision (cut from edge of disc)	1	0,92%
Total general	109	100,00%

- Incident duration:

Incident duration	Cases	%
no	108	99,08%
days	1	0,92%
Total general	109	100,00%

- Incident frequency:

Incident frequency	Cases	%
None	108	99,08%
only once	1	0,92%
Total general	109	100,00%

8.10.12. Clinical Safety – Other unexpected negative incidents

In 3% of cases, the application of ANF Devices can lead to other unexpected negative incidents, such as pain, and eye itchiness.

Other unexpected negative incidents?	Cases	%
no	106	97,25%
yes	3	2,75%
Total general	109	100,00%

- Specify:

Case	If yes, please specify:
1	Patient was not hydrated correctly. Effect of the discs lasted for 1 day then was advised to drink more then pain and tension relief came back the second day
2	Patient got fist relief, decreased pain then detox appeared: headache for a few hours with pain in heel and calf for 20 mn
3	Skin rash around L ear got worse as well as eyeball extremelly itchy. It took about 12 hours for the itchiness of the L eye to go away. Patient kept the discs 4 days, the 2nd tx was applied at day 6. Itchiness came back straight way. Advised the patient to drink much more

8.10.13. Clinical Safety – Severe adverse reaction, if any

No severe adverse reactions in 119 cases (0% of cases).

8.10.14. Clinical Safety – Summary of adverse events and adverse device effects

8.10.14.1. Detox List:

- Headache
- Fatigue
- Itching
- Dry mouth
- General discomfort
- Hives
- Light flu symptoms
- Nausea
- Shivers

8.10.14.2. Incident List:

- Skin incision (cut from the edge of Device)

8.10.14.3. Detox severity:

- Mild: 21 out of 29 cases.
- Medium: 7 out of 29 cases.
- Strong: 1 out of 29 cases.

8.10.14.4. Incident severity:

- Not measured, and no images of the incident have been taken or added to the case.

8.10.14.5. Treatment needed:

- Water intake.
- Wait until it goes away.

8.10.14.6. Resolution Detox:

- Resolution within minutes: 5 out of 29 cases.
- Resolution within hours: 18 out of 29 cases.
- Resolution within days: 6 out of 29 cases.

8.10.14.7. Resolution incident:

- Resolution within days: 1 out of 1 case.

8.10.14.8. Investigator judgment concerning the causal relationship with the device or procedure:

Detox symptoms: We conclude, on this basis, that these symptoms are related to the normal healing process of injuries and diseases and it is associated with the ANF Devices application. Although, it is still unclear when a patient could experience these symptoms. This could depend on the patient health status, intake of prescribed medication, diet habits, or patients' sensitivity.

8.10.15. Table compiling all observed device deficiencies that could have led to a serious adverse device effect, and corrective actions taken during the clinical investigation, if any.

- There has not been reported any serious adverse device effect in this investigation.
- No corrective action was needed in this investigation.

8.10.16. Subgroup analysis for special populations (gender, cultural subgroups)

8.10.16.1. Gender

- Female: 31,75 % of women experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	43	68,25%
Itching	3	4,76%
Dry mouth; General discomfort	2	3,17%
Fatigue	2	3,17%
Dry mouth	1	1,59%
Headache; General discomfort; Hives	1	1,59%
Headache; Dry mouth; Light flu symptoms; Fatigue	1	1,59%
Headache; Dry mouth; Fatigue; Nausea	1	1,59%
Fatigue; General discomfort	1	1,59%
Headache; Dry mouth; Light flu symptoms; Fatigue; Nausea	1	1,59%
General discomfort	1	1,59%
Headache; Shivers	1	1,59%
Headache	1	1,59%

Dry mouth; Fatigue; General discomfort	1	1,59%
Nausea	1	1,59%
Headache; Dry mouth; Fatigue	1	1,59%
Headache; Dry mouth; Fatigue; General discomfort	1	1,59%
Total general	63	100,00%

- Male: 21,74 % of men experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	36	78,26%
Headache	2	4,35%
Headache; Fatigue	1	2,17%
Shivers	1	2,17%
Headache; Dry mouth; Fatigue	1	2,17%
Hives; Itching	1	2,17%
Light flu symptoms	1	2,17%
Headache; Dry mouth; Itching	1	2,17%
Fatigue	1	2,17%
Headache; Dry mouth; Light flu symptoms	1	2,17%
Total general	46	100,00%

8.10.16.2. Group age

- Child, Teenager: 1 subject out of 4 experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	3	75,00%
Fatigue	1	25,00%
Total general	4	100,00%

- Senior and Old adults: 3 subjects out of 24 experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	21	87,50%
Itching	1	4,17%
Dry mouth	1	4,17%
Fatigue	1	4,17%
Total general	24	100,00%

8.10.16.3. General health status

- Detox symptoms in cases where the subject is suffering from other health issues.

Subjects suffering from other health issues; multiple other orthopedic complaints; immune system deficiencies; low-grade inflammation (invisible inflammations) ¸ autoimmune disorders; and/or cancer. 29,31 % of these patients experienced detox symptoms.

Any detox symptoms?	cases	%
NONE	41	70,69%
Headache	2	3,45%
Itching	2	3,45%
Fatigue	2	3,45%

General discomfort	1	1,72%
Headache; Shivers	1	1,72%
Headache; General discomfort; Hives	1	1,72%
Headache; Dry mouth; Itching	1	1,72%
Hives; Itching	1	1,72%
Light flu symptoms	1	1,72%
Headache; Dry mouth; Fatigue; Nausea	1	1,72%
Dry mouth; General discomfort	1	1,72%
Nausea	1	1,72%
Headache; Dry mouth; Light flu symptoms; Fatigue; Nausea	1	1,72%
Headache; Fatigue	1	1,72%
Total general	58	100,00%

- Detox Intensity in cases where the subject is suffering from other health issues.

Detox intensity	Cases	%
NONE	41	70,69%
Mild (little bit)	11	18,97%
Medium (moderate)	5	8,62%
Strong (a lot)	1	1,72%
Total general	58	100,00%

- Detox duration in cases where the subject is suffering from other health issues.

Detox duration	Cases	%
NONE	41	70,69%
hours	11	18,97%
days	3	5,17%
minutes	3	5,17%
Total general	58	100,00%

- Detox frequency in cases where the subject is suffering from other health issues.

Detox frequency	Cases	%
NONE	41	70,69%
only once	11	18,97%
every time the discs are applied	4	6,90%
not very often	2	3,45%
Total general	58	100,00%

- Other negative incidents on cases where the subject is suffering from other health issues:

No incidents were found in subjects with other health issues.

8.11. **Risk evaluation data**

8.11.1. ***Cases where there is a high number of Devices applied per session*** (more than 10 Devices).

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Detox symptoms in cases where there is a high number of Devices applied per session (more than 10 Devices): 33.33% of these patients experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	42	66,67%
Fatigue	3	4,76%
Headache	3	4,76%
Itching	2	3,17%
Fatigue; General discomfort	1	1,59%
General discomfort	1	1,59%
Dry mouth; Fatigue; General discomfort	1	1,59%
Headache; Dry mouth; Light flu symptoms; Fatigue; Nausea	1	1,59%
Headache; Fatigue	1	1,59%
Hives; Itching	1	1,59%
Light flu symptoms	1	1,59%
Dry mouth; General discomfort	1	1,59%
Nausea	1	1,59%
Headache; Dry mouth; Fatigue; General discomfort	1	1,59%

Shivers	1	1,59%
Headache; Dry mouth; Fatigue; Nausea	1	1,59%
Headache; Dry mouth; Light flu symptoms	1	1,59%
Total general	63	100,00%

- Detox intensity in cases where there is a high number of Devices applied per session (more than 10 Devices).

Detox intensity	Cases	%
NONE	42	66,67%
Mild (little bit)	15	23,81%
Medium (moderate)	5	7,94%
Strong (a lot)	1	1,59%
Total general	63	100,00%

- Detox duration in cases where there is a high number of Devices applied per session (more than 10 Devices).

Detox duration	Cases	%
NONE	42	66,67%
hours	12	19,05%
days	5	7,94%
minutes	4	6,35%
Total general	63	100,00%

- Detox frequency in cases where there is a high number of Devices applied per session (more than 10 Devices).

Detox frequency	Cases	%
NONE	42	66,67%
only once	13	20,63%
not very often	5	7,94%
every time the discs are applied	3	4,76%
Total general	63	100,00%

8.11.2. ***Cases where there is a high number of visits*** (more than 5 visits).

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Detox symptoms in cases where there is a high number of visits (more than 5 visits): 36% of these patients experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	9	64,29%
Headache	1	7,14%
Headache; Dry mouth; Fatigue; General discomfort	1	7,14%
Fatigue; General discomfort	1	7,14%
Dry mouth; General discomfort	1	7,14%
General discomfort	1	7,14%
Total general	14	100,00%

- Detox intensity on cases where there is a high number of visits (more than 5 visits).

Detox intensity	Cases	%
NONE	9	64,29%
Mild (little bit)	5	35,71%
Total general	14	100,00%

- Detox duration on cases where there is a high number of visits (more than 5 visits).

Detox duration	Cases	%
NONE	9	64,29%
hours	5	35,71%
Total general	14	100,00%

- Detox frequency on cases where there is a high number of visits (more than 5 visits).

Detox frequency	Cases	%
NONE	9	64,29%
only once	2	14,29%
not very often	2	14,29%
every time the discs are applied	1	7,14%
Total general	14	100,00%

8.11.3. ***Cases where there is a lack of compliance: patient might not be well-hydrated***.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Detox symptoms in cases where the patient might not be well-hydrated: 23.81% of these patients experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	16	76,19%
Headache	2	9,52%
Itching	1	4,76%
Fatigue	1	4,76%
Headache; Fatigue	1	4,76%
Total general	21	100,00%

- Detox intensity in cases where the patient might not be well-hydrated.

Detox intensity	Cases	%
NONE	16	76,19%
Mild (little bit)	3	14,29%
Strong (a lot)	1	4,76%
Medium (moderate)	1	4,76%
Total general	21	100,00%

- Detox duration in cases where the patient might not be well-hydrated.

Detox duration	Cases	%
NONE	16	76,19%
hours	3	14,29%
days	1	4,76%
minutes	1	4,76%
Total general	21	100,00%

- Detox frequency in cases where the patient might not be well-hydrated.

Detox frequency	Cases	%
NONE	16	76,19%
only once	3	14,29%
every time the discs are applied	2	9,52%
Total general	21	100,00%

8.11.4. ***Cases where there is a lack of compliance***: ANF Devices have not been applied on clean skin.

Probability: Medium.

Effects: Harmful.

Type of Risk: Moderate.

- Detox symptoms in cases where the ANF Devices have not been applied on clean skin: 1 out of 5 subjects experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	4	80,00%
Itching	1	20,00%
Total general	5	100,00%

- Detox intensity in cases where the ANF Devices have not been applied on clean skin.

Detox intensity	Cases	%
NONE	4	80,00%
Strong (a lot)	1	20,00%
Total general	5	100,00%

- Detox duration in cases where the ANF Devices have not been applied on clean skin.

Detox duration	Cases	%
NONE	4	80,00%
days	1	20,00%
Total general	5	100,00%

- Detox frequency in cases where the ANF Devices have not been applied on clean skin.

Detox frequency	Cases	%
NONE	4	80,00%
every time the discs are applied	1	20,00%
Total general	5	100,00%

8.11.5. ***Cases where there is a lack of compliance***: Protocol has not been used as intended. There are no cases in this situation.

8.11.6. ***Cases where high frequencies Devices have been applied***.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Detox symptoms in cases where high frequencies Devices have been applied. 36.36% of these patients experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	14	63,64%
Fatigue	2	9,09%
Headache; Dry mouth; Fatigue	1	4,55%

Headache; General discomfort; Hives	1	4,55%
Headache; Shivers	1	4,55%
General discomfort	1	4,55%
Dry mouth; General discomfort	1	4,55%
Headache	1	4,55%
Total general	22	100,00%

- Detox intensity in cases where high frequencies Devices have been applied.

Detox intensity	Cases	%
NONE	14	63,64%
Mild (little bit)	5	22,73%
Medium (moderate)	3	13,64%
Total general	22	100,00%

- Detox duration in cases where high frequencies Devices have been applied.

Detox duration	Cases	%
NONE	14	63,64%
hours	6	27,27%
minutes	2	9,09%
Total general	22	100,00%

- Detox frequency in cases where high frequencies Devices have been applied.

Detox frequency	Cases	%
NONE	14	63,64%
only once	6	27,27%
every time the discs are applied	1	4,55%

not very often	1	4,55%
Total general	22	100,00%

8.11.7. Cases where low frequencies Devices have been applied.

Probability: Low.

Effects: Slightly harmful.

Type of Risk: Trivial.

- Detox symptoms in cases where low frequencies Devices have been applied. None of these patients experienced detox symptoms.

8.11.8. Cases where medium frequencies have been applied.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Detox symptoms in cases where medium frequencies Devices have been applied. 28.95% of these patients experienced detox symptoms.

Any detox symptoms?	Cases	%
NONE	54	71,05%
Itching	3	3,95%
Headache	2	2,63%
Fatigue	1	1,32%
Light flu symptoms	1	1,32%
Headache; Fatigue	1	1,32%
Fatigue; General discomfort	1	1,32%
Shivers	1	1,32%

Headache; Dry mouth; Light flu symptoms	1	1,32%
Headache; Dry mouth; Light flu symptoms; Fatigue	1	1,32%
Headache; Dry mouth; Light flu symptoms; Fatigue; Nausea	1	1,32%
Headache; Dry mouth; Fatigue	1	1,32%
Dry mouth; General discomfort	1	1,32%
Hives; Itching	1	1,32%
Headache; Dry mouth; Fatigue; General discomfort	1	1,32%
Dry mouth; Fatigue; General discomfort	1	1,32%
Nausea	1	1,32%
Headache; Dry mouth; Fatigue; Nausea	1	1,32%
Dry mouth	1	1,32%
Headache; Dry mouth; Itching	1	1,32%
Total general	76	100,00%

- Detox intensity in cases where medium frequencies have been applied.

Detox intensity	Cases	%
NONE	55	72,37%
Mild (little bit)	16	21,05%
Medium (moderate)	4	5,26%
Strong (a lot)	1	1,32%
Total general	76	100,00%

- Detox duration in cases where medium frequencies have been applied.

Detox duration	Cases	%
NONE	55	72,37%

hours	12	15,79%
days	6	7,89%
minutes	3	3,95%
Total general	76	100,00%

- Detox frequency in cases where medium frequencies have been applied.

Detox frequency	Cases	%
NONE	55	72,37%
only once	11	14,47%
not very often	6	7,89%
every time the discs are applied	4	5,26%
Total general	76	100,00%

8.12. **Other benefits**

8.12.1. Improvement in pain sensation in cases where the main complaint is Low back pain.

A combination of ANF Devices can help patients with low back pain experience a reduction of pain of 81.08% immediately after applying the ANF protocol.

Pain Sensation Improvement	
Media / Mean	-81,0833333
Error típico / Standard error	2,98845403
Mediana / Median	-82,5
Moda / Mode	-90
Desviación estándar / Standard deviation	14,64037499
Varianza de la muestra / Variance	214,3405797

Curtosis / Kurtosis	1,932744298
Coeficiente de asimetría	1,319806466
Rango / Range	60
Mínimo / Minimum	-100
Máximo / Maximum	-40
Suma / Sum	-1946
Cases	24

- Improvement during daily activities in cases where the main complaint is Low back pain.

In 100% of the cases where the main complaint was low back pain, the patient experienced pain improvement during daily activities. The effects were considerably high in 96% of cases.

Pain improvement during daily activities	Cases	%
Much improved	12	50,00%
Very much improved	11	45,83%
Improved	1	4,17%
Total general	24	100,00%

8.12.2. Improvement in pain sensation in cases where the main issue is Acute.

A combination of ANF Devices can help patients with acute injury experience a reduction of pain of 74.68% immediately after applying the ANF protocol.

Pain Sensation Improvement	
Media / Mean	-74,6857143
Error típico / Standard error	4,52941301

Mediana / Median	-80
Moda / Mode	-100
Desviación estándar / Standard deviation	26,7963687
Varianza de la muestra / Variance	718,045378
Curtosis / Kurtosis	1,96899207
Coeficiente de asimetría	1,49197775
Rango / Range	100
Mínimo / Minimum	-100
Máximo / Maximum	0
Suma / Sum	-2614
Cases	35

- Improvement during daily activities in cases where the main issue is Acute pain.

In 97.14% of the cases where the main issue was acute pain, the patient experienced pain improvement during daily activities. The effects were considerably high in 77.15% of the cases.

Pain improvement during daily activities	Cases	%
Very much improved	15	42,86%
Much improved	12	34,29%
Improved	7	20,00%
Same	1	2,86%
Total general	35	100,00%

8.12.3. Improvement in pain sensation in cases where the main issue is Chronic.

A combination of ANF Devices can help patients with chronic injury experience a reduction of pain of 78.58% immediately after applying the ANF protocol.

Improvement in Pain Sensation	
Media / Mean	-78,5762712
Error típico / Standard error	2,26724232
Mediana / Median	-80
Moda / Mode	-60
Desviación estándar / Standard deviation	17,4150187
Varianza de la muestra / Variance	303,282876
Curtosis / Kurtosis	-0,31372824
Coeficiente de asimetría	0,683331
Rango / Range	70
Mínimo / Minimum	-100
Máximo / Maximum	-30
Suma / Sum	-4636
Cases	59

- Improvement during daily activities in cases where the main issue is Chronic pain.

In 100% of the cases where the main issue was chronic pain, the patient experienced pain improvement during daily activities. The effects were considerably high in 73% of the cases.

Pain improvement during daily activities	Cases	%
Very much improved	27	45,76%
Improved	16	27,12%
Much improved	16	27,12%
Total general	59	100,00%

8.12.4. Improvement in pain sensation in cases where the main problem is the nerve.

A combination of ANF Devices can help patients with nerve problems experience a reduction of pain of 62.14% immediately after applying the ANF protocol. The effects can be long-lasting.

Pain Sensation Improvement	
Media / Mean	-62,1428571
Error típico / Standard error	13,44553134
Mediana / Median	-75
Moda / Mode	-100
Desviación estándar / Standard deviation	35,57353216
Varianza de la muestra / Variance	1265,47619
Curtosis / Kurtosis	-1,63006472
Coeficiente de asimetría	0,360257062
Rango / Range	90
Mínimo / Minimum	-100
Máximo / Maximum	-10
Suma / Sum	-435
Cases	7

- Improvement during daily activities in cases where the main problem is Nerve pain.

In 100% of the cases where the main problem was the nerve, the patient experienced pain reduction during daily activities. The effects were considerably high in 86% of the cases.

Pain improvement during daily activities	Cases	%
Very much improved	6	85,71%
Improved	1	14,29%
Total general	7	100,00%

- Improvement duration in cases where the main problem is Nerve pain.

Pain improvement lasted for	Cases	%
continued time	6	85,71%
minutes	1	14,29%
Total general	7	100,00%

- Total pain reduction after all visits on cases where the main problem is Nerve pain.

Pain Sensation Improvement	*Columna2*
Media / Mean	-87,1428571
Error típico / Standard error	11,27878027
Mediana / Median	-100
Moda / Mode	-100
Desviación estándar / Standard deviation	29,84084768
Varianza de la muestra / Variance	890,4761905
Curtosis / Kurtosis	6,641282279
Coeficiente de asimetría	2,564406514
Rango / Range	80
Mínimo / Minimum	-100
Máximo / Maximum	-20
Suma / Sum	-610
Cases	7

8.12.5. Intended purpose – cases where the main complaint is chronic.

- Range of motion improvement in cases where the main complaint is chronic, and the intended purpose is a range of motion improvement.

In chronic cases where the intended purpose was a range of motion/mobility improvement, 97.14% of the patients experienced improvement, and in 71.43% of the cases the effects were considerably high.

Improvement in ROM/Mobility	Cases	%
Very much improved	14	40,00%
Much improved	11	31,43%
Improved	9	25,71%
Not relevant	1	2,86%
Total general	35	100,00%

- Quality of Life improvement in cases where the main complaint is chronic, and the intended purpose is Quality of Life improvement.

In chronic cases where the intended purpose was Quality of Life improvement, 92.5% of the patients experienced improvement, and in 85% of the cases, the effects were considerably high.

Improvement in Quality of Life	Cases	%
Very much improved	23	57,50%
Much improved	11	27,50%
Improved	3	7,50%
Worse	1	2,50%
Not relevant	1	2,50%
No change	1	2,50%
Total general	40	100,00%

8.13. Listing of deaths and reasons for death, if any

No deaths have been reported in this investigation.

9. DISCUSSION AND OVERALL CONCLUSIONS

9.1. Clinical performance, effectiveness, and safety results

9.1.1. Clinical performance

- A combination of ANF Devices designed by an ANF therapist alleviates pain.
- A combination of ANF Devices designed by an ANF therapist helps alleviate pain during daily activities.
- A combination of ANF Devices designed by an ANF therapist helps alleviate the swelling.
- A combination of ANF Devices designed by an ANF therapist helps improve the range of motion.
- A combination of ANF Devices designed by an ANF therapist helps improve the quality of life related to health.
- Benefits of applying ANF Devices are durable.
- Benefits of applying ANF Devices are multiple: pain reduction, swelling decrease, ROM improvement, and health-related quality of life improvement.
- Benefits of applying ANF Devices are significantly relevant.
- Patients are satisfied after the application of ANF Devices.
- Therapists are satisfied with the results of applying ANF Devices.

9.1.2. Clinical effectiveness

- In 100% of the cases where the intended purpose was “Pain reduction”, the patient experienced pain reduction (103 cases).
- In 84% of the cases where the intended purpose was “Swelling reduction”, the patient experienced swelling reduction (19 cases).
- In 97% of the cases where the intended purpose was “ROM/mobility improvement”, the patient experienced ROM improvement (69 cases).

- In 96% of the cases where the intended purpose was “Quality of Life improvement”, the patient experienced QoL improvement (79 cases).
- In 100% of the cases where the main complaint was low back pain, the patient experienced pain reduction during daily activities.
- In 100% of the cases where the main problem was the nerve, the patient experienced pain reduction during daily activities.
- In 97% of the cases where the main issue was acute pain, the patient experienced pain reduction during daily activities.
- In 100% of the cases where the main issue was chronic pain, the patient experienced pain reduction during daily activities.

9.1.3. Clinical safety

- A combination of ANF Devices designed by an ANF Therapist is safe to use.
- A combination of ANF Devices designed by an ANF Therapist is safe to use on vulnerable populations.
- A combination of ANF Devices designed by an ANF Therapist is linked to known adverse reactions.
- A higher number of ANF Devices applied corresponds with a higher incident rate of detox symptoms.

9.1.4. Assessment of benefits and risks

Based on the risk evaluation data, the type of risk as a consequence of not using the device as intended is mostly tolerable (slightly harmful effect and medium probability of occurring). Only when the Device is not applied on clean skin (contrary to the Instructions of usage), the type of risk can be moderate (harmful effect and medium probability of occurring). In all cases, the control measure is: ”Inform the user that if the discomfort lasts more than 24 hours, the patch should be removed”.

On this basis, we conclude that the benefit/risk ratio is positive for using ANF Devices for injury and disease alleviation.

9.1.5. Risk evaluation data

- Cases where there is a lack of compliance: Patient might not be well-hydrated.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Cases where there is a lack of compliance: ANF Devices have not been applied on clean skin.

Probability: Medium.

Effects: Harmful.

Type of Risk: Moderate.

- Cases where there is a high number of Devices applied per session (more than 10 Devices):

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Cases where there is a high number of visits (more than 5 visits):

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Cases where high frequencies Devices have been applied.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

- Cases where low frequencies Devices have been applied.

Probability: Low.

Effects: Slightly harmful.

Type of Risk: Trivial.

- Cases where medium frequencies Devices have been applied.

Probability: Medium.

Effects: Slightly harmful.

Type of Risk: Tolerable.

9.1.6. A combination of ANF Devices designed by an ANF therapist provides a positive Benefit / Risk ratio.

9.2. Discussion of the clinical relevance and importance of the results

This data reflects what many ANF Therapists have been experiencing during the usage of ANF Therapy® in regard to helping patients with complaints of injury or disease. This practical evidence of beneficial results should be taken into consideration for more studies in the future.

9.3. Specific benefits and special precautions

Required for individual subjects or groups considered to be at risk.

- Low back pain: A combination of ANF Devices designed by an ANF therapist helps alleviate pain in patients suffering from low back pain.
- Acute pain: A combination of ANF Devices designed by an ANF therapist helps alleviate acute pain.
- Chronic pain: A combination of ANF Devices designed by an ANF therapist helps alleviate chronic pain.
- Nerve pain: A combination of ANF Devices designed by an ANF therapist helps alleviate nerve pain.

9.4. Implications for the conduct of future clinical investigation

- Number of subjects.
- Baseline characteristics.
- Vulnerable population: Add Breastfeeding population.
- Follow-up period for each case.
- Incident severity.
- What is done for Detox/Incident resolution.

9.5. Limitations of the clinical investigation

- ANF Therapists might only be uploading successful cases.
- ANF Therapists might not be uploading the complete treatment (all visits where ANF Devices have been applied).
- ANF Therapists might have only access to limited ANF Devices, based on their education level.

9.6. Final conclusion

- The primary finding suggests that the application of ANF Therapy® Devices by ANF Therapists, is both effective in alleviating injuries and diseases and safe for implementation by ANF Therapists worldwide.
- A combination of ANF Therapy® Devices appears to improve injuries by diminishing pain, reducing swelling/edema, improving range of motion, and enhancing the overall health-related quality of life.
- Subsequent research should explore the potential impacts of ANF Therapy® Devices in various medical fields, particularly in the context of more severe pathologies.
- Further investigation is warranted to assess the feasibility of implementing ANF Therapy® Devices in the population of premature infants, babies, toddlers, and pregnant women.

10. ABBREVIATED TERMS AND DEFINITIONS

10.1. Abbreviated terms

10.1.1. **ANF**: Amino Neuro Frequency

10.1.2. **GSPR** = General Safety and Performance Requirements

10.1.3. **ROM**: Range of Motion.

10.1.4. **ADL** = Activities of daily living

10.2. Definitions

10.2.1. **Adverse device effect:** Adverse event related to the use of the investigational medical device.

10.2.2. **Adverse event:** Untoward medical occurrence, unintended disease or injury, untoward clinical sign in subjects related or not to the investigational medical device and whether anticipated or unanticipated.

10.2.3. **Serious adverse event**: An adverse event that led to any of the following:

10.2.3.1. Death: Serious deterioration in the health of the subject: Life-threatening illness or injury, permanent impairment, prolonged hospitalization, medical or surgical intervention.

10.2.3.2. Fetal distress, fetal death, a congenital abnormality, or birth defect (physical or mental impairment).

10.2.4. Risk evaluation - Effects

- Slightly harmful: When it causes minor skin injury (redness and/or itching) or physical discomfort such as headache, dizziness, nausea, or vomiting, which disappear within 24 hours.

- Harmful: When it causes mild skin injury (redness and/or itching) or physical discomforts such as headache, dizziness, nausea, or vomiting, which disappear within 24h.
- Extremely harmful: When it causes serious, temporary, or permanent deterioration of the health of the user or another person, of the health of the user or another person; causes the death of the user or another person; or represents a serious threat to public health.

10.2.5. Risk evaluation - Probability:

- Low probability: Damage will rarely occur (10% or less).
- Medium probability: Damage will occur on some occasions (more than 10% and less than 50%).
- High probability: The damage will occur always or almost always (50% or more).

10.2.6. **Risk evaluation -Type of risk**

		Risk Levels Consecuences		
		Slightly Harmful (SH)	**Harmful (H)**	**Very Harmful (VH)**
Probability	**LOW (L)**	Trivial Risk (T)	Tolerable risk (TO)	Moderate risk (MO)
	MEDIUM (M)	Tolerable Risk (TO)	Moderate risk (MO)	Important risk (I)
	HIGH (H)	Moderate Risk (MO)	Important risk (I)	Intolerable risk (IN)

10.2.7. Risk evaluation – Control measures and execution period

RISK	CONTROL MEASURES AND EXECUTION PERIOD
Trivial (T)	**No specific measures are required**
Tolerable (TO)	**No improvements are required. Ensure that the preventive measures are working properly: inform the user that if the discomfort lasts more than 24 hours, the patch should be removed.**
Moderate (M)	**Efforts should be made to reduce the risk. The implementation time of the measures will be immediate (as soon as it is known)**
Significant (**S**)	Stop using and selling until risks are reduced (immediate deadline)
Intolerable (**IN**)	Stop using and withdraw from the market (immediate deadline)

10.2.8. **Amino Neuro Frequency Device (ANF Device or Device):** Wearable non-transdermal adhesive patch made of a carbonized metal embedded with a specific frequency, a PET layer, and a Skin-friendly 3M adhesive layer used by ANF Therapists and ANF Practitioners for the intended purpose of injury and/or disease alleviation for pain relief, swelling reduction, range of motion improvement, and/or quality of life improvement, within musculoskeletal disorders, nervous system disorders, cardiovascular disorders, lymphatic disorders, and/or digestive disorders.

10.2.9. **High frequency Devices:** Pain & Inflammation (P&I) ANF Device P300 and above.

10.2.10. **Medium frequency Devices:** P&I ANF Device P200 until P280.

10.2.11. **Low Frequency Devices:** P&I ANF Device below P200.

10.2.12. **ANF protocol**: A combination of ANF Devices designed to accomplish the intended purpose of the device.

10.2.13. **Certified ANF Therapist:** Trained healthcare professional to use ANF Therapy® and create ANF protocols with the intended use of injury alleviation. The therapist has successfully passed the ANF Pain Program.

10.2.14. **Certified ANF Practitioner:** Trained healthcare professional to use ANF Therapy® and create ANF protocols with the intended use of injury and disease alleviation. The Practitioner has successfully passed both the ANF Pain and Holistic Program.

10.2.15. **Non-certified ANF Therapist/Student of ANF Therapy®:** Trained healthcare professional to use ANF Therapy® and create ANF protocols with the intended use of injury alleviation. The therapist is under the education of the ANF Pain Program.

10.2.16. **Non-certified ANF Practitioner/Student of ANF Therapy®:** Trained healthcare professional to use ANF Therapy® and create ANF protocols with the intended use of injury and disease alleviation. The Practitioner has successfully passed the ANF Pain Program and is under the education of the ANF Holistic Program.

10.2.17. **ANF Therapy® Method:** Developed by Dr. Mikel H-G Hoff; this method guides the healthcare professional on how to utilize the ANF Devices to approach and alleviate injuries and/or diseases in a holistic manner. Only ANF Therapists can use the ANF Devices on patients after attending an ANF Education designed by ANF Academy. Patented Model U202032252, ES1259974.

10.2.18. **ANF Education Program:** Any educational program delivered by ANF Academy.

10.2.19. **ANF Pain Program:** An educational program where the ANF Therapist learns and is competent about the ANF Therapy® Method

and how to utilize ANF Devices to approach and alleviate injuries and inflammation in a holistic manner.

10.2.20. **ANF Holistic Program:** An educational program where the ANF Practitioner learns and is competent in the ANF Therapy® Method and how to utilize ANF Devices to approach and alleviate injuries, diseases, and inflammation in a holistic manner.

10.2.21. **ANF Pain Case Entry:** Cases uploaded by ANF Therapists and ANF Practitioners through a webform. These cases are done during normal clinical practice using ANF Devices under normal conditions of use following the ANF Therapy® Method.

10.2.22. **ANF Edu Guidelines Compliance** is based on the patient-specific protocol, which considers the number and consecutiveness of visits, the patient´s regular water consumption, proper placement of ANF Devices on clean skin, and the correct execution of the protocol as intended.

10.2.23. **Group Age:** Premature born (fewer than 37 weeks gestational age). Baby (before 1 year of age). Toddler (1 - 3 years old, recently learned to walk). Child (3 - 12 approx. puberty). Teenager (12 approx. - 18 years old). Young Adult (18 - 39 years old). Middle-aged Adult (40 - 59 years old). Senior Adult (60 – 79 years old). Old Adult (above 80 years old).

10.2.24. **Injured body part/Wounds and Injuries:** Damage inflicted on the body as the direct or indirect result of an external force, with or without disruption of structural continuity.

10.2.25. **Pain**: An unpleasant sensation induced by noxious stimuli which are detected by nerve endings of nociceptive neurons.

10.2.26. **Swelling/edema**: Abnormal fluid accumulation in tissues or body cavities. Most cases of edema are present under the skin in subcutaneous tissue.

10.2.27. **Range of motion, articular**: The distance and direction to which a bone joint can be extended. Range of motion is a function of the condition of the joints, muscles, and connective tissues involved.

10.2.28. **Quality of Life:** A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral, and social environment, as well as health and disease.

10.2.29. **Activities of Daily Living**: The performance of the basic activities of self-care, such as dressing, ambulation, or eating.

10.2.30. **Clinical Benefits**: The positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health.

10.2.31. Informed consent:

10.2.31.1. Informed consent to participate in the Post Market Follow Up is not given to the patient since this post-market study is intended to monitor and assess the clinical performance, effectiveness, and safety of the ANF Device when worldwide ANF Therapists are using the medical device in their own will, for both therapist and patient under a regular clinic visit.

10.2.31.2. Informed consent, which confirms that the patient has been informed of ANF Therapy® by the ANF Therapist and is willing to receive the application of ANF Devices, is part of the therapist´s own clinic report system.

10.2.32. **Use error**: User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user.

11. ETHICS

11.1. Communication with the ethics committee:

This Post Market Study has been cleared from Ethics Committee's initial submission. See attached

12. INVESTIGATORS AND ADMINISTRATIVE STRUCTURE OF CLINICAL INVESTIGATION

- **Evaluator:** Irina Heinisuo Berná
- **Qualification:**
    - Bachelor's degree in Physiotherapy. University of Malaga, Spain, 2003.
    - Master's degree in Health Sciences: Innovation and Investigation on Health Care. University of Cádiz, Spain, 2010.
- **Experience with the Device under evaluation** since 2017.

13. SIGNATURE

Irina A. Heinisuo Berná

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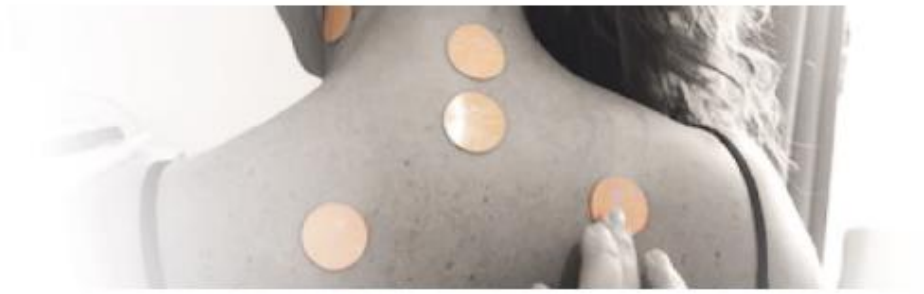
15. ANNEXES TO THE REPORT

15.1. ANF Pain Case Entry



ANF PAIN CASE ENTRY

Join our goal to show the power of ANF to the World

This ANF Pain Case Entry section is made to create a Clinical Evaluation report and analyze the benefit / risk ratio when using ANF Therapy on orthopedic injuries.

The questionnaire includes a range of items: list selection, multiple choice, single choice, yes/no questions, short written answer, upload image/s, bar rating scale, and ANF Discs selection. Most items are mandatory (*).
Carefully read the help text and be precise on your answers.

Symptom assessment tool:

» Pain bar rating scale 0-100. Pain level during palpation, passive movement, or active movement of the main complaint. Zero means "no pain," and 100 means "the worst possible pain."
» Scoring categories (very much improved, much improved, improved, same / no change, worse)
» Duration: (none, minutes, hours, days, weeks, continued).
» Satisfaction bar rating scale 0-100. Zero means "no satisfied," and 100 means "very satisfied".

Pain

» Pain before ANF: bar rating scale 0-100.
» Pain after ANF (5-60 minutes): bar rating scale 0-100.
» Pain improvement during daily activities: Scoring categories.
» Duration of pain improvement.
» Pain after 1 or more ANF applications (end of treatment): bar rating scale 0-100.

ROM / Mobility

» Improvement in ROM / Mobility: Scoring categories.
» Duration of ROM / Mobility improvement.

Swelling

» Improvement in swelling: Scoring categories.
» Duration of swelling improvement.

Quality of life

» Improvement in QoL: Scoring categories

» Duration of QoL improvement.

Any unexpected benefit? Yes, No. If yes, specify.

Therapist satisfaction: bar rating scale 0-100.

Patient satisfaction: bar rating scale 0-100.

You will need some images to upload into the webform for each case that you submit:

Mandatory:

» Protocol of the first visit.

If applicable:

» Protocols of the following visits.

» Images and/or videos before and after ANF.

» Picture/s of skin, in case of unintended skin lesion.

Thank you for contributing to a successful future of ANF Therapy!

ENTER YOUR CASE Here

Enter ONE CASE AT A TIME. You can enter as many as you like

!! IMPORTANT!! Only Pain, ROM, Swelling and / or Quality of life

---

Why this?

Being a MD1 product we are obliged to gather Post Market Evidence and Result/Risk Performance Studies

REWARDING?

YES! Soon you will have efficiency study to show your patients and other practitioners

&

The cases that is uploaded will be evaluated by ANF Academy and those applicable for the studies will be awarded per included case with a disc or Master Class voucher for:

€3 per case (including protocol)

€10 per case (including BEFORE & AFTER pictures)

As soon as the Case is evaluated, you will be notified and once a month you can require a voucher (min 30€) to be made available for your next order

16. LIST OF TABLES

Table 1:

Table 2:

Combination of Discs
P150;VC1;LUX1;VK1;ACA;P300;HD2;HXH;P130;MCT;LUX2;BF2;HD4;P350;P280;NX2;SC6
P411;ACA;P-15;AS;HD4;M2
P200;P-9;P-15;P311;P271;P-17;ACAS;AGLS;MR;MCS
ACA;AGL
MT;ACA;P150;E+6;VC1;VK1;AGL;P300;VD1;P350;P-9;SC1;P400;EDM;HD4;NX3
ACA;AGL;MC;AS;P200;P-9;P130;NX3;HD2;BF2
P200;P-9;ACA;MC
ACA;AGLS;MCS;P-15;P140;P400;P450
P271;MCS;AGL;P-9;HD2;P130;ACAS;P200
ACA;BF2;NX2;P200;AGL;E+1;E+6;P-9;P130;P271
P-9;SC10;P200;ACAS;AGL;ACA;SC7;NX3;BF3
ACA;E+6
P130;MCT;AGL;P-9;P200;E+6;E-6;ACA;P-1
ACA;NX2;HXH;BF;P300;P311;P240;P-5;CR1;MCS;WXC
P200;P205;P-9;MCS
ACA;P-1;P130;HD2;MC;P200;P217
P200;P-9;MC;AS;AGL;P217
ACA;P200;E+6
P217;P271;P-9;ACA;AGL;NX2;BF2;MCS
ACA;P200;MC
P311;P200;AGL
ACA;P200;P-9;SC4;P311;P350;ACAS;SC6;P-15
P-9;P-1;P200;P130;MCS;AGLS;ACAS;AS
ACA;P580;MC;EDM
PTX6;MF3;VC1;SC7;PH9;VD1;P-17;P580;P300;PH14;PH3;AGL;P590;P460;MCT;P565;HD4;SC10;PH12
ACAS;AGL;M2;MT;VC2;VD2;VK1;VB12;HD3;HD4;HD2;NX3;NX4;CR2;DP2;MC;MCS;PH10;PH17;PH4;P200;P280;P311;P400;P620;P500;P-9;P-17;P-5;P130;WXC3;WXC5;TYGAG;RXC2;SPL2;SPL3;HA2;BF3;BF4;CR4;P580;KY;SK2;P
P-1;P-9;P200;P130;ACAS;AGLS;MCS
ACAS;AGLS;E-10;E+10
P130;P200;P-1;P-9;P411;MCS;ACAS;AGLS
ACAS;HXH;PH4;P-17;P620;MPX;P-15;PH10;AGL;HD2;E+10;P280;M2;TXS;P580
P200;P130;AS;P217;AGL
ACAS;PH17;P590