A Brief Overview of Biofeedback Electro-Stimulation Technology (***BEST***™*) based ***Avazzia***™* Devices

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Abstract

Biofeedback Electro-Stimulation Technology **(*BEST*™) is briefly reviewed and an explanation of therapeutic applications and neurophysiology based upon electron loading, i.e., increased cellular capacitance, and stimulation of nonmyelinated C and myelinated A nerve fibers to secrete neuropeptides leading to a cascade of multiple other neuro-active substances such as neurotransmitters, histamine and 5-HT (serotonin) is presented. In addition, neuropeptide synthesis is up-regulated leading to a quantitative increase in endogenous neuropeptide production by C fibers.**

***BEST*™ impulses induce neuropeptides secretion by primarily C nerve fibers, and have profound and wide-ranging effects, triggering complex regulative chains and cascades. Multiple biochemical pathways utilizing many types of neuro-mediators, hormones, and cytokines are involved. Although peptide half-life in body fluids is relatively short, other mediators in the cascades survive for many hours. Some regulatory peptides act on genomic activity to alter gene expression and change biochemical synthesis. *BEST*™ electrical signals can reprogram tissues locked into chronic vegetative and dysfunctional states by inducing bolus synthesis of regulatory peptides (RP).**

***BEST*™ impulses also are relayed through afferent© neural pathways to the CNS and give rise to various 1) segmental spinal reflexes by efferent signals sent from the cord to organs associated with that segment or back to the local tissue receiving the impulse; 2) systemic reactions such as endorphin induction by efferent§ signals descending from the cortical and subcortical areas of the brain i.e. pain reduction.**

***BEST*™ impulses have a direct effect on blood perfusion. Clinically observable and well-defined increases in tissue perfusion at the treated areas are due to neuropeptide-induced vasodilatation, particularly *Substance P*. A combination of *BEST*™-induced axon reflexes also releases other vaso-active substances such as kinins, prostaglandins, cytokines, and nitric oxide. The end result is that blood flow to a treated area is significantly increased. Other neuropeptides and endocrine secretions released by *BEST*™ impulses mediate inflammation. Complement fixation and tissue injuries due to immune aggression are**

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* ***Avazzia*** ™ and ***BEST*** ™ are trademarks of Avazzia Inc., Dallas Texas

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♥ an afferent nerve conducts impulses from peripheral nerve endings to the brain (CNS)

♣ an efferent nerve conducts impulses from the brain (CNS) to peripheral receptors

suppressed, and cellular immunity is enhanced by macrophage proliferation, activation, chemotaxis, and clearance of extracelluar debris.

***BEST*, based upon older electro-stimulation concepts, has redefined existing technology with novel waveforms, improved circuitry, and cleaner signaling. Signaling is focused and intensified for narrow applications or is expanded with unique signaling combinations and frequency ranges for increased therapeutic flexibility. The *Avazzia* unit is the first generation of *BEST*. Compared with the earlier Russian electro-stimulation devices, *Avazzia* generates cleaner and more precisely defined wave forms and possesses both newer (patent pending) settings that expand clinical versatility and vastly improved operational reliability.**

Key Words: Avazzia, BEST, Micro-current, Neuropeptides, Nitric Oxide, Redox Potential, Acupuncture

Introduction and History of Development

Electro-stimulation devices **(ESDs)** were developed in Russia in the mid-seventies by A. Karasev, based at Sochi University, and extensively refined by Professor A.N. Revenko (neurologist) and Ya.Z. Grinberg (electrical engineer) and many physicians and scientists based in Taganrog.[1] They were first to achieve repeatable therapeutic results using electrical signals to stimulate the immune system. **ESD**s were created for use by the Russian military and space programs with the advantages of being inexpensive, lightweight, space saving, and a practical substitute for pharmaceutical therapy. Pharmacy supplies on board space vessels were reduced, saving space and weight. In 1986 the first electro-stimulation device passed technical and clinical trials and was given permission by the USSR Medical Council to be used in hospitals and in homes. **ESD**s are carried by the Russian Military and are used to treat shock and as a substitute for morphine on the battlefield. It is known that Russian **ESD**s were probably developed at a much earlier date than officially stated. Before their release to the world, they remained closely guarded state secrets. After the formal dissolution of the USSR, **ESD** technology was declassified and released to the world for humanitarian relief as a gesture of good will and a furtherance of Perestroika.

The original **ESD** high failure rate (40% within first year) was due to overly complex circuitry, inferior components, and other reliability and signal quality issues. Engineers at *Avazzia Inc.* of Dallas, Texas, have further redefined the **ESD** concept. *Avazzia Inc.* produced the ***BEST*** concept and based its ***BEST*** family of devices upon a superior and redefined concept: simplification by redefining **ESD** waveforms to create unique, focused areas of neurological signaling.

A primary mission for *Avazzia Inc.* was to design and develop ***BEST*** devices for effective muscular rehabilitation and retraining, as an aid for pain relief, alleviation of edema via increased perfusion, lymphatic drainage, and a variety of other inflammatory and degenerative conditions. Some ***BEST*** models are classified by FDA as Exempt Class II Biofeedback devices and require a prescription from a health practitioner.†

BEST therapy utilizes *redefined ESD* concepts as a complementary method of promoting the body's own healing processes through neurological signalling by electronic biofeedback and increasing the electron/ATP content (cellular redox potential) of tissue.

***BEST*: a Cybernetic Therapy**

Cybernetics is defined as: *the science of communication and control processes within systems. Control is based on communication both within the system and with the external environment and influences the actions of the system to bring it into some desired future state or to maintain homeostasis. Cybernetics includes the concepts of auto-regulation and feedback as well as the transmission and self-correction of information, and can be applied not only to machines like*

† Biofeedback-controlled electro-stimulators are regulated by the United States Food and Drug Administration under the provision of the U.S. Code of Federal Regulations, Vol. 21, Section 882.5050, Generic Name: Biofeedback Device, Product Code: HCC, Class II. The FDA has exempted certain Class II devices from the 510(k) pre-market notification requirement in a Notice published in the Federal Register, January 21, 1998, p. 84, including battery-powered biofeedback devices for prescription use in relaxation training and muscle re-education.

CFR 21 Sec. 882.5050 *Biofeedback device (a) Identification. A biofeedback device is an instrument that provides a visual or auditory signal corresponding to the status of one or more of a patient's physiological parameters (e.g., brain alpha wave activity, muscle activity, skin temperature, etc.)so that the patient can control voluntarily these physiological parameters. (b) Classification. Class II (special controls). The device is exempt from pre-market notification procedures in subpart E of part 807 of this chapter when it is a prescription battery-powered device that is indicated for relaxation training and muscle reeducation and prescription use, subject to 882.9.*

computers but also to living organisms, including humans, and to complex organizations and societies. [2]

Cybernetics then, is the theory of automatic control systems. The nervous system and brain can be viewed as an automatic communication and control system utilizing electrochemical impulses as signals. ***BEST*** is also an electrical control system, external to the body, that interfaces directly with the skin and transcutaneously communicates with the internal peripheral nervous system for the purpose of therapeutic intervention. This is possible because of the development of modern high-speed microprocessors, which are able to establish a "cybernetic loop" between electronic instrument and living body. The body's response can be measured with respect to a signal sent out from the instrument to initiate the loop. When a signal is emitted and penetrates deep into the tissue, the impedance of the tissue (analogous to resistance in DC circuits but dynamic in nature) modulates the waveform of the return signal as it transverses back to the instrument. [3] The software inside the instrument may be used to discern and evaluate the signal and modulate the next emitted signal. The degree of modulation is based upon the impedance of the return signal. This sets up a constantly changing interactive bio-loop possessing nonrepeating multiple signals. Eventually the change in impedance signal diminishes in significance until a plateau occurs.

Redox potential is an exceptionally valuable tool for energetic evaluation of cellular metabolism.[4] It is a representation of overall electron activity within cells and tissues. Oxidation is the loss of electrons and/or hydrogen atoms and/or the gain of oxygen by molecules. Reduction is the gain of electrons and/or hydrogen atoms and/or the loss of oxygen. [5] [6] It must be clarified that in nature, free electrons do not actually exist in aqueous solutions. They exist in a homogeneous blend and are oftentimes being transferred from one atom or ion to another. Therefore, in living systems it is negative and positive electrical charges that are actually transferred. [7]

The energy is ultimately stored in phosporalated nucleotide bonds like ATP [8] and ethylene bonds of isoprenoids (vitamins A, D, E, and K), cytochrome, flavinoid, and porphyrin pigments and unsaturated lipids comprising cell membranes.[9] When tissue becomes saturated by electrical micro-currents, cellular redox potential (charge) is maximized and effective cellular-signaling

stimuli are achieved. Impendence increases due to electron saturation. Further signaling past this point is not effective, and the unit automatically signals to cease activity.

Avazzia BEST Neurophysiology

BEST devices generate electrical impulses that are physiologically similar to neurological impulses generated by C nerve fibers embedded in most tissues and consist of 85% of all nerves found in the body and to a much lesser extent on "fast" pain blocking A fibers.[10] C-type fibers are small and nonmyelinated, with a diameter of 1-2 mkm.[11] C fibers are responsible for slow diffuse pain, but more importantly nerve endings secrete neuropeptides capable of blocking pain perception via afferent signaling to the cortical centers in the brain.[12] Stimulation of acupuncture points and/or embedded afferent C fibers transmits impulses via the cord to the dorsal medulla and thalamic areas of the brain, which produce nitric oxide and a host of other neuroactive mediators.[13] Nitric oxide then acts as a neurotransmitter for induction of opioid peptide production, i.e. endorphins.[14] [15] [16]

A class of neuropeptides secreted locally is termed *Regulatory Neuropeptides (RNP).* RNP within C fibers directly increases further peptide synthesis, neurotransmitters, serotonin, histamine, and other peptide hormones production by modifying genomic activity, up-regulating gene expression, and enzyme synthesis.[17]

A-fiber axons are surrounded by a myelin sheath created by Schwann cells. Schwann cells are glial, circumferential support cells of the peripheral nervous system (PNS): These cells generate extensive sheets that wrap the axons repeatedly to form lipid rich myelin. The myelin sheath acts as insulation on a wire and is essential for rapid conduction of impulses along the large nerve axons. Meylinated A fibers are responsible for sharp fast pain.[10]

Although ***BEST*** signals have some neuro-secretory effect on these fibers, the vast majority of effect and response involves C fibers.

Fibroblastic Connective Tissue: A Conduit for Electrons

A *BEST*™ device communicates with the neuro-endocrine system through direct touch of the skin, sending a signal through the epidermis and dermis into underlying fascial planes and is transmitted through connective tissue to the C and A nerve fibers.

Connective tissues are comprised of mostly *collagen* with some *elastin.* Because of its unique triple helix structure and macro-porous nature, water binds to collagen fibers.[18] The bound layer of water is structured by hydrogen bonding and electrostatic properties of the triple helix and forms a continuum throughout the entire body--a *collagen liquid crystal continuum (CLCC)*. Layers of structured water bound onto collagen fibers provide proton conduction pathways for rapid intercommunication throughout the body. Electro-magnetic energy flows and flux in connective tissues along lines of collagen and flowing along molecules of structured water. The entire fibro-collagen matrix contained in somatic and visceral tissues function as a coherent whole: that is, a continuum.[19] Fibrous collagenous tissue therefore displays the greatest conductivity and least impedance (resistance) to current of all the tissues in the body.[20]

Ligaments, tendons, and outer capsules of organs and muscles (aponeurosis) are easily apparent. The sheath of areolar tissue invests the entire muscle termed the *epimysium*.[21] Muscles encapsulated by epimysium are anatomically grouped based on function, with each muscle forming separate functions of extension or flexion, yet forming spaces or *fascial tissue planes* between muscle layers. Fascial planes can be viewed as a continuum of interstitial space between muscles, bounded and defined by the epimysiun of muscles. If one studies acupuncture points and meridians, one will observe a correspondence to the fascial muscle planes.[22] Points on the skin are very closely aligned with superficial and corresponding subdermal (deep) fascia, especially where multiple fascial planes intersect within the body.

Acupuncture points on the skin are the interface for the CLCC. It has been shown that acupuncture points have much lower electrical impedance (lower resistance and higher conductivity to the flow of electrons) than surrounding skin and are in effect, sumps that will draw electrons (and interestingly enough also photons [23]). Electrons flow along fascial planes

comprising of CCLC, which define *acupuncture meridians*.[21 24] Fibrous capsules and sheaths of nerves, ligaments, tendon, bone (periostium), even fibro-elastic tissue embedded in blood vessels all network in an integrated reticulum to carry electrons throughout the body. Internal organs are encapsulated in the thorax and abdomen with pleural and peritoneal layers, as well as possessing a stromal skeleton, and these also facilitate electron flow. Robert O. Becker defined a perinueral system consisting of epi/peri-neurium and Schwann cells of the peripheral nervous system, and glial, ependymal cells of the central nervous system. Activity is independent of neuronal tracts and propagates a unique electrical current. The perineural system functions as both a support/protective structure and a separate signaling and electron-carrying conduit. [25 26]

BEST devices actually seek decreased impedance on skin by sticking (dramatic increase in friction) to acupuncture or electron deficient sump points when gliding the instrument over the skin. The area may comprise injured or diseased tissue or may be associated with an organ or corresponding structure with that anatomical segment. Electrons supplied by a ***BEST*** unit placed at the correct location on the skin are channeled by the integrated system of connective tissue within the body to the lowest electron deficiency. The normal energetic equilibrium between various tissues and organs is restored, and the redox potential of the body is recharged.

Restoration of Dysfunctional Cells

Changed electrical properties of diseased or dysfunctional tissue with respect to healthy tissue are attributed to increased cellular water retention, increased Na^+ (sodium) content, and altered membrane permeability, changes in tissue density, and orientation of cells. [3 27 28 29] The conductivity is a measure of the mobility of ions in the extra cellular fluid in the presence of an electric field. A tissue's aqueous composition (ratio of extra cellular to intracellular volume) determines travel of current; therefore, electrical conductivity is tissue-specific.[3] Tissues normally vary in aqueous content; moreover, cells that are damaged (i.e. display pathology) retain water, possess increased impedance, and therefore lose electrons.[30] By definition,

increased impedance also means decreased membrane capacitance; that is, decreased ability to store electrons as an energy reserve for ATP synthesis in mitochondria.

Lack of energy causes disruption in the osmotic gradient and electrolyte balances normally maintained by the cell, leading to an influx of sodium ions to the interior of the cell, and water follows the sodium. Reiterating the loss of electrons in cellular membranes due to increased impedance and decreased capacitance leads to chronic swelling and tissue water retention--edema. Cellular redox potential is decreased.

Damaged cells become electropositive with respect to surrounding normal cells. ***BEST*** intervention restores electro negativity (electrons) to deficient cellular membranes therefore restoring the redox potential of the cell, i.e., recharging their biological batteries. It has been shown that stimulation with currents from 50-1000 micro amps can increase tissue ATP concentrations in rats by 300-500%.[31] Amino acid transport through the cell membrane and consequent protein synthesis is also increased by as much as 40%.[23] Therefore charging the dielectric, the cell membrane, will increase intracellular ATP in damaged cells, providing additional metabolic energy. Edema diminishes as homeostatic electrolyte and osmotic gradients re-establish themselves.

Russian doctors developed the concept of vegetative dysfunction of neural tissue in particular, and all tissues in general.[32] When one tissue or organ is depleted of electrons then the metabolic function of the tissue degenerates, and the body makes adjustments by pulling electrons from other tissues in a balancing act to maintain the highest level of capacitance (i.e. redox potential, charge) possible for energy resources available. Organs are paired so that deficient organs will borrow electrons from their partner to remedy the deficiency. This process continues until the donating organ degenerates, which in turn borrows from wherever possible. The body continues to compensate for electron deficiency and signaling patterns, exacerbating in a downward spiral to a terminal event.

Because neuropeptides, neurotransmitters, and nitric oxide (NO) are all highly energetic molecules, their synthesis requires large amounts of ATP. Presynaptic nerve cells have the high

numbers of mitochondria per cell, and they are located in the dendrites in close proximity to presynaptic junctions and neurotransmitter synthesizing areas of the cell.[33] [34]

BEST devices send signals designed to modify the body's abnormal signal. The resulting stimulation and response continues in dampened oscillation until normalcy is achieved. Thus, with modern biofeedback, the body's abnormal electrical signalling can be retrained.

Damaged tissues lock into a pattern of abnormal signaling as other organ systems adjust to the abnormal tissue. The adaptive reaction of the organism to the pathological change in environment allows for the maximum length of survival. In the body a great variety of manifestations of adaptive reactions are capable of existing.

Clinically, tremendous energy at the cellular level is required to affect a permanent change from a refractory dysfunctional state back to optimal homeostasis. Identifying energetic deficiencies and supplying electrons or identifying excess electrons and removing them until a normal redox potential is achieved has not been an accepted paradigm for western medicine. However, it has been extensively studied and well understood in oriental and modern Russian medicine. Cultural and financial pressures have forced these societies to seek solutions that are more economical than wholly pharmaceutical-based approaches to therapeutics.

Nakatoni MEAD Profiling for Energetic Dysfunction of Organs

A reliable energetic function profile of organs and related systems can developed with a ***Nakatoni MEAD***‡ (Meridian Energy Analysis Device) instrument, utilizing six acupuncture points on each hand and foot. The ***MEAD*** measures electron deficiency or excess (redox potential) of each meridian with respect to an established mean within three standard deviations and plots the profile graphically on a chart. The profile correlates well with standard diagnostic blood chemistries and appears to be a more sensitive indicator of impending pathology in that energetic changes appear in the organ before biochemical blood markers can exceed a detectable threshold with current lab analysis. Pathological degeneration of an organ is associated with

‡ Meridian Energy Analysis Devices Enterprises, Medpex Private Limited, Taiwan

electron deficiency, and the farther below the mean, the greater the degree of degeneration and malfunction of the organ. Inflammation and free radical damage is associated with electron excess and the farther above the mean, the greater the inflammatory process. The profiles of various organs can then be viewed in real time and with respect to each other, and an overall interpretation can be derived. The results are repeatable and quantifiable.

BEST devices normalize pathological signals by amplifying electrons and supplying electrons to energy deficient areas of the body in the case of degeneration or removing electrons in the cases of inflammation. Example: 1) Retraining atrophied tissues, muscles in particular, to contract, or nullifying and removing overactive body electrons (inflammation); 2)Muscle spasms reduction of (induction of NOS and vasodilatory neuropeptides, release of existing NO, increased perfusion, increased oxygenation, reduction and removal of lactic acid and free radicals) and removal of pain (induction of endorphins).

When ***BEST*** devices are applied to acupuncture points that correspond to a particular organ, a "dosage" of electrical stimulation impulses is delivered to the body via the built-in and/or remote electrodes in direct contact with the skin surface.

Therapeutic results can be evaluated and be adjusted if needed by retesting with the **MEAD** instrument after treatment. A four-hour interval after treatment is necessary for energy equilibration between tissues and must be observed before accurate data can be recorded for evaluation.

Increasing the Electron Capacitance of damaged tissue

A mechanism of action is the electron recharging of tissue. Tissues in the body actually possess an oxidation/reduction potential in which cells can be viewed as an electro-chemical gradient across a membrane much like a storage battery. [35] Voltage is the force that pushes electrons through a circuit or across a membrane to produce a current or flow of electrons or ions. Electrons flow from areas of higher concentration to lower concentration until equilibrium is achieved. The potential difference of electrons outside (less concentration) the cell membrane

with respect to the inside (greater concentration) is the potential difference or voltage. When the electrons move, the volume of flowing electrons is measured in amperes.

A capacitor stores electrons much like a tank stores water, releasing or storing when demand is present. An electronic capacitor usually consists of conducting plates or foils separated by thin layers of an insulating dielectric (as air or mica) with the plates on opposite sides of the dielectric layers oppositely charged by a source of voltage and the electrical energy of the charged system stored in the polarized dielectric. [36]

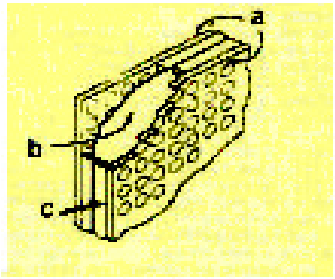

Figure 1

An electronic capacitor consists of two conducting plates ***(c)*** separated by a nonconducting plate ***(b)***. The gap ***(a)*** determines the potential difference (voltage).

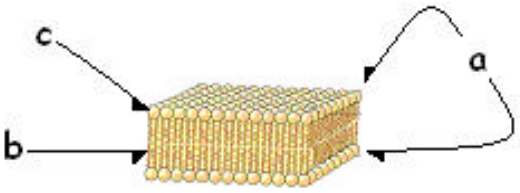

Figure 2

A cell membrane consists of lipid molecules with hydrophilic (electron conducting) carboxylic acid groups ***(c)*** and hydrophobic (electron insulating) hydrocarbon tail chains ***(b)***. The membrane thickness is the gap ***(c)***. The membrane acts as a dielectric to store electrons and transfers them to the cytoplasm upon demand.

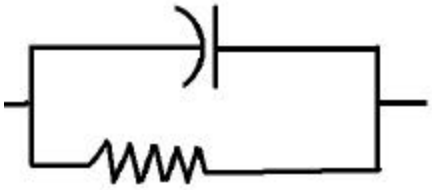

Figure 3

The circuit diagram at the left (Figure 3) consists of a resistor and a capacitor in parallel. When a load is incurred electrons bypass the capacitor and flow through the resistor to perform work. When there is no load the electrons flow to the capacitor for storage until a load is again incurred. Cell membranes are capacitors and micro-tubular cytoskeletons are the resistor; mitochondrial respiratory activities generate the demand (load).

Anything that resists the flow of electrons from one place to another is called a “resistor” (in alternating current, it is called “impedance”). Anytime a current exists, there is a magnetic field ninety degrees from the current and flowing in the direction of the current.

The cell membrane is a capacitor connected to the peripheral cytoskeleton acting as a resistor, in parallel. This electronic circuit creates a constant flow of electrons into the cytoplasm. If there is an excess of electrons flowing down the pathway, the excess is stored in the capacitor. If there is a deficiency of electrons flowing, the capacitor provides some from its storage to keep the current constant. It should be noted that the extra cellular fluid and the cells are wired in series.

In electronic circuits, electrons will always attempt to flow from the area of highest voltage to the areas of lowest voltage. In an organ system composed of many cells, each cell will send electrons to any cell with a lower voltage as shown in the diagram above. Thus there will be a common voltage in any given organ within the ability of the electrons to flow as dictated by local impedance

BEST **mediated transcellular membrane signaling of DNA and activation of peptide synthesis**

In 1974 Pilla developed a model of cell signaling and gene expression where the molecular components of cell membranes reflect current expression of chromosomal DNA within the nucleus.[37] The function and structure of protein and receptor sites embedded in/on the membranes in particular are controlled by chromosomal DNA via Messenger DNA. Pilla hypothesized the function of a cell at any instant in time is determined by a feedback loop between chromosomal DNA and macromolecules liberated from the membrane by means of an enzyme derived from messenger RNA activity within the cell. The induction activity of these membrane-bound proteins is strongly modulated by changes in the concentration of divalent ions (such as calcium Ca^{++} and magnesium Mg^{++}) absorbed on the membrane.[34 38 39]

BEST may electrically elicit these ionic changes and signal the nucleus to switch chromosomal gene expression “on” through cAMP for neuropeptide production.

In C fibers the process of membrane depolarization carried out by the influx of sodium ions seems to be followed by an increase in intracellular Ca^{++} concentration, thereby triggering the cyclic AMP transduction cascade for activating DNA/gene expression and subsequent peptide synthesis in neurons susceptible to the ***BEST*** stimulus.

Pilla confirmed the existence of cellular “windows” for signaling that open most effectively when certain frequencies, pulse widths, and pulse amplitudes are present. These findings support ***BEST*** technology and its perfected, clearly defined waveforms.

Enhanced Blood Perfusion, Vasodilatory Neuropeptides, and Nitric Oxide

Nitric oxide (NO), a short-lived molecule, has been identified as a potent biological mediator.[40] It plays an active role in many physiological processes such as vasodilatation, neural function, and inhibition of platelet aggregation, as well as in pathological processes such as inflammation.[41] [42] [43] Immunological, activated monocyte and NK white blood cells synthesize NO, which contributes in part to their cytotoxic activity against tumor cells and bacteria. [44]

NO is synthesized from the oxidation of the terminal guanido nitrogen atom of L-arginine by a family of nicotinamide adenine dinucleotide phosphate (NADPH)-dependent enzyme, the NOS (nitric oxide synthetase).[43] It has been shown that micro-currents applied to acupuncture points 1.) mediate vasodilatation locally through nitric oxide [45] [46] 2.) signal afferent nerves via dorsal root ganglia to medulla thalamic tracts to the CNS and mediate opiod peptide synthesis and analgesia.[13] [15] [16] NO is a primary vasodilator affecting the endothelial and smooth muscle cells of blood vessels. [47] [48] The induction of vasoldialtory neuropeptides and associated NO synthesis is a crucial aspect of the potential use of ***BEST*** therapy as an aid in wound healing, peripheral neuropathy, and ischemic conditions like thrombo-phlebitis and intermittent claudication of the limbs. Depletion of the nitric oxide pool in tissue inhibits healing and regeneration of normal metabolic functions due to stasis of extra cellular fluid and lymph flow. Ischemia leads to tissue acidification, degradation of the extra cellular milieu, and a further breakdown of cells. Local nitric oxide production is essential for adequate tissue perfusion and oxygenation of damaged tissue by its local vasodilatation mechanism.[41] Neural peptide production plays a role in perfusion as well as the local and systemic up-regulation of both substances.

Overcoming neural habituation and refractoriness to stimuli

Accommodation: the rise in the threshold during the passage of a constant, direct electric current because of which only the make and break of the current stimulates the nerve. [3]

Habituation: 1.) the gradual adaptation to a stimulus. 2.) extinction or decrease of a conditioned reflex over time by repetition of the conditioned stimulus. [3]

Afferent neurons exhibit phenomenon known as *neuronal habituation*, where refractoriness develops to repeated stimuli.[30] The nerve no longer responds to predictable signals and either ignores them or develops alternative neural pathways to circumvent the stimuli and continue to transmit pain or aberrant signals to the CNS. Therefore, bombarding tissue with repeated, uniform and predictable signals rapidly become useless in stimulating nerve fibers to release secretions.

Law of Dubois-Reymond◈: To electrically stimulate a nerve, there must be a sudden variation in current flow to prevent accommodation.

Systematic variation of the pulse amplitude, frequency, interval, and clustering such that no two impulses exhibit the same waveform, discourages neural habituation. In the course of treatment, waveforms emitted from certain modes in ***BEST*** devices are continuously changing (if it is repeated, it reappears only after a lengthy interval). Moreover the impedance of the tissue is constantly changing the waveform of the next emitted signal to ensure a different waveform until equilibrium is achieved, at which point a maximum dose of signaling has been delivered.

An important response to a ***BEST*** impulse is the release of regulative neuropeptides and cytokines. The signal stream, comprising waveform, signal strength, voltage, current, and frequency, can be varied in a number of ways, either through preselection by the operator or automatically by the software programmed into the device. The "dosage" can be delivered automatically or overridden at the discretion of the operator, with guidance from visual and audio indicators. Digital LED and sound displays or both

◈ Father of modern electrophysiology, he conducted foundational research on electrical activity in nerves and muscles German Physiologist 1818-1896

give guidance to the operator as dynamic real-time indicators of function and endpoint achievement of objectives.

A single pulse may be preselected for a specific repeat rate over a specific frequency range. The signal may also be "modulated" either by altering the ratio of "time-on" to "time-off" signaling or by changing the pulse waveform by selecting one of a series of set damping factors. These "modulations" can either be applied individually or together. Each individual impulse can be adjusted for amplitude, frequency, and dampened waveform.

A cluster of pulses may be packaged into discrete bursts and may be repeated at a fixed or varying frequencies and intervals. The individual pulses in these cluster bursts themselves can be modulated for either random or periodic interval spacing to give a concentrated (deep) or diffuse (shallow) penetration.

Automatic cycling of both the pulse interval rate over a set frequency range and the waveform-damping factor is also possible. These cyclical modes can again be utilized either individually or together.

The power output can be set by the operator to be detectable but comfortable for the patient. It can also be adjusted during application should this be desired. These impulses have been tailored to mimic the electrical discharges of the nervous system in order to elicit the organism's response with optimum efficiency and minimum disruption to cell function, depending upon the unique requirements of the presenting pain disease dynamics (or lack of same).

General Contra-indications to *BEST* Therapies

Following are descriptions of general hazards that could result in injury to the user or the patient, or lead to product damage. Specific warnings and cautions are found in relevant sections of the ***BEST*** manual. While ***BEST*** products are safe and no adverse reports have been received or documented, caution is advised for professional models until training is received. Training provides the opportunity for maximum utilization of therapeutic benefit. Individuals with a pacemaker or other electronic implants or who are intoxicated, pregnant, or suffering from emotional or mental conditions should not use ***BEST*** products. ***BEST*** electrodes should not come in contact with metal surfaces or be allowed to get wet during operation. When using ***BEST*** devices these basic precautions should be observed to reduce the risk of personal injury or damage to the circuitry voiding the warranty.

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