

Pulsed Electro-Magnetic Field (“PEMF”) Therapy

Benefits of PEMF Therapy	Page 2
Differences in PEMF Therapy Products	Page 3
Brief History of PEMF	Page 3
How PEMF Therapy Works	Page 3
PEMF Therapy and Circulation	Page 4
PEMF Increases Cellular Membrane Permeability	Page 6
PEMF Increases Cell Metabolism	Page 7
PEMF Increases Energy Storage and Cellular Activity	Page 7
PEMF Increases Cellular Membrane Flexibility and Elasticity	Page 9
PEMF Stimulates Cellular Communication and Replication	Page 9
PEMF Increases Cellular Genesis (Cellular Growth and Repair)	Page 9
- <u>PEMF Increases Blood Vessel Growth & Osteogenesis</u>	Page 9
- <u>PEMF and the spine</u>	Page 10
- <u>PEMF on bone and cartilage</u>	Page 10
PEMF and Immune Response	Page 11
PEMF Therapy Decreases Inflammation	Page 12
PEMF Therapy Reduces Pain	Page 12
PEMF Therapy Blocks Pain	Page 14
PEMF and tendonitis	Page 16
PEMF and intestines	Page 16
PEMF and the brain	Page 16
PEMF and multiple sclerosis (“MS”)	Page 16
PEMF Systems, Inc’s sponsored study SAWC poster: “Use Of Pulse Electromagnetic Field Therapy For Non-healing Leg Ulcers”, Henry Ford Health, Detroit, MI	Page 18
PEMF Systems, Inc’s Products Are The Most Technologically Advanced	Page 20

Benefits of PEMF Therapy

PEMF therapy has proven to be beneficial for many conditions and diseases and to improve many physical and physiological functions. PEMF therapy is a non-contact, non-invasive, non-pharmacological and effective treatment for many conditions.

In the past 30 years, more than 3,000 sham controlled, double-blind, university level medical studies worldwide have demonstrated that PEMF therapy is a safe and effective treatment for a variety of medical conditions and that it promotes and helps maintain general cellular health and function.

Clinical evidence shows that PEMF therapy reduces pain associated with trauma from accidents, sports injuries, surgeries and burns as well as pain from disease and degeneration.

PEMF therapy improves these conditions in many ways, including by mechanical, electrical, chemical, and magnetic processes within the cells of the body.

In 1995, Siskin and Walker provided a summary of clinical results on soft tissue damage. No adverse effects were noted, and the following positive effects were reported:

- ***Decreased pain***
- ***Reduced inflammation***
- ***Increased range of motion***
- ***Faster functional recovery***
- ***Reduced muscle loss after surgery***
- ***Increased tensile strength of ligaments***
- ***Faster healing of skin wounds***
- ***Enhanced capillary formation***
- ***Acceleration of nerve regeneration***
- ***And decreased tissue necrosis***

Brief History of PEMF

The principals of Pulsed Electro-Magnetic Field (PEMF) therapy were first described by Nikola Tesla in 1898. In 1956, Dr. Kyoichi Nakagawa, Japan, advanced the theory that humans were subjected to the Earth's magnetic field and that it had bio-magnetic effects.

In the 1960s, Dr. Becker gives an autobiographical account of his life experiences with bio electro-magnetics in his famous book "The Body Electric". He discovered a host of other bioelectric effects within the body such as electro-stimulating limb regeneration in mammals and further experimented with the piezoelectric properties of bones, skin and other tissues.

In 1974, Bassett et al. successfully used pulsed magnetic fields to treat non-union fractures. In 2000, Lorrain characterizes the electromagnetic field: "any time-varying magnetic field is accompanied by a time-varying electric field".

In 2004, Dr. Abraham Liboff introduced significant physics principles into the field of bio-electromagnetics as he studied the electromagnetic effects on the flux of ions and complex biological systems.

Various types of PEMF products have been accepted by the regulating bodies in many countries and are sold all over the world.

Market access was granted by the US FDA to PEMF therapy products for:

- ***Non-union bone fractures since 1979***
- ***Cortical and peripheral stimulation since 1991***
- ***Urinary incontinence and pelvic floor stimulation since 1998***
- ***Muscle stimulation since 1998***
- ***Cervical stimulation since 2004***
- ***Depression and anxiety since 2006.***

Other countries have also recognized the positive effects of PEMF therapy on health:

- ***Israel has accepted the use of PEMF products for migraine headaches.***
- ***Canada has accepted PEMF products for powered muscle stimulation.***
- ***The European Union has accepted the use of PEMF therapy in many areas including healing and recovery from trauma, degeneration, and the treatment of the pain associated with these conditions.***

Differences in PEMF Therapy Products

- Power Level

The magnetic energy produced by the various PEMF products can be as little as that of the Earth's magnetic field to more than 10,000 times as powerful. The lower power products are generally used for cellular health and bone healing. The higher power products are generally used for recovery of trauma from accidents, sports injuries, and surgery, as well as for control and improvement of degenerative diseases. Both low power and high-power products help reduce pain, but the higher power products are more effective in doing so.

- Continuous or Pulsed Waveform

Although there are exceptions in both types, most low power PEMF products have a continuous waveform while most high power PEMF products have a pulsed waveform.

- Shape of Waveform

The continuous waveform PEMF products can produce a square, a saw tooth, a sine, or a custom waveform. The pulsed output PEMF products usually produce a biphasic short duration pulse.

- Pulse Rate

Many low power PEMF products have preset pulse rates to choose from according to the various manufacturers' individual theories. Most high power PEMF products have a user variable control of the pulse rate.

- Duration of Treatment

Depending on the power level of the PEMF product, the treatment duration can be from three minutes to several hours.

How PEMF Therapy Works

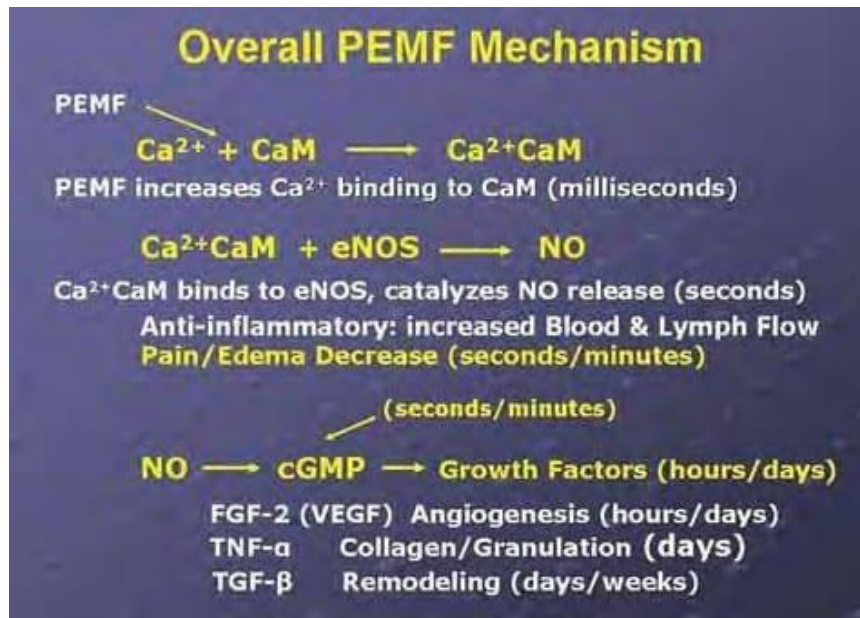
Many cells in the body produce nitric oxide (NO), a radical gas and a key vertebrate biological messenger that plays a role in many biological processes. The vascular endothelium production of NO is particularly important in the regulation of blood flow. Abnormal production

of NO, as occurs in variety of diseases, can adversely affect blood flow and other vascular functions.

By the mid-1990s, researchers were investigating the effects of electrical and PEMF signaling on intracellular calcium ion (Ca^{2+}), specifically the binding of Ca^{2+} to Calmodulin (CaM) present in tissue repair. The most recent studies on the PEMF transduction pathways concentrate on the Ca/CaM-dependent NO cascades, the growth factor cascades involved in tissue healing.

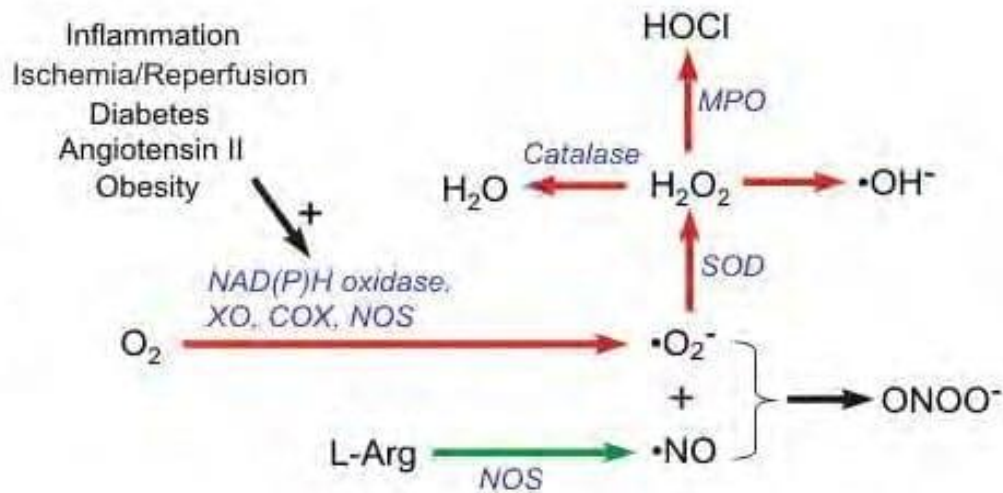
It is now understood that PEMFs modulate the calcium-binding kinetics to Calmodulin. Calcium/Calmodulin (Ca/CaM) then activates nitric oxide synthase (NOS) in several different isoforms.

When injury occurs, large amounts of nitric oxide are produced by long-lived inducible nitric oxide synthase (iNOS). In this cascade, tissue levels of nitric oxide persist, and the prolonged presence of this free radical is pro-inflammatory. This accounts for the leaky blood vessels syndrome associated with pain and swelling. In contrast, the endothelial and neuronal nitric oxide synthase isoforms (respectively eNOS and nNOS) produce nitric oxide in short bursts that can immediately relax blood and lymph vessels. These short bursts of nitric oxide in turn lead to the production of cyclic Guanosine Monophosphate (cGMP), which drives growth factor production. Interestingly, iNOS is not dependent on CaM, while the constitutive nitric oxide synthase or cNOS (eNOS or nNOS) cascade is dependent on the binding of Ca/CaM. Therapies, such as PEMF therapy, that can accelerate Ca/CaM binding may therefore impact all phases of tissue repair, from initial pain and swelling to blood vessel growth, tissue regeneration and remodeling as shown in the following diagram:



PEMF Therapy and Circulation

NOS, also known as the vascular endothelium-derived relaxing factor or 'EDRF' is bio-synthesized endogenously. The endothelial neural NOS (nNOS, Type I) serves as a transmitter in the brain and in different nerves of the peripheral nervous system to stimulate vasodilation, blood flow and to signal the surrounding smooth muscles to relax. When the endothelium is intact, NO is continually being produced by cNOS in the blood vessels. The Ca/CaM-dependent activity of cNOS produces vascular relaxation.



NO Intracellular Mechanisms

Under normal conditions, the Ca independent activation of iNOS is very low. Bacterial endotoxins or cytokines, such as tumor necrosis factor (TNF) and interleukins, stimulate the activity of iNOS causing inflammation. During inflammation, the amount of NO produced by iNOS may be 1,000-fold greater than that produced by cNOS. When NO is formed, it is highly reactive (its lifetime is a few seconds), yet it diffuses freely across membranes, primarily because superoxide anions (O_2^-) have a high affinity for NO. The unpaired electron of O_2^- binds very rapidly to NO which also has an unpaired electron. The reaction between NO and O_2^- effectively scavenges NO and reduces its bioavailability. This leads to vasoconstriction, increased platelet-endothelial cell adhesion, platelet aggregation and thrombus formation, increased leukocyte-endothelial cell adhesion, and morphologic changes in blood vessels including cell proliferation. Superoxide anions and their products have tissue damaging effects and are thus very important in cardiovascular pathology and pathophysiology.

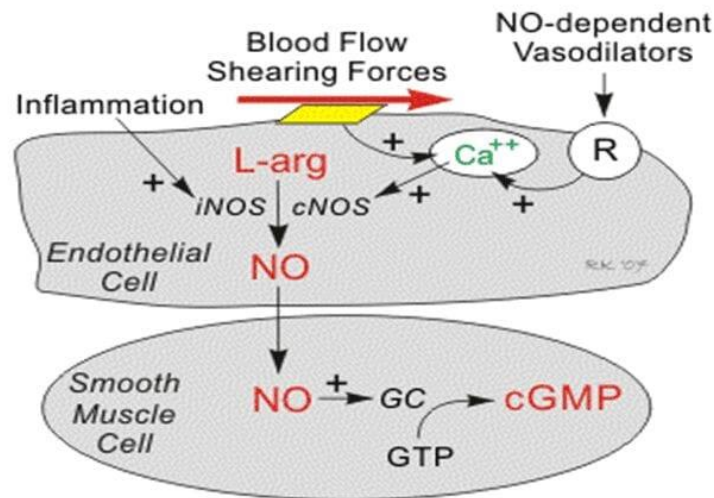
NO also binds avidly to the hemoglobin (Hgb) in red blood cells and to the enzyme guanylyl cyclase found in vascular smooth muscle cells and most cells of the body. When NO is formed by the vascular endothelium, it rapidly diffuses into the blood where it binds to Hgb breaking it down. Additionally, it diffuses into the adjacent smooth vascular muscle cells where it binds to and activates guanylyl cyclase. The enzyme catalyzes the dephosphorylation of Guanosine Triphosphate (GTP) to Cyclic Guanosine Monophosphate (cGMP), which serves as a second messenger for many important cellular functions, particularly for signaling smooth muscle relaxation.

As blood flow increases, so does the oxygen intake. PEMF therapy has been proven to effectively increase blood flow and provide muscle relaxation with better oxygenation of the muscle tissue.

As a highly reactive gaseous molecule, NO is an ideal transient paracrine (between adjacent cells) and autocrine (within a single cell) signaling molecule that has direct and indirect vascular action, including the following:

- **Direct vasodilation (flow dependent and receptor mediated)**
- **Indirect vasodilation by inhibiting vasoconstrictor influences**
- **Anti-thrombotic effect - inhibits platelet adhesion to the vascular endothelium**

- **Anti-inflammatory effect - inhibits leukocyte adhesion to vascular endothelium scavenges superoxide anion.**
- **Anti-proliferative effect - inhibits smooth muscle hyperplasia**



Many studies have demonstrated that PEMF therapy affects many transduction pathways and the Ca/CaM-dependent nitric oxide cascades involved in tissue repair. By modulating intracellular Ca/CaM, the eNOS and nNOS produce NO in short bursts that can immediately relax blood and lymph vessels.

By increasing the production of vascular endothelium NO when its production is impaired or its bioavailability is reduced, PEMF therapy can successfully help improve conditions and diseases associated with vasoconstriction (e.g., coronary vasospasm, elevated systemic vascular resistance, hypertension), thrombosis due to platelet aggregation and adhesion to vascular endothelium, inflammation by up regulating leukocyte and endothelial adhesion molecules, vascular hypertrophy, stenosis, hypertension, obesity, dyslipidemias (particularly hypercholesterolemia and hypertriglyceridemia), diabetes (both type I and II), atherosclerosis, heart failure, tissue repair and aging.

As demonstrated above, PEMF Therapy affects many processes in the cells and tissues of the body that can be specifically identified. They in turn improve many conditions in the body.

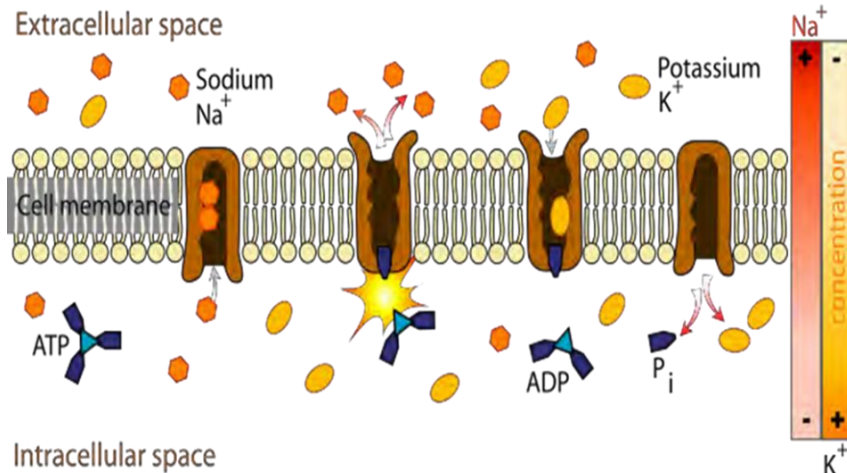
PEMF Increases Cellular Membrane Permeability

As early as 1940 it was suggested that magnetic fields might influence membrane permeability as it affects the transmembrane potential ("TMP") and the flow of ions in and out of the cells. Healthy cells in tissue have a voltage difference between the inner and outer membrane referred to as the resting TMP ranging from -70 to -80 mV. This causes a steady flow of ions through the membrane's voltage-dependent ion channels. In damaged cells, the TMP is raised from -50mV to -15mV causing an increased cations inflow through the Na⁺ and CA²⁺ channels. As their concentration rises, interstitial fluid is attracted to the inner cellular space causing swelling and edema.

The application of PEMF therapy to damaged cells accelerates the re-establishment of normal TMP in the nucleus reducing swelling and increasing the rate of healing. As the electromagnetic field pulses temporarily hyperpolarize and depolarize the cell membrane, the ion channels open and close allowing a more efficient ion exchange, as with the Na/ K pump, and increasing cellular oxygenation and nutrition. (Sansaverino).

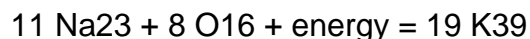
PEMF Increases Cell Metabolism

It has since been established that magnetic fields can influence ATP (Adenosine Triphosphate) production; increase the supply of oxygen and nutrients via the vascular system; improve the removal of waste via the lymphatic system; and help to re-balance the distribution of ions across the cell membrane.



For proper metabolism, the Na⁺/K⁺ pump within the membrane forces a ratio of 3Na⁺ ions out of the cell for every 2K⁺ ions pumped in. The Na⁺/K⁺ pump uses energy derived from ATP to exchange Na⁺ for K⁺ ions across the membrane.

An impaired Na⁺/K⁺ pump results in edema (cellular water accumulation) and fermentation, a condition favorable to cancerous activity. French researcher Louis C. Kervran demonstrated that Sodium plus Oxygen plus Energy (ex: magnetic energy) in the nucleus transmutes into Potassium as:



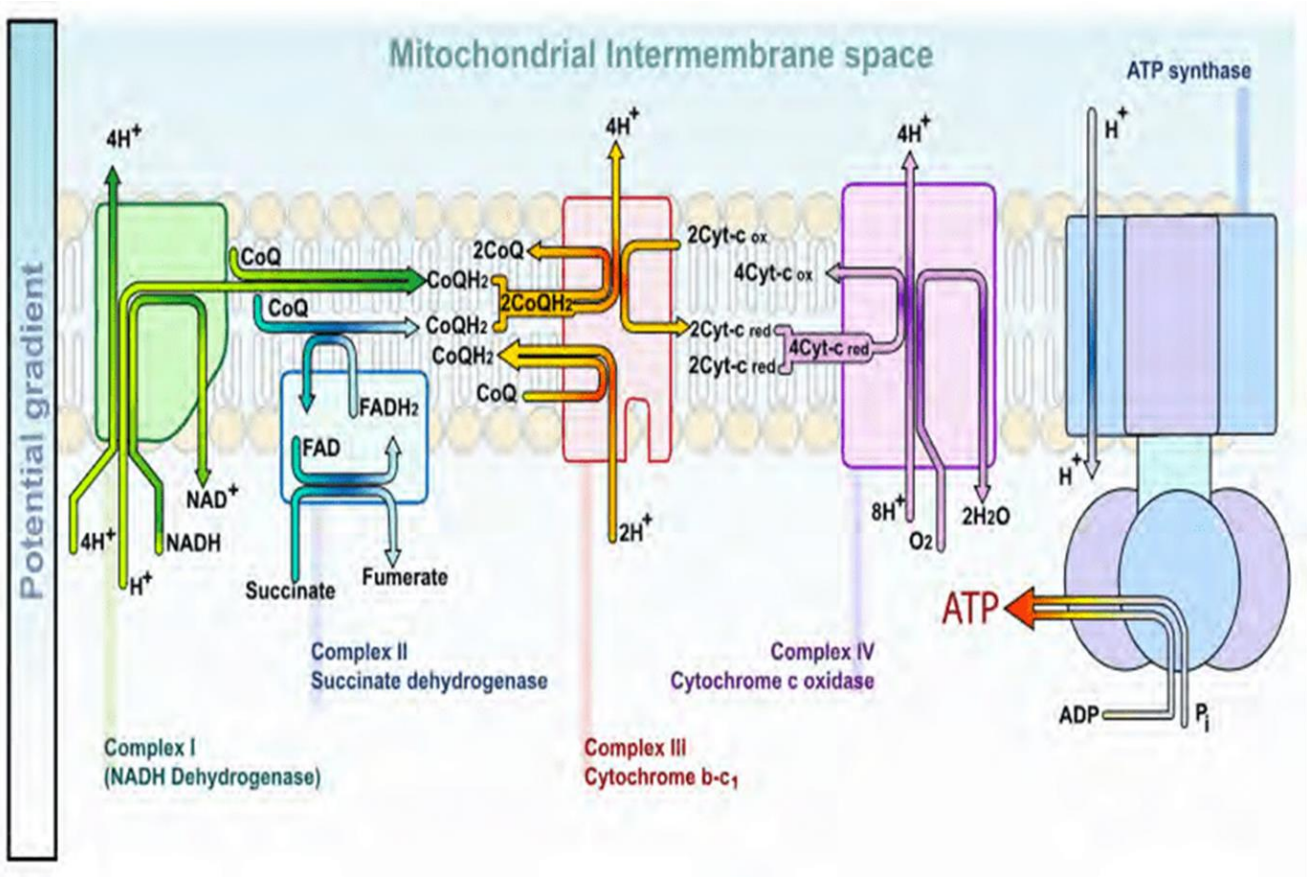
As a result, utilization of oxygen in the cells increases and the body increases production of its own energy supplier (ATP). The body's natural regulatory mechanisms are reinforced, toxins and waste products are more rapidly broken down and healing processes accelerated.

PEMF Increases Energy Storage and Cellular Activity

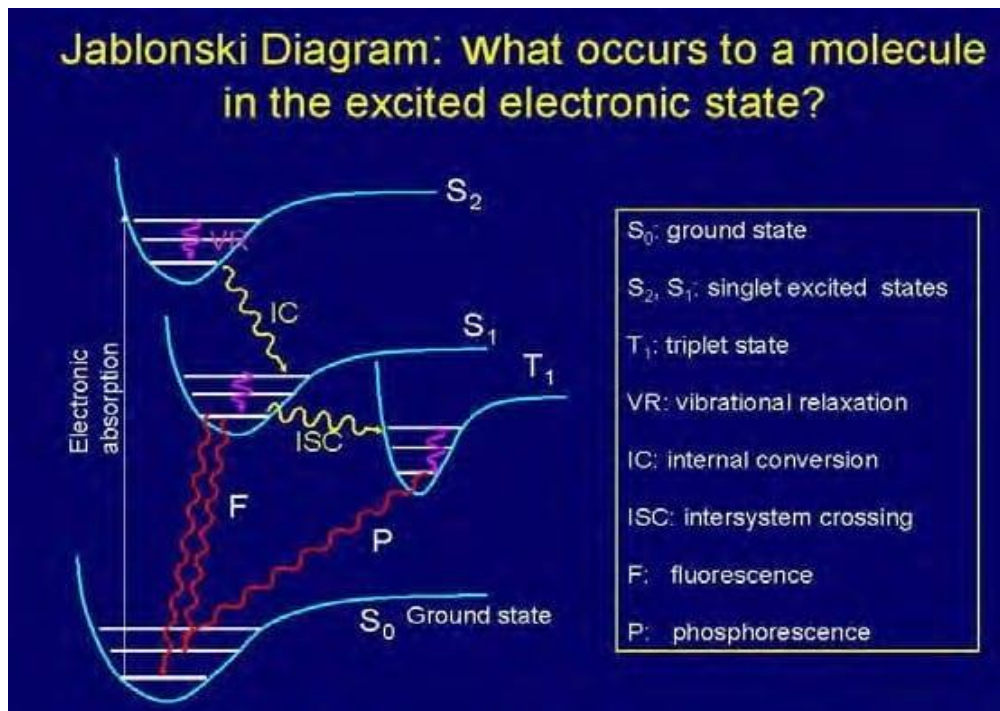
As the pulsed fields expand and collapse through a tissue, the protein molecules, such as the cytochromes in the cells' mitochondria, gain electrons and, in doing so, store energy by converting ADP to ATP molecules more rapidly.

The ATP molecules store and transport the energy that is then used in all the metabolic functions of living cells.

PEMF therapy provides sufficient energy to affect the magnetic resonance of the atom as the electron is energized. The magnetic resonance of the electrons at the atomic level also exhibits a change, a phase shift that disturbs and breaks the once orderly pathways of communication that is usually transmitted from atom to molecule, molecule to cell, cell to tissue, and tissue to organ.



PEMF seems to confuse the specific inherent magnetic resonance and temporarily modify it in each atom, molecule, cell, and thus, tissue and organ. In doing so, the phase shift influences the physical and chemical characteristics of the physiological markers.



PEMF Increases Cellular Membrane Flexibility and Elasticity

A study entitled “Modulation of collagen production in cultured fibroblasts by a low-frequency pulsed magnetic field” by Murray J. et.al. (Biochim Biophys Acta) shows that PEMF therapy successfully increases membrane flexibility by increasing the synthesis of collagen within the fibroblasts, a crucial protein that supports membrane elasticity. In doing so PEMF therapy increases tissue and muscle flexibility and, therefore, increases range of motion, and that usually within minutes.

PEMF Stimulates Cellular Communication and Replication

DNA synthesis is linked to pulsed, low intensity magnetic fields (Liboff et al, 1984; Rosch et al, 2004). Proteins, as conductors of electricity, are subject to electrophoresis. The Ribonucleic Acid (“RNA”) messengers that are synthesized from a Deoxyribonucleic Acid (“DNA”) template during transcription mediate the transfer of genetic information from the cell nucleus to ribosomes in the cytoplasm and serve as a template for protein synthesis.

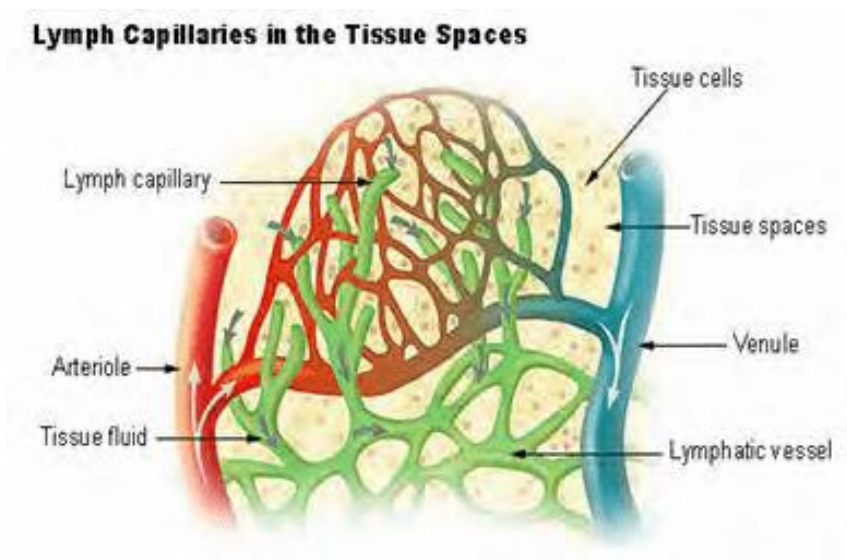
Dandliker et al. (1997) show that DNA conducts electrons along the stacked bases within the DNA double helix, electro-magnetic fields may initiate transcription of the precursor mRNA by accelerating electrons moving within the DNA helix (McLean et al, 2003). Therefore, the flow of information to and from genes may be linked to changing magnetic fields (Einstein, 1977; Goodman et al, 1983).

PEMF Increases Cellular Genesis (Cellular Growth and Repair)

In December 2004, the Swiss Medical Tribune stated that PEMF therapy provided: “improvement of blood circulation, relief from pain, improvement of bone healing and the stimulation of nerve cells”.

- PEMF Increases Blood Vessel Growth & Osteogenesis

A study done at the New York University Medical Center (Institute of Reconstructive Plastic Surgery, NY, NY, USA) demonstrates in vitro and in vivo that electro-magnetic fields increase angiogenesis, the growth of new blood vessels through the endothelial release of the fibroblast growth factor-2 (“FGF-2”). The delivery of PEMF therapy in low doses identical to that currently in clinical use significantly increased endothelial cell proliferation and tubulization, which are both important processes for vessel formation.



The ability of PEMF to increase cell proliferation seems unique to the endothelial cells releasing a protein in a paracrine fashion (or signaling to adjacent cells and other types of cells) to induce changes in neighboring cells and tissues. The coordinated release of FGF-2 suggests that PEMF therapy may facilitate healing by augmenting the interaction between osteogenesis and blood vessel growth. The fibroblast and endothelial cells are made to go embryonic due to drastic changes in ionic concentrations in the cells' cytoplasm and therefore the cells' nuclei. These ionic concentrations react with the cell DNA opening some gene sets and closing others.

PEMF therapy has proven efficacious in increasing the flow of ions and nutrients through the lymph capillaries as well as blood and interstitial fluid circulation. Vital organs such as the liver, kidneys and colon are able to rid themselves of impurities through the same processes, thus detoxifying the body and allowing better organ functionality.

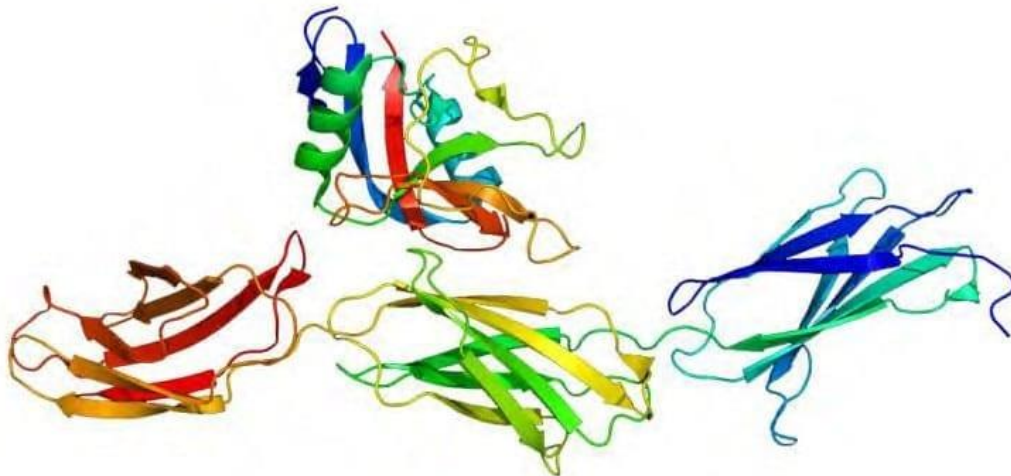
- PEMF and the spine

Long-term studies such as those by Marks RA. (*Richardson Orthopaedic Surgery, TX, USA*) and Richard A. Silver, M.D. (*Tucson Orthopaedic & Fracture Surgery Associates, Ltd., Tucson, AZ, USA*) demonstrate that adjunctive treatment with PEMF is effective in promoting spinal fusion following PLIF procedures across all patient subgroups by stimulating osteoblast proliferation.

- PEMF on bone and cartilage

In a study entitled: "*Modification of biological behavior of cells by Pulsing Electro-magnetic fields*", Ben Philipson, Curatronix Ltd. (*University of Hawaii School of Medicine, HI, USA*) demonstrates that PEMF application increases bone density, promotes bone union by electric current induction stimulating cell membrane permeability and allowing more ions across. This affects the activity of intracellular cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), and accelerates osteoblast differentiation.

In healthy joints, movement generates electric currents in the joint. The electrical field protects and regenerates the cartilage, surrounding bone, and connective tissues (tendons, ligaments...). In the joint space, chondrocytes produce a cartilaginous extracellular matrix that supports and increases the space between individual cells. This matrix consists mostly of collagen type II and aggrecans.



Proteoglycan Aggregate

Injuries and osteoarthritis alter the electrical field in the joint and thus disrupt the normal mechanism of preservation and regeneration of the cartilage. The ability of the cartilaginous tissue to withstand compressive stress is reduced. Once the destructive process has begun and the delicate integrity of healthy resting chondrocytes in maturational arrest is disturbed, phenotypic dedifferentiation of the chondrocytes may become hypertrophic.

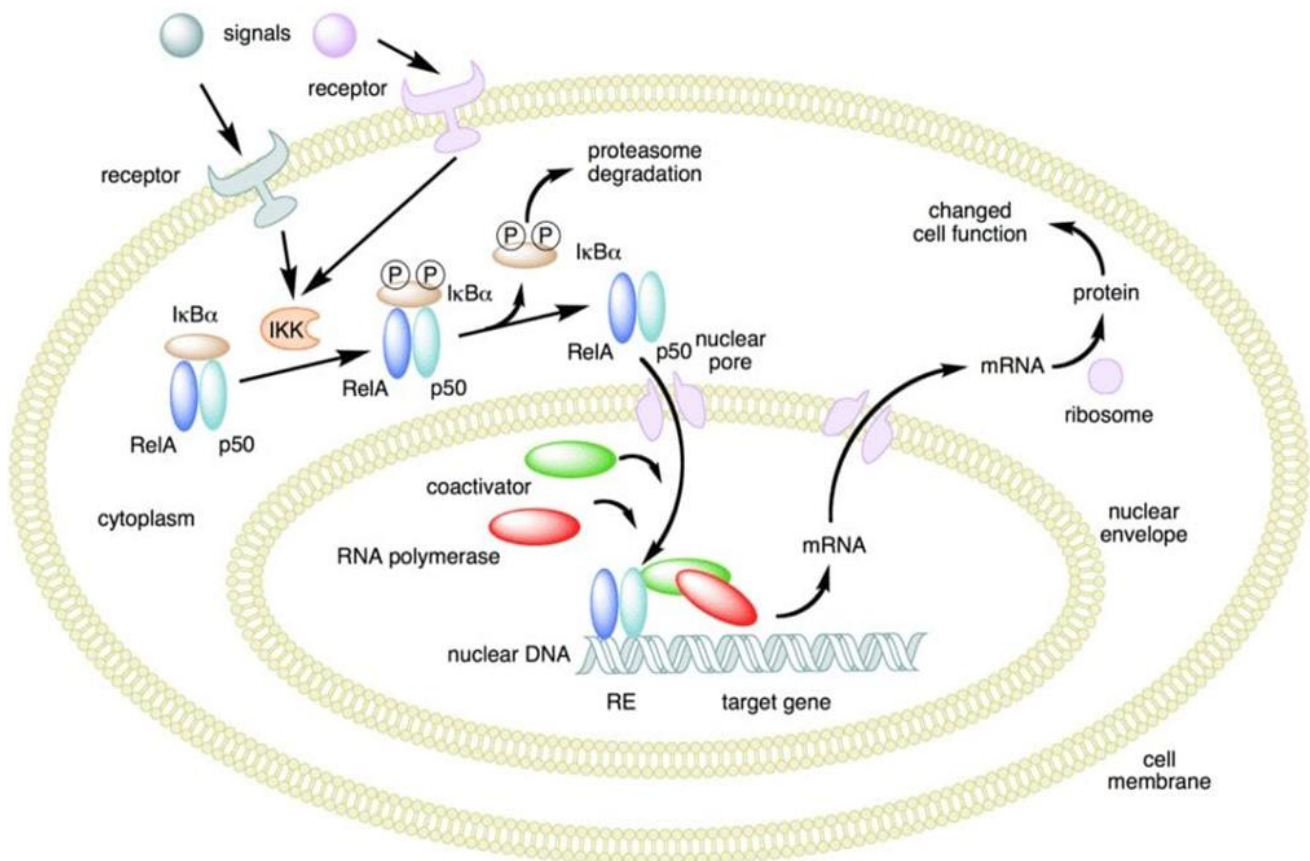
“Severe joint inflammation following trauma, arthroscopic surgery or infection can damage articular cartilage, thus every effort should be made to protect cartilage from the catabolic effects of pro - inflammatory cytokines and stimulate cartilage anabolic activities. Previous pre-clinical studies have shown that PEMFs can protect articular cartilage from such catabolic effects and prevent its degeneration resulting in chondroprotection.” (Zorzi C et Al., Arthroscopy journal July 2007)

PEMF stimulation increases the partial oxygen pressure and calcium transport. Repair and growth of cartilage is thus stimulated, preventing grinding of the bones.

PEMF and Immune Response

With a lifetime of a few seconds, NO is highly reactive and diffuses freely across cell membranes. As PEMF therapy effectively stimulates NO production, it also improves paracrine and autocrine communication. NO is also generated by phagocytes (monocytes, macrophages, and neutrophils) and, as such, is part of the human immune response.

NO has been demonstrated to activate NF-κB in peripheral blood mononuclear cells, an important protein complex that controls the transcription of DNA and a transcription factor in iNOS gene expression in response to inflammation.



NF-κB mechanism of action

NO plays a key role in regulating the immune response to infection and is implicated in processes of synaptic plasticity and memory (see above). The vascular endothelium uses NO to signal the surrounding smooth muscle to relax. This results in vasodilation and increased lymphatic and blood flow providing better oxygenation, transport of white blood cells and antibodies, and input of phagocytes into the cells, thus promoting cellular health and immune response.

PEMF Therapy Decreases Inflammation

Several factors contribute to inflammation including injury, surgery, tissue damage, poor localized circulation with swelling and edema. The formation of edema with swelling, bruising and discoloration of soft tissue is an inflammatory response and inflammation causes pain. When a cell is traumatized, its electrical charge is diminished. Thus, normal cell functions and operations shut down. Cells that are scarred or fibrotic with adhesions have a TMP charge of about -15 mV, degenerative or immune-compromised cells about -30 mV instead of a normal a normal -70mV. When the resting TMP is raised, the cells reach the +30mV threshold for the pre-synaptic terminals to release the chemical neurotransmitter that causes pain and inflammation more quickly and readily. Swelling and bruising occur, and more pain is transmitted along the nerves to the cells. Communication pathways necessary for healing to begin are interrupted. Numerous clinical studies have demonstrated that PEMF Therapy sends a mild electromagnetic current that effectively recharges cells and thus, lowers the cell TMP reducing pain and inflammation.

During inflammation, the amount of NO produced by iNOS may be 1,000-fold greater than that produced by cNOS. When NO is formed, it freely diffuses cross membranes, primarily because superoxide anions (O_2^-) have a high affinity for and rapidly bind with NO reducing its bioavailability. This leads to vasoconstriction, increased platelet-endothelial cell adhesion, platelet aggregation and thrombus formation, increased leukocyte-endothelial cell adhesion, and morphologic changes in blood vessels including cell proliferation. As PEMF therapy effectively stimulates NO production, it can successfully help improve conditions and diseases.

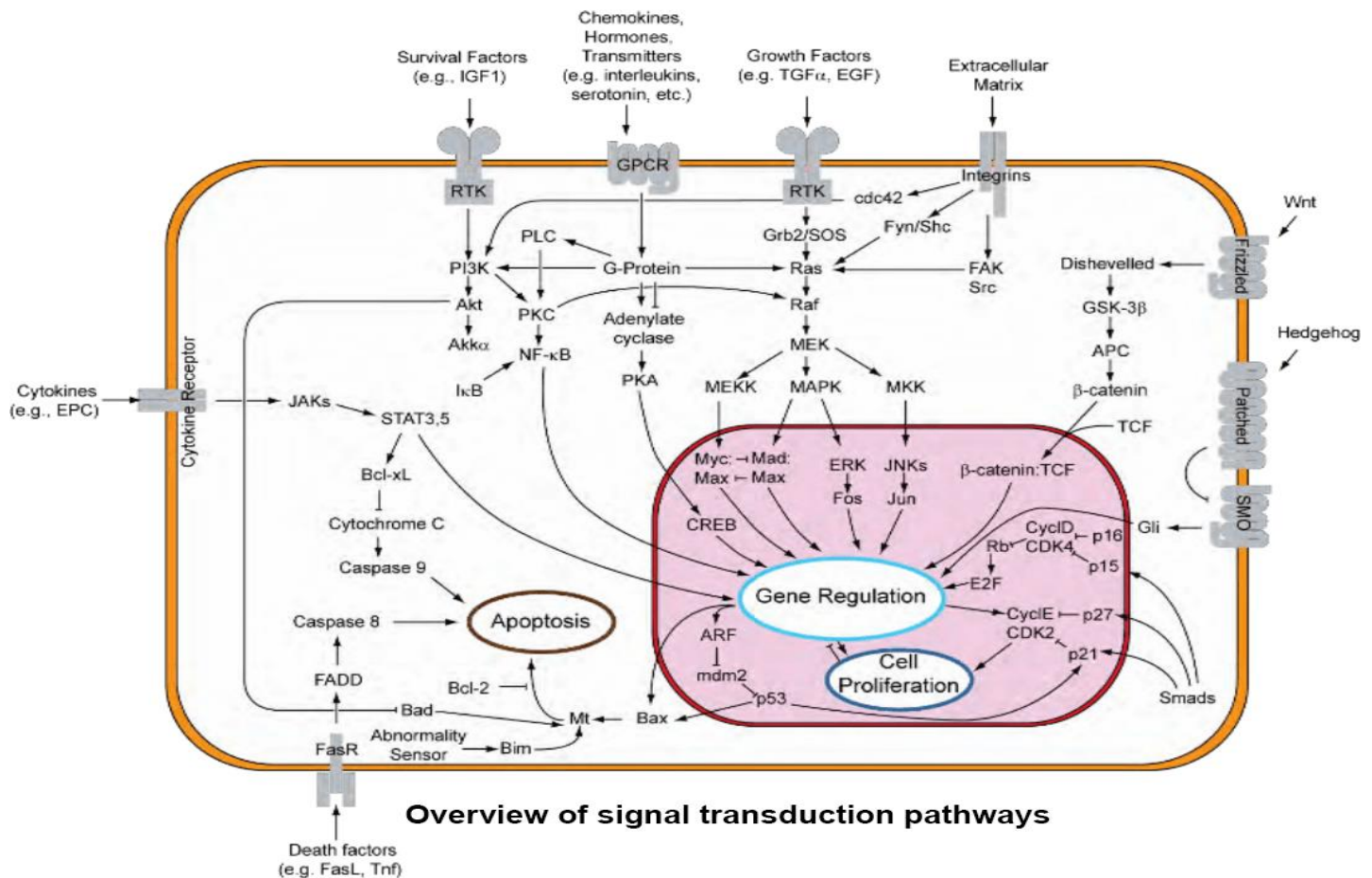
PEMF Therapy Reduces Pain

One of the most significant effects of PEMF therapy is the improvement of painful conditions regardless of their origin. Pain mechanisms are complex and have peripheral and central nervous system aspects.

During the last 100 years, theories of pain mechanism have evolved from specificity and summation models to the popular Gate Control Theory has become the most important development in the field of pain management (Melzack/Wall/Casey, 1989).

Signal transduction is a mechanism by which a mechanical or chemical stimulus to a cell triggers a specific cellular response. In transmembrane receptors, half of the receptor is outside the cell and the other half on the inside. A signal, such as a chemical signal, binds to the outer half of the transmembrane receptor which then changes its shape to convey the signal inside the cell. There may be cascades of signals, one after the other. The signal creates a change in the cell, either in the cytoplasm or in the DNA of the nucleus.

In a chronic pain state, the pain signal generated can occur in the central nervous system without any peripheral noxious stimulation. Scientific evidence shows that acute persistent pain eventually sensitizes wide dynamic neurons in the dorsal horn of the spinal cord, the wind-up phenomenon, constituting the basis of developing chronic pain syndromes (Kristensen, 1992).



Persistent and excessive pain has no biological positive or necessary function. It is harmful to our well-being. Therefore, pain needs to be treated as early and as completely as possible and not to be left alone (Adams et Al. 1997).

Soft tissue pain generally stems from local inflammation and can be depicted as musculo-skeletal, neurologic, vascular, and referred visceral - somatic or articular (Cailliet, 1991). In many patients, inflammation causes pain that limits range of movements and daily activities.

Early reports of applying electrical current to treat pain date back to before 1800 (Ersek, 1981). Many studies have demonstrated the positive effects of PEMF therapy on patients with pain from a wide variety of conditions. Some studies focused on the rapid short-term relief while others demonstrate the long-term benefits. PEMF therapy has successfully been used for the control of pain associated with rotator cuff tendinitis, multiple sclerosis, carpal tunnel syndrome, and peri-arthritis (Battisti et Al. 1998; Lecaire et Al. 1991). PEMF therapy has also successfully been used for treatment of migraine, chronic pelvic pain, neck pain, and whiplash injuries (Rosch et Al. 2004).

In a March 2003 publication on Pain Management with PEMF Treatment, Dr. William Pawluk explains: "Magnetic fields affect pain perception in many ways. These actions are both direct and indirect. Direct effects are neuron firing, calcium ion movement, membrane potentials, endorphin levels, nitric oxide, dopamine levels, acupuncture actions and nerve regeneration. Indirect benefits are on circulation, muscles, edema, tissue oxygen, inflammation, healing, prostaglandins, cellular metabolism, and cell energy levels... Short-term effects are thought due to a decrease in cortisol and noradrenaline, and an increase in serotonin, endorphins and enkephalins. Longer term effects may be due to CNS and/or peripheral nervous system

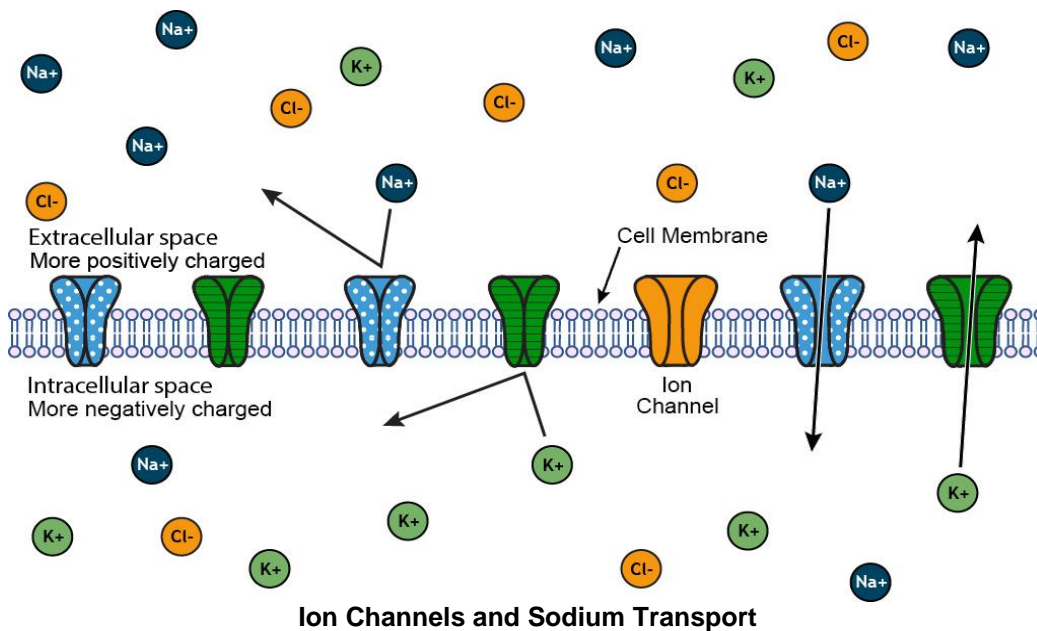
biochemical and neuronal effects in which pain messages are altered; and the pain is not just masked as in the case of medication”.

PEMF Therapy Blocks Pain

The TMP is the voltage difference between the interior and exterior of a cell often due to ion gradients, particularly proton gradients.

Differences in concentration of ions on opposite sides of a cell membrane produce the TMP. Sodium (Na^+) and chloride (Cl^-) ions are in high concentrations in the extracellular region while potassium (K^+) ions and large protein anions are in high concentrations in the intracellular region.

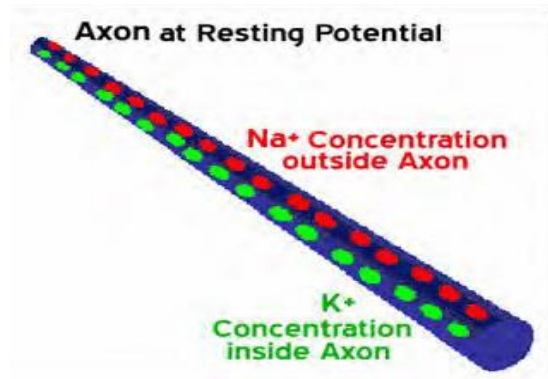
The opening and closing of ion channels to transport ions (Na^+ , Ca^{2+} , K^+ , Cl^-) in and out of cells through the membrane produce a local change in the transmembrane potential (“TMP”) which causes a rapid flow of electrons to other areas of the membrane, thus generating an electric current. In electrically excitable cells such as neurons, the TMP is used to transmit signals from one part to another.



In their baseline states, both non-excitable and excitable cells have a TMP at a relatively stable value called the resting potential. The interior of a cell has a negative baseline voltage relative to the outside. The Na^+/K^+ -ATPase helps maintain resting potential.

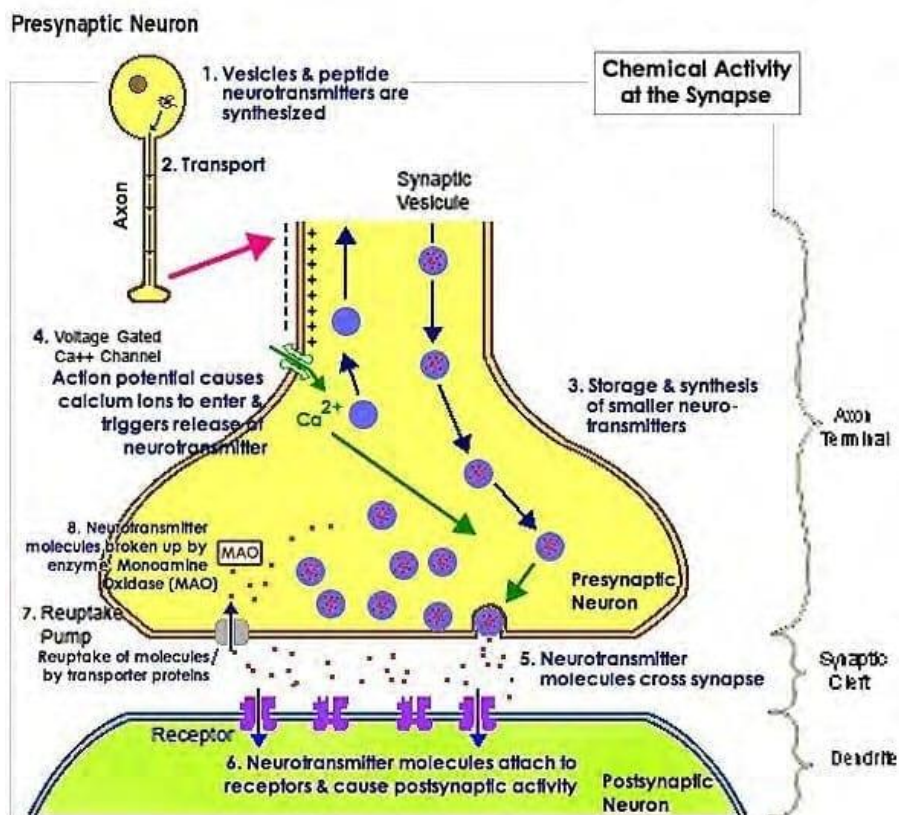
Neurons have typical resting potential values ranging from -70 to -80 mV (milli Volts) and each axon has its characteristic resting potential voltage. The opening and closing of the ion channels induce a change in the resting potential called a depolarization if the interior voltage rises (say from -70 mV to -65 mV), or a hyper polarization if the interior voltage decreases (say from -70 mV to -80 mV).

In excitable cells, a depolarization evokes a short-lasting all-or-nothing event called an action potential where the TMP undergoes a sudden spike often reversing its charge; special types of voltage-dependent ion channels that remain closed at the resting TMP can be induced to open.



Dr. D. Laycock, Ph.D. Med. Eng. MBES, MIPEM, B.E d., inspired by the works of Adams et Al. (1997) lectured on PEMF therapy and Pain Reduction: "It is necessary to understand the mechanism of pain transmission to understand how pain blocking can take place with PEMF therapy..." A pain signal is transmitted by an electric signal along the nerve cells interrupted by pre-synaptic terminals, then by a chemical signal across synaptic gaps between neurons. When a pain signal arrives, it temporarily depolarizes the nociceptive cell and raises the TMP to +30mV from a normal -70mV. The +30mV threshold is needed to cause the release of a chemical neurotransmitter from a synaptic vesicle contained within the membrane at those terminals.

The Na⁺ channels close when the inside of the axon becomes sufficiently positive, about +30 mV. The Na⁺ channels closing limit the ability of Na⁺ ions to enter the axon. Now K⁺ ions are free to cross the channels and leave the axon because of the greater concentration of K⁺ on the inside and reverse the voltage levels. The action potential is therefore not the movement of voltage or ions but the flow of these ion channels opening and closing moving down the axon.



This exchange of Na⁺ and K⁺ triggers exocytosis of neurotransmitters via synaptic vesicles contained within the membrane. The neurotransmitters diffuse into the synaptic gap and chemically transfer the pain signal across the synaptic gap to chemical receptors on the post-synaptic nerve cell. The cell then returns to its previous level of -70mV.

Research by Warnke, 1983; (Warnke, et al 1997) suggests that PEMF therapy lowers the TMP to a hyperpolarized level of -90mV thus preventing the pain signal from triggering the neurotransmitter exocytosis as the TMP can only be raised to +10mV. This potential is well below the threshold of +30mV necessary to release the relevant neurotransmitters into the synaptic cleft and the pain signal is effectively blocked”.

PEMF and tendonitis

The department of rheumatology at Addenbrookes Hospital showed a 65% total success and 18% improvement rate with the use of PMFT for the treatment of persistent rotator cuff tendonitis.

PEMF and intestines

An experimental study by Nayci A. et.al. Cakmak M, Aksoyek S, Renda N, Yucesan S. (Department of Pediatric Surgery, Mersin University Medical Faculty, Turkey) demonstrated that electro-magnetic field stimulation provided a significant gain in anastomotic healing in both small and large intestine, and a significant increase in both biochemical and mechanical parameters.

PEMF and the brain

Grant G. et.al. of the Department of Neurosurgery, Stanford University, CA, USA observed that exposure to PEMF attenuated cortical ischemia edema on MRI and reduced ischemic neuronal damage as he stated:” *PEMF stimulation may accelerate the healing of tissue damage following ischemia. Preliminary data suggest that exposure to a PEMF of short duration may have implications for the treatment of acute stroke*”.

PEMF and multiple sclerosis (“MS”)

Scientific studies have demonstrated the effects of PEMF on nerve regeneration, brain electrical activity (electro-encephalography), neurochemistry, and immune system components, all important effects for disease pathology and clinical symptoms in MS. Evidence from many studies showed a significant increase in alpha EEG magnitude, a significant improvement in the PS combined rating for bladder control, cognitive function, fatigue level, mobility, spasticity, and vision. Sandyk R. summarizes recent clinical work on the therapeutic effects of PEMF in MS: “*A host of biological phenomena associated with the disease involving interactions among genetic, environmental, immunologic, and hormonal factors, cannot be explained on the basis of demyelination alone and therefore require refocusing attention on alternative explanations, one of which implicates the pineal gland as pivotal. The pineal gland functions as a magnetoreceptor organ. This biological property of the gland provided the impetus for the development of a novel and highly effective therapeutic modality, which involves transcranial applications of PEMF flux density*”.

The many studies cited herein and listed thereafter demonstrate that PEMF treatment stimulates many aspects of cellular activity. In doing so, PEMF therapy promotes

neural regeneration and brain function, and improves neuro-muscular function and general health.

Beyond the complex mechanisms by which it operates remain the health benefits associated with PEMF therapy. PEMF therapy increases blood circulation in and around damaged tissue, and effectively helps damaged cells heal. Generally, PEMF therapy produces one main effect; it stimulates the cell metabolism by increasing the flow of electrons and ions across the cell membrane. This effect involves a chain of processes in the human body, which leads to improvement of health without side effects including:

- *Decreased inflammation, swelling and pain*
- *Accelerated detoxification of cells and organs*
- *Increased blood flow by angiogenesis with the formation of new capillaries*
- *Enhanced macro circulation by mechanically de-clumping blood cells, by alternately dilating and constricting vessels*
- *Improved circulation with mechanical contraction and relaxation of blood vessels*
- *Improved interstitial fluid circulation*
- *Increased supply of oxygen, ions and nutrients to cells*
- *Increased partial oxygen pressure*
- *Improved elimination of carbon dioxide and waste products away from the cells*
- *Activation of cellular and molecular processes enhancing the internal self-regulating mechanisms of the body*
- *Stimulation of cellular repair mechanisms*
- *Stimulation of inter cellular communication*
- *Increased cellular genesis promoting bone, cartilage, tendon and soft tissue growth*
- *Increased collagen production with associated enhanced cellular and tissue elasticity*
- *Stimulation of the Na/K pump by increased opening of the ion channels in the cell membrane*
- *Increased calcium transport and absorption for stronger bones, joints, and muscles*
- *Increased ATP production by excitation and increased transport of electrons in the mitochondria*
- *Stimulation of RNA, DNA and protein biosynthesis by electron and energy transfer*

Because of its many positive biological effects, PEMF therapy helps the body's natural processes and promotes healing.

PEMF Systems, Inc. sponsored a study conducted with two its products of different power levels that was recently presented at SAWC (the Symposium on Advanced Wound Care) of Fall 2023 in Las Vegas, NV and the results are presented in the following poster.

Abstract

Introduction: Pulsed electromagnetic field (PEMF) therapy has proven to be effective in acute tissue healing and pain reduction. It encourages the growth, maintenance and healing of living cells, soothes muscle pain and stiffness, and improves tissue oxygenation and blood circulation. It is hypothesized that by inducing a mild electrical magnetic current into damaged cells, PEMF therapy slows or stops the release of pain and inflammatory mediators, increases blood flow of the cells, and re-establishes normal cell interaction. With reduced inflammation, pain decreases, energy increases, and faster tissue healing occurs.

Objective: We conducted a study on the clinical efficacy of PEMF therapy to improve clinical outcomes for patient with chronic venous leg ulcers.

Methods: The study was designed as a prospective randomized, double blinded study to test the benefits of PEMF therapy. Patients who met the inclusion criteria were instructed on the use of the device and daily pain score recording. The wounds were treated biweekly with routine care, measured and underwent standardized photography. The study duration was 16 weeks for each individual. Randomization was performed after enrollment to the PEMF unit or a placebo unit (Pemf Systems, Inc. Sherman Oaks, CA). Only the study coordinator knew which device was provide to the patient.

Results: 33 patients completed the study. No patient sustained any harm from the devices. Six patients received placebo devices and 27 received active devices. In the treated group, wound area went from 17 ± 15 cm to 2 ± 3 cm² and wound circumference improved from 175 ± 113 to 13 ± 13 mm. These were both clinically and statistically significant ($p < 0.01$). For the control group, area went from 13 ± 14 cm to 11 ± 14 cm² ($p = 0.06$) and circumference from 157 ± 82 to $97 \pm$ mm ($p = 0.12$), see table 1. Pain score rating and medication use were both significantly better for the treated group compared to control, table 2. Fig 1 and Fig 2 show examples of progressive healing with PEMF.

Conclusion: Our results confirm the vulnerary potential of PEMF therapy for patients with chronic venous stasis ulcers when combined with standard evidence-based care. Because of the short study interval, we were only able to document improved healing trajectory not necessarily complete healing. We were also able to document improved pain control with this technology. Pain control may translate to less inflammation and suggest a mechanism of action in this clinical setting. Further work is needed to better elucidate mechanism and long-term efficacy.

Da

Table 1.

	Pre-Treatment
Area (cm2)	Control: 13 ± 14.5 PEMF: 17 ± 15
Circumference (mm)	Control: 157 ± 82 PEMF: 175 ± 113

Table 2.

	Control
Pain score**	6 ± 2
MQS III**	24 ± 12

**Pain score and MQS III value used data from up and data collections considerations.
* $p < 0.05$ significant

Patier

Figure 1
47 y.o male 3 year history of chro

Before



Therapy For Non-healing Leg Ulcers

avani Ramanujan MD; Aamir Siddiqui MD,

ic Surgery

n, Detroit, Michigan

ta

Post- Treatment	p-value
Control: 11±14	0.06
PEMF: 3±3.2	<0.01*
Control: 97±98	0.12
PEMF:13±13	<0.01*

Treated	p-value
4 ± 2	<0.01*
14 ± 7	<0.01*

the second 8 weeks of the study to avoid ramp

nt Photos

nic venous ulcer.

After completion of PEMF therapy



Figure 2

36 y.o female 6 month history of injury to left medial leg

Before

After completion of PEMF therapy



Bibliography

- Rohde, C. H., Taylor, E. F., Alonso, A., Ascherman, J. A., Hardy, K., & Pilla, A. A. (2015). Pulsed Electromagnetic Fields Reduce Postoperative Interleukin-1 β , Pain, and Inflammation. *Plastic and Reconstructive Surgery*, 135(5), 808e–817e. <https://doi.org/10.1097/prs.0000000000001152>
- Markov, M. S. (2007). Expanding Use of Pulsed Electromagnetic Field Therapies. *Electromagnetic Biology and Medicine*, 26(3), 257–274. <https://doi.org/10.1080/15368370701580806>
- Sisken, B. F., & Walker, J. (1995). Therapeutic Aspects of Electromagnetic Fields for Soft-Tissue Healing. In *Advances in chemistry series*. American Chemical Society. <https://doi.org/10.1021/ba-1995-0250.ch015>
- Moor, A. N., Vachon, D. J., & Gould, L. J. (2009). Proteolytic activity in wound fluids and tissues derived from chronic venous leg ulcers. *Wound Repair and Regeneration*, 17(6), 832–839. <https://doi.org/10.1111/j.1524-475x.2009.00547.x>
- Harden, R. N., Weinland, S. R., Remble, T. A., Houle, T. T., Colio, S., Steedman, S., & Kee, W. G. (2005). Medication Quantification Scale Version III: Update in Medication Classes and Revised Detriment Weights by Survey of American Pain Society Physicians. *The Journal of Pain*, 6(6), 364–371. <https://doi.org/10.1016/j.jpain.2005.01.350>

PEMF Systems, Inc's Products Are The Most Technologically Advanced

Every PEMF product manufacturer has different theories about the most effective pulse rate, amount of magnetic energy, shape of waveform and treatment time. However, no actual research to determine if any of these parameters are preferable has ever been done nor which are the best pulse rates, the best amount of magnetic energy, the best wave form, or the best treatment duration to treat the various conditions PEMF Therapy can treat.

Most PEMF manufacturers on the market offer products with factory preset controls that are unchangeable with settings they have arbitrarily selected.

PEMF Systems, Inc. has developed innovative Pulsed Electro Magnetic Field ("PEMF") therapy products for nearly two decades and is a fully accredited medical product manufacturer with ISO 13485 Certification. All our models are fully safety tested.

PEMF Systems, Inc's digital products are different and unique as they incorporate a revolutionary advancement in PEMF Therapy. Our digital models have both a high power and a low power PEMF Therapy device running concurrently to provide a more effective and broad spectrum treatment than any other PEMF product on the market.

All our digital models are computer controlled and totally programmable. This is revolutionary and completely changes the way PEMF products operate. This also means that we can modify our digital models programs to deliver optimum healing therapy as additional PEMF medical studies are done, and new information is learned,.

PEMF therapy is effective, non-invasive, reduces pain and inflammation, and improves mobility. PEMF therapy provides patients with faster rehabilitation. And with faster recovery and rehabilitation, PEMF therapy also improves the perception patients have of the quality of healthcare they receive.