Industry White Paper:
Non-Invasive Interactive Neurostimulation

physiokey

sanakey

NON-INVASIVE INTERACTIVE NEUROSTIMULATION

An evidenced-based approach to neurostimulation therapy

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Introduction and background

Pain is the most under managed vital sign in a clinical setting[1] [2]. It is estimated one in five Australians lives with chronic pain including adolescents and children. This prevalence rises to one in three people over the age of 65. One in five GP consultations involves a patient with chronic pain and almost five percent report severe, disabling chronic pain. The economic cost of chronic pain in Australia is estimated at $34.3 billion per annum. It is the nation's third most costly health problem, ranking only after cardiovascular disease and musculoskeletal conditions.

The impact on the nation's productivity is significant, with losses estimated at $11.7 billion per annum (34 percent of total pain-related costs). This equates to 36.5 million workdays lost each year. The cost to the health system is approximately $7 billion per annum. It is estimated that half of the economic cost of chronic pain could be saved by providing effective and timely treatment [3].

Chronic pain conditions may have a major effect on the body physiology, functional status, work productivity, treatment costs, and on mental status [4]. Pain stimulates the adrenergic nervous system, increases heart rate, blood pressure, and causes arteriolar constriction [5]. Decreased physical activity due to pain may increase the incidence of pulmonary infections, deep venous thromboembolism, mortality and morbidity. All of this negatively effects the quality of life in chronic pain patients.

NSAIDS are the most commonly used pain relief medications. Opioids are alkaloid analgesics used for the treatment of moderate to severe pain conditions. Long-term regular use of opioids can lead to tolerance, physical dependence, poisoning and in high doses, even death. It is estimated there were approximately 100 deaths in 2009 related to the use of over-the-counter (OTC) opioids, and based on the trend this is likely to have increased in recent years [6]. The most serious health risks include: suppression of breathing; tolerance leading to escalation of dosing; and breaking down in the body at different rates for different people [7].

Concerns arising from the overuse of analgesic medications and opioid addiction have increased the need in non-pharmacological treatment for pain management including the development of devices using modern technology to relieve pain[8].

Non-invasive interactive neurostimulation (NIN) is a relatively new development in transcutaneous electrical nerve stimulation which may offer solutions to many of the application problems experienced with conventional TENS treatment.

Transcutaneous electrical nerve stimulation (TENS) describes a range of battery powered electrical stimulation devices applied directly to intact skin, delivering electrical current to peripheral sensory nerve fibres [9] [10] to elicit physiological responses, most commonly pain relief. The tenet of TENS is found in Wall and Melzack's gate control theory which suggests that large nerve fibre activation can modulate pain sensation conducted in small fibre nerves, by gating or blocking the transmission within central nociceptive pain pathways[11] [12].

Although the use of TENS contributes a component in multidisciplinary treatment programs for acute and chronic pain, especially for its low benefit-risk ratio and limited contraindication profile is considered, studies of TENS have produced limited statistically significant results [13]. This has been compounded by a lack of consistency in approaches to using TENS, both clinically and in research[14] [15].

The mechanism by which TENS suppresses pain is that it stimulates A-beta suppressing fibres and 'overwhelms' the C-pain fibres in the body. The effects are similar to that of continually rubbing a painful spot: after a while, the pain lessens because the area becomes numb. From a holistic perspective though, this is not the best way to manage pain, since the TENS unit relieves pain not through body awareness (which allows the system to self-regulate and correct), but through lack of awareness (which may not allow for self-regulation and correction). This is a possible explanation as to why the effects of TENS treatments are often temporary.

Non-invasive Interactive Neurostimulation (NIN) differs from conventional TENS in both the electrode configuration and the inbuilt circuitry that enables automatic adjustment to changing tissue impedance. Together these result in the delivery of higher density and amplitude of stimulation than is currently available with conventional TENS device specifications and electrode configurations[16] [17] [18].

Interactive Neurostimulation means that the stimulation responds to changes in the electrical property of the skin and tissue. The device waveform automatically adjusts as the impedance of the treatment area varies from one point to another as the device is moved or varies as a result of response to the stimulation. This technical advancement facilitates a number of differences in the application of the device which are aimed at optimising the clinical outcome. Those include, the identification of optimal treatment points and the delivery of a very high amplitude and high density stimulation.

physio**key** and sana**key**[19] represent a dynamic advancement in the technology of electrical stimulation which facilitates unique applications, offering the user a highly flexible treatment tool. The nature of the physio**key** and sana**key**'s interactive neurostimulation allows for a unique evidenced based application that optimises certain treatment parameters and thus achieves consistently good results across a broad range of conditions, both acute and chronic in nature. It is easy to use and completely portable around the clinic, hospital or treatment centre yet enables a scientific method of delivering the optimal treatment for each and every patient. The 3-step protocol of **scan, treat and assess** integrates easily into current treatment practices and produces consistent results for the treatment of many painful conditions, providing not only direct therapeutic effect, but also activates the natural defences of the body[16 20].

physio**key** practitioner device
ARTG ID 230724

sana**key** personal/patient device
ARTG ID 260053

Non-Invasive Interactive Neurostimulation relies on the body's mechanism of adaptation ensuring dynamic equilibrium and homeostasis. Regulation of the body's vital functions is achieved through close connection and interaction of the nervous and endocrine systems.

The effects of these systems result in the release of biologically active chemical modulators, called neuromediators. Examples of these neuromediators:

- amine: acetylcholine, noradrenalin, adrenalin, dopamine, serotonin epinephrine, norepinephrine, histamine
- amino acids: glycine, glutamic, aspartic and gammaaminobutyric acid.
- purine nucleotides: adenosine, cytidine, guanosine, thymidine
- neuropeptides: enkephallin, neuropeptide Y, cholecystokinin, substance P, neurotensin.

During physio**key** and sana**key** therapy it is the neuropeptides that are the most important chemical modulators. Neuropeptide-producing nerve fibres make up more than 70% of the body's neural tracts and can therefore be stimulated from many areas of the skin. The main goal of physio**key** therapy is to induce the secretion of a sufficient amount of neuropeptides to relieve pain and initiate a healing response. This is achieved by active feedback mechanisms, damped, bi-phasic, sinusoidal impulses and individualised treatment [21].

The most unique characteristic of physio**key** and sana**key** is that they can induce changes in the parameters of its impulse automatically and in accordance with the body's response to the device. While conventional physiotherapeutic devices are passive, physio**key** and sana**key** involve active feedback. The devices do this by monitoring the skin's impedance and then changes the electrical impulse it emits accordingly.

The characteristics of the physio**key** and sana**key** impulses are such that the probability of excitation of the thin neuropeptide-secreting neural fibres is higher than conventional methods of electrotherapy [22 23 24].

physio**key** and sana**key** therapy functions on two physiological principles: that the body has its own healing capabilities and that we can promote this ability to heal by stimulation of the areas of the brain responsible for regulation of the autonomic nervous system and homeostasis. physio**key** and sana**key** technology is hypothesised to produce both local effects - by stimulating the skin, muscle and blood vessels - as well as a general influence - by an effect on nervous and endocrine systems.

It is further hypothesised that the pattern of physio**key** and sana**key** impulses stimulate nervous pathways via '**key**points' on the skin in an effort to restore and to improve the regulation of the disease-affected organs and tissues. The physio**key** and sana**key** device function is aimed at stimulating the skin surface with specifically shaped impulses. Constant measurement of electric skin parameters enables an intelligent feedback mechanism via a patented modulation algorithm.

The physio**key** and sana**key** devices are small, hand-held transdermal neurostimulators that contain a cutaneous impedance sensor, delivering non-invasive, computer-modulated electrical stimulation via the patient's skin and involves damped, bi-phasic, sinusoidal impulses with little discomfort to the patient. These impulses stimulate both the A delta fibres, responsible for the quick, shallow first pain, and the C fibres, known to maintain the state of hyper-excitability of the painful area and the spread of the hyperalgesic state to nearby neurons.

It has been shown that an electrical stimulus activates C fibres when an intensity higher than the threshold for A fibres is used. Due to the device's delivery of high amplitude oscillating waveforms in millisecond dosages, small unmyelinated C fibres can be stimulated to a higher degree than with other forms of electrotherapy. Stimulation of 'C' fibres has been shown to activate the right and left anterior insula and the frontal operculum of the brain. The anterior insula are responsible for perception of pain and the maintenance of homeostasis within the body [21].

When sufficiently stimulated, 'C' fibres also trigger local neuro- and regulative-peptide release with resultant pain relief and healing. The physio**key** and sana**key** impulse is carried via afferent nerve fibres to regulatory centres in the brain which in turn responds via efferent nerve fibres. The physio**key** interprets this response and, via computer modulation, results in its next impulse being modified accordingly which further provides information back to the brain to either amplify or dampen the pathological signals initiating pain.

Every physiokey and sanakey treatment is designed to optimise four main aspects of any neurostimulation treatment to ensure better and lasting results. Research has shown that the optimisation of various treatment parameters can significantly increase the effectiveness of neurostimulation across a broad range of painful conditions. Missing any one of these parameters could significantly reduce or even negate any clinical benefit from the treatment [14] [25].

Optimal Treatment Points.

The physiokey and sanakey identify areas of low skin impedance. The low impedance of the skin is caused by an increase in the galvanic or sympathetic skin response [26] [27]. These areas of low skin impedance relate to major nerve branches trigger points, acupuncture points, and localised areas of sympathetic skin response. Research has shown that targeting these points gets a better clinical result.

Melzack et al [28] compared the spatial distribution and associated pain patterns of trigger points and traditional acupuncture points using body maps compiled by several authors and concluded that there was a high degree of correlation (71%) for both criteria. In essence, these are treatment points which will respond best to electrical stimulation; their locations vary and are unique to each patient. Much like manual therapists scan muscles with their hands before deciding where best to apply pressure based upon finding trigger points and adhesions, a physiokey practitioner identifies the most responsive cutaneous nerves based upon relative skin impedance differences.

This scanning methodology ensures patient specific, multiple and varied treatment locations to elicit the most effective pain relief. Melzack showed that treating major nerve branches, trigger points, and secondary areas on the dermatome, in addition to the area of pain, with high amplitude stimulation provided the most effective and sustained pain relief as opposed to lower amplitude treatment delivered only to the point of pain. Scanning for and then targeting areas of low impedance with physiokey and sanakey key as well as points of pain ensures all of these aspects are included in a physiokey and sanakey protocol.

High Amplitude Stimulation.

The physiokey and sanakey deliver safely and comfortably a much higher amplitude signal than would normally cause muscle contraction with a TENS or interferential. This is made possible by the interactive neurostimulation and the fixed electrode head - the practitioner is able to deliver direct stimulation without uncomfortable muscle contraction [29] [30] [31] [32] [33] [34] [35] [36].

Variable Frequency.

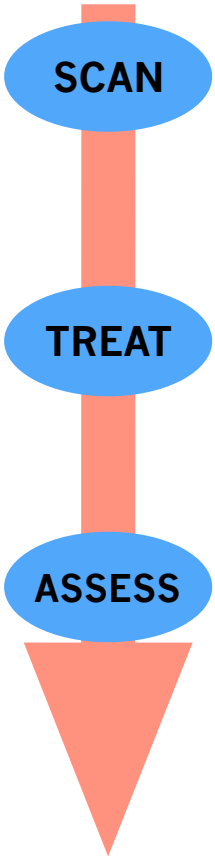
A range of analgesic mechanisms are activated when varying frequencies are used. The physiokey has a frequency range from 5 - 460Hz. All physiokey and sanakey protocols ensure that a broad range of frequencies are delivered in every single treatment [37] [38]

Prevention of Accommodation.

Research has shown that treating too often, treating too long, and treating in fixed frequencies causes the body to stop responding to neurostimulation after a period of time, sometimes as little as four 20-minute treatments [39] [40] . physiokey and sanakey protocols focus on delivering short infrequent treatments to multiple treatment points that change in every treatment, and by using a wide range of frequencies, the physiokey and sanakey ensures patients continue to respond to treatment over the full treatment course.

physiokey and sanakey treatment protocol

Every physiokey and sanakey treatment follows a 3 step protocol



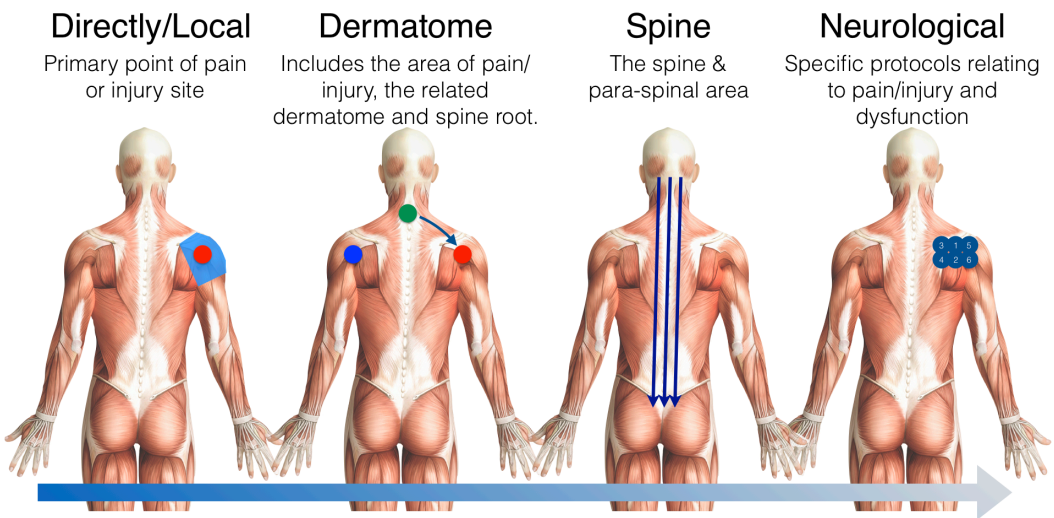
Scan for **Key**points
Keypoints are low skin impedance points/areas on the skin where;

1. the physio**key** and sana**key** electrode drags ('sticks to the skin'),
2. the physio**key** and sana**key** impulse feels stronger,
3. the sound of the physio**key** and sana**key** get quieter,
4. the colour of the skin in the area being treated has a pronounced change.

Treat Keypoints
Use the physio**key** and sana**key** electrode to clear **key**points.

Assess Treatment Outcome

physiokey and sanakey treatment protocols progress from simple to more complex



physiokey and sanakey observed clinical effects

- Pain Relief:
- Autonomic responses from the patient:
  - Sympathetic – in some cases patients may begin to perspire, heart beat and blood pressure increases slightly, and the patients feels warm,
  - Parasympathetic – after 10 to 15 minutes of physiokey therapy, most patients become relaxed, their heartbeat slightly decreases, and their blood pressure normalises;
- Post physiokey therapy– most patients report having prolonged deep sleep 'first time in years';
- Range of motion increases due to muscular relaxation;
- Microcirculation – increased – directly under the physiokey and sanakey electrode one can see erythema after a few minutes of application;
- Feeling of well-being, lightness, relaxed, sleepy, but not tired.

physiokey and sanakey intended use

- Acute and chronic pain
- Increased blood circulation
- Passive muscle stimulation
- Improvement and recovery of function.
- ARTG identifier (Australia) physiokey 230724 and sanakey 2560053

Contraindications

- On-demand-type cardiac pacemaker or other electrically powered implant.
- Electrode placement over malignant tumours.
- Use over open wounds.
- Patients prone to seizures.
- Alcohol intoxication.
- Pregnancy.

sanakey personal / patient device

sanakey two treatment application modes in one device

Bio-Regulation

Bioregulation mode delivers interactive neurostimulation to the body's physiological systems via skin areas in order to provide pain relief and functional restoration.

There are 5 special programs available.

Key-phoresis

Key-Phoresis mode is a modified iontophoretic mechanism to facilitate the absorption of external substances such as creams, lotions and gels.

physiokey practitioner device

physiokey three treatment application modes in one device

Bio-Regulation

Bioregulation mode delivers interactive neurostimulation to the body's physiological systems via skin areas in order to provide pain relief and functional restoration.
There are 11 special programs available.

Diagnostic

Diagnostic mode allows the identification of optimal treatment points and individualised therapy through numerical readings. The readings are used to give information for the optimal location and duration of therapy.

Key-phoresis

Key-Phoresis mode is a modified iontophoretic mechanism to facilitate the absorption of external substances such as creams, lotions and gels.

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