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MEETING PAPERS

Pulsed Signal Therapy® for the treatment of musculoskeletal conditions: a millennium paradigm

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Abstract

Reports and reviews from various sources, including the World Health Organization and United Nations Population Division, confirm the general increasing trend in the ageing population groups worldwide. There are over 150 types of musculoskeletal conditions, with rheumatoid arthritis, osteoarthritis, osteoporosis, low back pain and limb trauma, accounting for the greatest impact on the population at large. Osteoarthritis (OA) is predicted to become the fourth leading cause of disability by the year 2020. The most common medication prescribed for OA is non-steroidal anti-inflammatory drugs (NSAIDs). These have long been associated with numerous adverse effects, are costly and short-term in their 'therapeutic' effect. Pulsed Signal Therapy® (PST™) is an innovative treatment modality for musculoskeletal conditions. It has been commercially available since 1992, is currently employed in at least 800 clinics and/or medical institutes, and to-date, no adverse effects have been reported. Furthermore, it is non-invasive, non-pharmacological, painless, with long-term follow-up, and sustained efficacy. When connective tissue is injured and physiological signalling is disturbed or absent, PST™, as the external, biophysical signal (stimulus) of physiological energy parameters and waveform, passively induces 'fluid flow' in the injured area, creating 'streaming potentials', that induce biophysical-biochemical coupling, subsequent signal transduction, to activate repair and regenerative processes. In doing so, it restores the innate, physiological signalling to enable these regenerative and repair processes to continue naturally.

Key words: biophysical-biochemical coupling, electromagnetic, mechanotransduction, musculoskeletal conditions, osteoarthritis, PST, Pulsed Signal Therapy.

INTRODUCTION

Over 150 disorders and syndromes, which are usually progressive and associated with pain, may be classified as musculoskeletal conditions.[1] They are generally broadly categorized as joint diseases, physical disability, spinal disorders and conditions resulting from trauma.[1] Of these, those conditions with the greatest impact on society include rheumatoid arthritis (RA), osteoarthritis (OA), osteoporosis (OP), low back pain and limb trauma, because they are the leading causes of morbidity, disability and job loss, and are also costly to health systems.[1] Moreover, as the ageing of most population groups continues to increase, their impact is expected to increase accordingly.[1]

Osteoarthritis (OA) is a non-inflammatory joint disease of one or more small joint systems, which mainly affects articular cartilage.[2] It is associated with ageing and mostly affects the weight-bearing joints – that is, the joints that have been continuously stressed throughout the years, including the knees, hips, fingers and lower spine area.[2] Primary OA is related to ageing and cartilage degradation occurs as a result of wear and tear.[3] Secondary OA either occurs as a result of another disease, disorder or condition, for example, obesity, or

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is traumatically induced.[3] Osteoarthritis represents one of the most common chronic diseases in the world, affecting all racial and ethnic groups. There are numerous medical modalities currently available for OA treatment, ranging from simple home treatments, including paraffin baths and heat, to those at the other end of the treatment spectrum, namely surgery. The prescription drugs available for OA treatment such as NSAIDs, have long been associated with undesirable, untoward effects, high costs and short duration of 'therapeutic' effects. More recently COX-2 inhibitors, referred to in the Epilogue, have been introduced and have summarily come under scrutiny for their adverse effects. It is not surprising therefore that scientists continue their endeavour to find a more desirable form of treatment modality for OA.

Pulsed Signal Therapy® (PST™) is a patented medical technology, developed over 20 years of intense scientific research. It has been commercially available since 1992 and is currently employed in at least 800 clinics and/or medical institutes, worldwide. A score of clinical trials and studies have demonstrated PST™ therapeutic success and long-term benefits for the treatment of musculoskeletal conditions, most notably OA. Over ten well-designed *in vitro* studies have confirmed these clinical data. PST™ has been shown not only to be safe and effective, but is painless, non-invasive, non-pharmacological, with long-term follow-up, sustained efficacy and an absence of any known adverse effects.[4]

Before dwelling into an insight of the electrophysiology of the joint, biophysical-biochemical coupling and the role of PST™, perhaps a brief introduction to PST™ as a treatment modality may be warranted.

THE FUNDAMENTALS OF PST™

PST™ is based on pulsed electromagnetic field therapy, but differs in its array of unique energy parameters

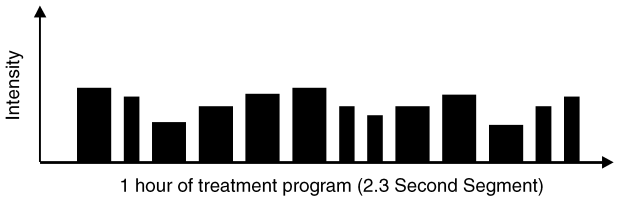


Figure 1 Pulsed Signal Therapy® (PST™)

(refer to Table 1 for a comparison). All PST™ devices have received regulatory approval as medical devices according to the International Medical Device Directive (MDD) 93/42/EEC and EN ISO 13485. They consist of a magnetic field generator, connected to a ring-shaped coil, or other applicator, by means of an electronic interface, that produces a pulsed DC magnetic field of 0.28 W, with field intensity not greater than 20 Gauss (maximum) and frequency 5–24 Hz, and emits a proprietary signal, quasi-rectangular in waveform (Fig. 1). There are a number of different devices available, with coil sizes optimally suited for the treatment of the specified joint(s) or body area(s). In general, there are devices for the treatment of the peripheral joints/extremities (knees, shoulders and wrists), the spine (cervical, thoracic and lumbar axial vertebral bodies), tinnitus and dental disorders, including temporomandibular joint disorder (TMJ). There are also other devices specifically designed for veterinary use. The development of a multifunctional kombi device, PST-Osteo® (arthrosis, osteoporosis, fibromyalgia), was completed in early 2004, for the treatment of osteoporosis (OP), fibromyalgia and/or OA. With this device, the entire body, from the shoulders to the pelvic girdle, is ideally treated. As the patient lies in the device, the coil is lowered to the anterior aspect of the thorax, as far as possible, around the body accordingly. In this way, induction of PST™ treatment is attained with greater efficacy and efficiency.

Table 1 Comparison of energy characteristics

Device parameter	Magnetic field therapy	PST™
Electromagnetic properties	Piezoelectric	Biological signal
Energy form	Alternating current	Direct current
Frequency	44–77 Hz	1–30 Hz
Waveform	Sinusoidal	Quasi-rectangular
Field Strength	2G	12.5G
Energy driver	Voltage control	Pulsed DC
Duty cycle	< 50%	> 50%
Pulse frequency	Continuous	Pulse-modulated
Frequency source	Fixed frequency source	6 frequency sources
Implementation	Diode (biasing)	Free-wheeling diode

PST™ 'ON WHEELS'!

In a society governed by time and money, the PST™ original equipment was embodied in a miniaturized format to enable patients to administer treatment at his/her own convenience at home, office – virtually, anywhere! The treating physician, or therapist, carries out the first treatment with the PST Mobil®, and instructs the patient accordingly. Thereafter, it is safely and conveniently packaged into a wheeled cart, as used on board airplanes, for easy transport.

BIOPHYSICAL-BIOCHEMICAL COUPLING IN RELATION TO PST™

The joint is composed of connective tissue – soft (cartilage), dense (ligaments and tendons) and hard (bone). As a structural tissue, cartilage consists of approximately 60–80% water and an intercellular matrix of basic substances, namely proteoglycans, glucoproteins and collagen (filaments), manufactured by the cartilage cells (chondrocytes).[5] Attached to the proteoglycans are several glycosaminoglycan (GAG) chains, possessing negatively charged sulphate (SO_4^{2-}) and carboxyl (COO^-) groups.

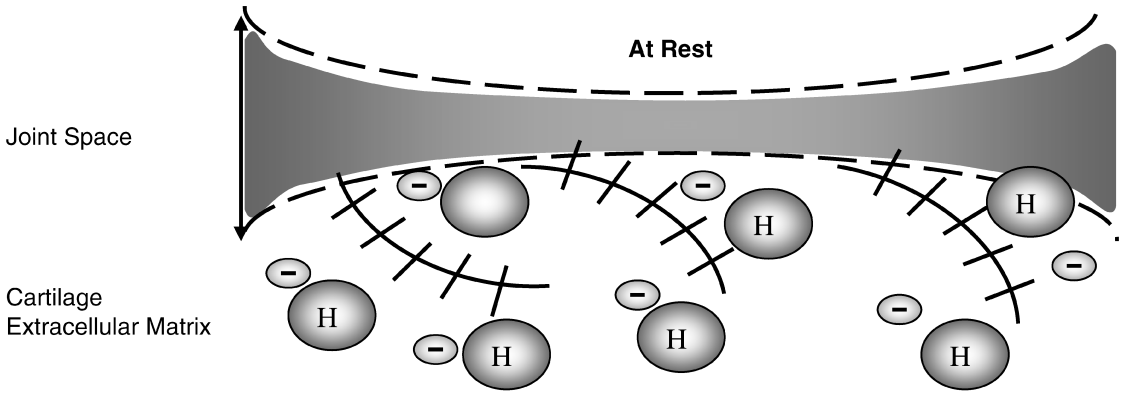
Biophysically, when a healthy joint is subjected to a load or mild stress (walking, for example), hydrogen protons (of water) are forced through the extracellular matrix (ECM), into the synovial space, leaving a net, negative charge within the matrix. This mechanotransduction causes a small, pulsed energy signal, piezoelectric signal ('streaming potential'), to be generated in the ECM.

Biochemically, one can envision cells to be 'hard-wired' to respond to external stimuli, including fluid flow. Although several hypotheses have been proposed linking physical forces to intracellular signalling pathways, in many cases, the molecular mechanisms of mechanotransduction remain elusive. Some research studies have suggested that the biochemical coupling occurring at the cellular membrane occurs through the integrin-cytoskeleton-nuclear matrix scaffold, ionic channels within the cell membrane, G-protein-dependent pathways, and/or linkage of the cytoskeleton with the phospholipase A, and/or C, pathways.[6–8] Recently, for example, Tschumperlin *et al.* from the Department of Environmental Health, Harvard Medical School, Massachusetts, US, found that compressive stress shrinks the lateral intercellular space surrounding epithelial cells, triggering cellular signalling via autocrine binding of epidermal growth factor family ligands to the epidermal growth factor receptor.[9] Autocrine ligands are constantly shed, collapsing into the lateral intercellular space, increasing the local ligand concentrations, enabling sufficient receptor signalling to occur.[9] In another recent study, Vassilios *et al.* working on cells of the mammalian brain, reported that the transient receptor potential (TRP) super-family of ion channels act as cellular sensors, translating external signals (stimuli) into changes in membrane excitability and increased intracellular calcium.[10] These receptor-operated channels are activated by G-protein-coupled receptor (GPCR) and receptor tyrosine kinase (RTK) stimulation. To prevent continuous calcium influx, Clapham *et al.* further demonstrated that growth factor stimulation initiates a response termed 'rapid vesicular insertion of TRP' (RiVIT), whereby TRPC ion channels are rapidly translocated to the cell surface from vesicles held in reserve just under the plasma membrane.[10] Ergo, these and other studies show that biochemical coupling, signalling pathways and the response elicited as a result thereof, are diverse and dependent on the type of tissue targeted and the 'incoming' biophysical signal – different signals trigger different coupling mechanisms in different tissues, to activate appropriate pathway(s). Communication of the signal to adjacent cells may occur through cell processes connected by gap junctions.[6,11]

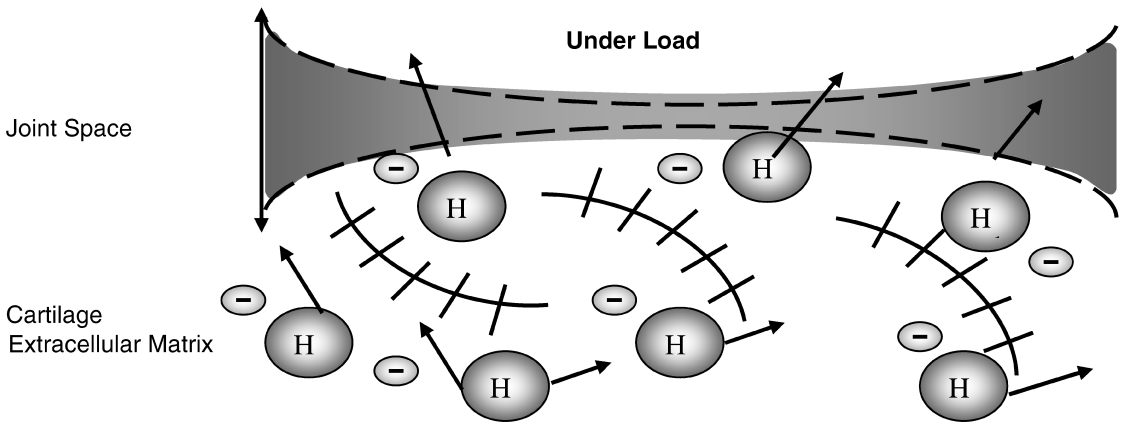
The pending question: Where does PST™ play a role? When a joint surface is progressively worn down as a result of non-physiological loading, including overweight, incorrect positioning, inactivity and changes in the synovia, due to infection, attrition and eventual destruction of the cartilage eventually occurs. As a result, the innate mechanotransduction, biophysical-biochemical coupling, signal transduction and resultant effector cell response, is weak, fails to elicit a response, or is totally absent, such that regeneration and repair processes gradually decrease and/or cease. In such cases, PST™ acts as the external biophysical signal (stimulus) of physiological energy parameters and waveform. It passively induces 'fluid flow', creates 'streaming potentials', to trigger biochemical coupling, signal transduction and elicitation of the repair and regenerative processes (Fig. 2). In cartilage, for example, this passive induction and transduction into an electric (electromagnetic) phenomenon, results in the stimulation of chondrocytes to produce essential matrix components, including proteoglycan and collagen, without having to subject the affected tissues to any load.

TREATMENT PROTOCOL AND INDUCTION OF TREATMENT

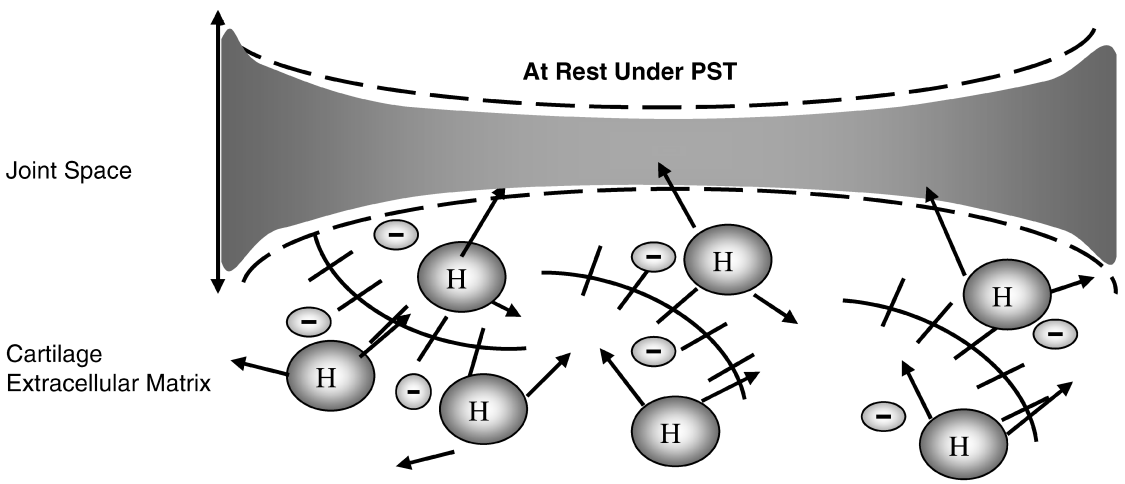
The most unique feature of PST™ is undoubtedly its patented signal. Intense scientific investigations into



Charge equilibrium between hydrogen protons and negative charge carriers in the extracellular cartilage matrix



Creation of a streaming voltage potential in the ECM during loading caused by the 'compression' of fixed negatively charged fluid forced out of cartilage tissue with forced movement displacement of the hydrogen protons (joint flexion)



Generation of Streaming Potentials flow in the Joint caused by forced movement of hydrogen protons in the ECM through alternating PST signals as stimulation of chondrocytes in the connective tissue matrix

Figure 2 Mechanism of action of Pulsed Signal Therapy.

the electrical properties of tissue, including conductivity, enabled development of this signal of unique energy parameters. Unless a signal's energy parameters lie within the physiological range of the particular tissue, the desired tissue response/process will not be induced. Ergo, since the unique PST™ signal is in the 'biological window' of connective tissue, it mimics the electrical (electromagnetic) signalling naturally occurring in the body and sets the regenerative and repair processes in motion.

A full therapy course consists of nine or twelve one-hour daily treatments, administered on consecutive working days, with allowed interruption of a maximum of 48 hours over the weekend. Twelve treatments are carried out for the vertebral column (cervical/thoracic/lumbar spine, shoulders, hips) and/or full body (thorax). PST™ administration is strictly reserved for qualified physicians and health professionals who have been licensed to do so, after successful completion of a specially formulated training course. This course was designed in conjunction with the treatment protocol and provides hands-on training with each specific device, and in addition, knowledge on how to conduct a double-blind trial, how to obtain an accurate history of the patient and how to perform a thorough physical examination, before and after treatment.

STUDIES SUPPORTING PST™ THERAPEUTIC POTENTIAL

Over 25 rigorously controlled clinical trials have been conducted globally with PST™ at well-respected universities, medical clinics and/or centers, as well as their affiliated medical institutions (Tables 2 and 3). These have served to consistently verify PST™ long-term follow-up success. In addition to clinical trials, expansive *in vitro* and scientific imaging, research studies (Table 4), have been carried out to elucidate PST™ postulated mechanisms of action, its efficacy and the safety profile of its unique patented signal.[12] These *in vitro* studies have also substantiated and confirmed the *in vivo* clinical trials.

Clinical and *in vitro* studies

These have included double-blind and other open-label randomized clinical trials in over 100,000 patients, including Europe (France, Italy and Germany), the US and Canada (Tables 2 and 3). In addition to OA, temporomandibular joint pain and morbus tinnitus have been widely studied in Europe, leading to regulatory approval under the international MDD 93/42/EEC and ISO 9001.[13] A four-year study was launched in 1990, at a Yale University-affiliated teaching hospital, to investigate PST™ therapeutic benefits for sport and other traumatic joint injuries, with encouraging data and results.[14,15] The clinical benefits were confirmed in 1997 in a study conducted in Canada with PST™, investigating its effects in the treatment of chronic pain due to traumatic soft tissue injury (degenerative joint disease, muscle/ligament/tendon injuries, disc degeneration-herniation).[16] As a result, a large number of sport-type injury clinics have been established in Europe and Asia since 1996, and PST™ is available at most European soccer team sites, including the German athletic team that requested PST™ at the Sydney 2000 Olympic Games and the German water polo team for the Olympics in Athens, 2004, as well as many other world-class sportsmen and women, teams and international events (Oliver-Sven Büder, German shotputter; Nicolas Kiefer, German tennis player; Mark Dzemski, a boxer; Jamir Rednapp, Tottenham Hotspur, Liverpool, England footballer; Darren Gough, Essex England cricketer; international ski teams; FC Kaiserslautern and Borussia Mönchengladbach football teams; Stuttgart and Hamburg Ballet groups [Germany], to name a few).

In these clinical trials, pain was evaluated using WOMAC, and later OMERACT III, validated instruments of outcome measurements. Functionality was measured using WOMAC and modified Ritchie scales, as well as global evaluations of improvement by the patient and physician.

With the ageing population, another connective tissue disorder that has established itself as an endemic health problem is osteoporosis (OP). According to a special report 'Fighting Osteoporosis', 30 April, 2004, OP is a disease of global proportions and affects more than 200 million people worldwide. It affects both women and men, over 20 million women and 5 million men in the US alone.[17] Statistics show that every 30 seconds, someone in the European Union suffers a fracture as a result of OP, that one in three women, and one in eight men, will suffer at least one OP-related fracture during their lifetime, and that approximately one-third of women aged 60–70, and two-thirds of women aged 80 or older, are affected. In the US alone, over 2 million men, 65 or older, suffer from OP. By the year 2050, the number of hip fractures worldwide is expected to rise from 1.7 million (in 1990) to 6.3 million.[17] Although a diverse number of medications are currently available on the market for the prevention and treatment of OP, they are not met without serious side-effects, including thrombosis, cardiovascular effects,

Table 2 Completed clinical studies/USA

Nature of study	Institution where study was conducted	Study director(s)	Publication	Comments
DB-1 (Initial Pilot) A double-blind trial of the clinical effects of pulsed electromagnetic fields in osteoarthritis.	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	T.P. Greco, Richard Markoll	*Journal of Rheumatology* 1993; 20, 456–60	Good to very good results, with high statistical significance
DB-2 (2nd Pilot) A double-blind trial of the clinical effects of pulsed electromagnetic fields in osteoarthritis	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	D.H. Trock, A.J. Bollet	*Journal of Rheumatology* 1993; 20, 456–60	Good to very good results, with high statistical significance
DB-3 The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee	Three trial centers under a protocol from Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	D.H. Trock, R. Roseff, M. Spiegel	*Journal of Rheumatology* 1994; 21, 1903–1911	Good to very good results, with high statistical significance for pain, pain on motion; and for both the patient's, and physician's, global assessment
DB-4 The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the cervical spine		E. Heller, R.M. Higley, R.H. Dyer, Jr., W.K. Miner, S.H. DeWitt		
Open initial trial Prospective study using extremely low frequency electromagnetic induction therapy in the treatment of patients with inflammatory and non-inflammatory arthritis	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	T.P. Greco, R. Markoll		Good to very good results, with high statistical significance
Open Trial 1 A Prospective study using extremely low frequency electromagnetic induction therapy in the treatment of patients with inflammatory and non-inflammatory arthritis	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	R.H. Dryer, Jr., W.K. Miner, S.H. De Witt		Good to very good results, with high statistical significance
Open Trial 2 A prospective study using extremely low frequency electromagnetic induction therapy in the treatment of patients with inflammatory and non-inflammatory arthritis	Three Trial Centers under a protocol from Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	D.H. Trock, R. Roseff, M. Spiegel, E. Heller, R.M. Higley		Good to very good results, with high statistical significance
Pulsed Signal Therapy: treatment of chronic pain due to traumatic soft tissue injury	McGill University, Vancouver, Canada	C. Hershler, A. Sjaus	*International Medical Journal* 1999; 6, 167–73	High statistical significance. This study also showed that PST™ is as effective for the treatment of STI, as it is for OA

Table 3 Completed clinical studies/Europe

Nature of study	Institution where study was conducted	Study director(s)	Publication	Comments
Efficacy of pulsed electromagnetic therapy (PST) in painful knee osteoarthritis. (French publication)	Cochin Hospital, Paris, France	S. Perrot, M. Marty, A. Kahan, C.-J. Menkés	1. American College of Rheumatology presentation, November 1998. 1. *Arthritis Rheum* 1998; 41, S. 357 2. *Arthritis Rheum* 2002; 222, 101–4	Good to very good results, with high statistical significance
PST – A proposal for a chondro-protection with physical methods. (Italian publication)	Niguarda Hospital, Milano, Italy	M. Cossu N. Portale	*La Riabilitazione-Revista di Medicina Fisca e Riabilitazione* 1998; 31, 51–9	The results confirmed that PST™ has a beneficial effect at the end of therapy, and long-term too
The use of Pulsed Signal Therapy (PST) in the treatment of arthritis of the hand. (Italian publication)	Niguarda Hospital, Milano, Italy	M. Cossu, C. Leuci, N. Sias	*La Riabilitazione-Revista di Medicina Fisca e Riabilitazione* 000; 33, 109–14	High success rate post 6-months [76.19% (VAS); 80.95% (algofunctional index)]
The use of Pulsed Signal Therapy (PST) in osteoarthritis of the knee. (Italian publication)	Niguarda Hospital, Milano, Italy	M Cossu, N. Sias, G. Devito	*La Riabilitazione-Revista di Medicina Fisca e Riabilitazione* 001; 34, 213–18	High statistical significance
Procedural proposal for patients suffering with osteoarthritis of the knee by means of PST vs. placebo	University of Siena, Siena	R. Marcolongo		High statistical significance
Preliminary results of the treatment of osteochondral knee injuries, with Pulsed Signal Therapy. (Italian publication)	Università degli Studi di Catania	M. Di Martino, S. Avondo, T.C. Russo, M.G. Onesta, G. Sessa	*Atti del Congresso della Società Medico-Chirurgica Catanese* – Novembre 2002	High statistical significance
Long-term results achieved by Pulsed Signal Therapy (PST). (Italian publication)	Niguarda Hospital, Milano, Italy	M. Cossu, C. Leuci	*La Riabilitazione-Revista di Medicina Fisca e Riabilitazione* 1999; 32, 11–5	PST™-effects were long-term, that is, decreased pain intensity and improved functionality, prevailed, at 1 years post
Prospective, clinical verification study of PST in gonarthrosis, coxarthrosis and degenerative disorders of the lumbar spine	PST™ Treatment Center Munich, TU Munich	S. Frhr von Gumppenberg M. Faensen, H. Martin, R. Breul	1. *Medycyna Sportowa* 1998, XIV, 31–34. 1. Poster Presentation: *14. GOTS Kongress für Sport orthopädie und Sportstrauma-tologie* 25–27 June 1999, München 2. Presentation: *Norddeutsche Orthopäden-vereinigung e.V. 48. Jahrestagung*, Münster, 17–19 June, 1999	High statistical significance

Table 3 *Continued*

Nature of study	Institution where study was conducted	Study director(s)	Publication	Comments
Multicenter-study of the clinical effect of Pulsed Signal Therapy in arthrosis of the knee (gonarthrosis, grade II and III, Kellgren.) (German publication)	Ludwig-Maximilians-Universität, Munich	M. Faensen, R. Breul	*Orthopädische Praxis*, 2001; 37, 701–9	High statistical significance
Permanent Prospective Study (VITAL) (Pooled data)		R. Breul, F. Hahn, D. Rost		High statistical significance; further documentation and analysis of the patient data
Pulsed Signal Therapy in the treatment of anterior disk displacement without reduction. (An observational study; pilot study to the double-blind, below) (German publication)	Humboldt-Universität, Berlin	I. Peroz, Y.-H. P. Chun, J.-F. Roulet, K.-P. Lange	*Deutsche Zahnärztliche Zeitschrift mit Deutsche Zahn-, Mund- und Kieferheilkunde* 1999; 54, 284–7	
Pulsed Signal Therapy for the treatment of temporomandibular arthropathy – preliminary results of a double-blind study	Humboldt Universität, Berlin	G. Karageorgi, I. Peroz, Ch. Schwerin, Y.-H. Chun, O. Bernhardt, J.-F. Roulet *et al.*		Significant reduction in pain, and an improvement in moving & opening the lower jaw
Morbus tinnitus (a pilot study)	Medical practice(s)	K. Pfeiffer *et al.*		Goebel-Hiller Scores – definite & significant improvement in 52% of patients, increasing in the long term
Chronischer mobus tinnitus (a pilot study)	Medical practices in Munich	K. Pfeiffer, R. Markoll, R. Breul		A definite improvement at 3 months post-PST® treatment, which increased in the long term
Three prospective clinical trials conducted in Berlin, Nuremberg and Munich, Germany, on chronic tinnitus (Grades, II, III, or IV)	Three prospective clinical trials conducted in Berlin, Nuremberg and Munich	M. Dornacher, G. Buschmann, K. Pfeiffer *et al.*		Increasing trend in improvement at the end of treatment and six weeks post. At 12 weeks post-treatment, 26% were unchanged, 52% were very significantly improved, and 22% were completely symptom free

Table 4 Completed *in vitro* studies

Nature of study	Institution where study was conducted	Study director(s)	Publication	Comments
The stimulation of chondrocyte metabolism by pulsed magnetic fields	North Shore University Hospital, New York (affiliated with Cornell University), USA	D.-A. Grande, A.J. Bollet, R. Markoll	Draft, 1992	*In vitro* bovine cartilage explants maintained in organ culture, showed statistically significant differences in sulphate incorporation, post-PST™ exposure ($P < 0.05$), suggesting PST™ increases proteoglycan synthesis
Pulsed Signal Therapy (PST) enhances the proteoglycans concentration in human chondrocyte cultures	Institute of Rheumatology, University of Siena, Siena, Italy	F. Nerucci, A. Fioravanti C. Tofi, K. Righeschi, R. Marcolongo, R. Markoll	1. *BEMS Twenty-Second Annual Meeting Abstract Book*, Munich, Germany, June 11–16, 2000: 48. 2. *Ann Rheum Dis*. 2002; 61, 1032–33	Human articular chondrocytes were cultured in the presence and absence of IL-β and subjected to PST™. A significant ($P < 0.05$) increase in proteoglycan concentration was measured in cultures exposed to PST™, compared to control cultures. Both qualitative and quantitative investigations were conducted
Pulsed Signal Therapy (PST) stimulates mitosis of human chondrocytes in culture	Praxis für Orthopädie und Sportstraumatologie Cologne, Germany	H. Gierse, R. Breul, M. Faensen, R. Markoll	Singapore Humanitas Press, In Proceedings: *Tenth International Conference on Biomedical Engineering. Singapore* December 2000; 473–474	Human chondrocyte cell cultures exposed to PST™ attained statistically significant higher mitosis-rates, than chondrocytes in untreated cultures
The PST effect on 3-dimensional chondrocyte culture: an in vitro study	University Center, Charité, Humboldt University, Berlin, Germany	I. Krüger, T. Knedel, J. Zimmermann, M. Sittinger, M. Faensen	1. Presentation: PST™ Symposium, Salzburg, Austria; May 19, 2001. 1. Presentation: 1st Biennial Meeting of the ETES – 2001 2. ICRS Symposium, Freiburg, Germany; November 7–10, 2001	In general, biochemical analysis of meniscal and articular chondrocyte cultures showed increased collagen and proteoglycan synthesis in cultures exposed to PST™, compared to control cultures
The clinical effect of PST™ in gonarthrosis – analysis of synovial fluid	Auguste-Victoria-Hospital Berlin, University of Erlangen	D. Schuppan, M. Faensen R. Markoll D. Ferreira	In press	Two-tailed paired *t*-test showed statistically significant ($P < 0.05$) differences between pre- and post-PST™ treatment for MMP-1/protein, tenascin-C/protein, MMP-9/collagen IV and MMP-9/TIMP; and also in all pain intensity and ADL parameters assessed. PST™ appears to regulate/ control the release of MMP, and other matrix parameters, during joint remodelling

gastrointestinal effects, among others. More so, until recently, with the synthetic development of the parathyroid hormone, teriparatide, no medication increased bone formation, but merely decreased bone resorption. Furthermore, in OP treatment, improvement of bone architecture and quality cannot be ignored. Pooled data from an OP pilot study of postmenopausal women treated with PST™, demonstrated an increasing trend in bone formation, post-PST™ treatment. The percentage increase in bone formation at 6 months post-treatment was almost 6% (internal data). Amid conventional treatment options available and demands for alternative therapies, such promising findings prompted initiation of a long-term, multicenter, post-marketing surveillance with PST™, in the treatment of postmenopausal women with OP. Currently, this multicenter, clinical study is underway in Germany.

In vitro studies

The clinical efficacy of PST™ is strongly supported by published *in vitro* studies (Table 4).

The Grande study, conducted in 1992, was the first study reporting the *in vitro* effect of PST™ on bovine cartilage explants, maintained in organ culture.[18] Data obtained showed a statistically significant effect ($P < 0.05$), as measured by sulphate incorporation. This is indicative of GAG production, and therefore proteoglycan synthesis. Subsequent studies conducted at both the University of Siena's Institute of Rheumatology[19] and Humboldt University, Berlin[20] confirmed these results. Of particular interest is the study conducted at the University of Siena. This study focused on both the biochemical and morphological effects of PST™ on human articular chondrocytes cultured in the presence and absence of interleukin-1β (IL-1β) and subjected to PST™. Cells treated with IL-1β (a pro-inflammatory cytokine) showed massive cell destruction, including vacuolization.[21] In retrospect, healthy cells stimulated with PST™ show no tendency to destruction or damage, but remained in a healthy state. Qualitatively, using transmission electron microscopy (TEM) and scanning-electron microscopy (SEM), morphological regeneration and restoration of cellular moieties, as well as structural integrity, could be observed in chondrocyte cell cultures destroyed by IL-1β and thereafter subjected to PST™. Quantitatively, proteoglycan synthesis by chondrocytes was measured.[21] It was postulated that PST™ results in electric and magnetic stimulation of receptors, ionic movement, including calcium, across cell membranes, to stimulate DNA transcription and protein synthesis.[22–24] These findings collaborate with other studies demonstrating electric stimuli and PEMF-enhanced cartilage repair processes, increased [^{3}H]-thymidine incorporation into the DNA of chondrocytes (proliferation), as well as $^{35}SO_4$ uptake (GAG production).[18,22,23,25]

In 2000, Gierse *et al*. conducted a study in Cologne, Germany, exposing human chondrocyte cell cultures to PST™. They reported statistically significant higher mitosis rates (almost two-fold), compared to chondrocytes in untreated cultures.[26]

A study, conducted at the University of Erlangen, Germany, investigated the effect of PST™ in joint remodelling. The literature reports that one of the underlying causes of OA is an imbalance of the physiological degradation and repair processes of joint cartilage.[27] OA leads to cartilage loss, damage to bone, intra-articular ligaments, as well as tendons and also causes inflammation of adjacent soft-tissues.[27,28] OA is characterized by an unopposed degradation of cartilage proteoglycans and collagens by a spectrum of proteinases.[23] There are essentially four classes of enzymes responsible for the degradation of the ECM components in OA, namely cysteine and aspartic proteinases that act intracellularly at acidic pH, and serine and matrix metalloproteinases (MMPs) that act extracellularly at neutral pH.[29] MMPs are considered the most important enzymes in ECM degradation. However, these MMPs can also initiate repair processes, setting the stage for regeneration of the injured tissue.[30–34] Matrix parameters, including MMPs, -1, -2, -3, and -9, TIMP1 (tissue inhibitor of metalloproteinase); collagens IV and VI, as well as tenascin-C (TC) and hyaluronan (HA), were measured pre- and post-PST™ treatment. Synovial fluid was effused from both healthy and arthritic knees of 21 patients, pre- and 6-weeks post-PST™ treatment. Fluids were analysed in relation to connective tissue proliferation, collagen IV and collagen VI synthesis, as well as HA and associated matrix protein, TC. The level of matrix parameters was correlated to changes in clinical parameters such as performance, pain intensity and activities of daily living (ADL), that were assessed using VAS (Visual Analog Scale). Data showed statistically significant increases in ratios of measured parameters of interest, that correlated with improvement in clinical symptoms, including ADL, post-PST™ treatment. In general, PST™ appears to regulate the release of MMP and other matrix parameters, during joint remodelling, such that connective tissue cells (and associated cells) may be reactivated to commence regeneration of the matrix and its components. These study results are currently in press.

Imaging study

It is often said 'A picture is worth a thousand words . . .' In order to enhance, and further substantiate, the potential therapeutic effects of PST™, it was decided to employ another technique, namely Kirlian photography, in order to establish whether the effect of PST™ on energy fields in OA patients, could be corroborated. This technique produces photon images in the presence of a high-frequency electrical field to generate a spark discharge around animate or inanimate objects that are believed to reflect its energy flow characteristics.[35] A > 300-patient study, confirmed significant changes in energy fields following PST™ treatment, thereby illustrating its ability to restore the efficient transmission of the electromagnetic stimulus, hampered in damaged tissue.[35]

INDICATIONS AND LIMITATIONS

Anecdotal information regarding the therapeutic potential and applications of PST™ in other medical disorders is available, and in some cases pilot studies have been conducted to verify results. PST™ medical applications include:

1. Anterior cruciate ligament surgical repair and rehabilitation, tendinitis, fresh bone fractures and stress fractures, ankylosing spondylitis, meniscus tears, spondylolisthesis and hernia disci;
2. Fibromygalia, asceptic necrosis, bilateral avascular necrosis of the femur neck;
3. Metatarsalalgia, carpal tunnel syndrome;
4. Osteoporosis;
5. Morton's syndrome (Morton's neuroma), epilepsy (non-responsive to medication);
6. Referred sciatic nerve pain;
7. Delayed poliomyletitis syndrome (sequela);
8. Plantar fascitis;
9. Diabetic neuropathy;
10. Migraine headaches;
11. Atrophy of the plantar metatarsal fat pad;
12. Acute burns.

There are no contraindications for PST™; however, the following cases are generally carefully considered, for medical/insurance/legal reasons:

- Pregnancy;
- Those with pacemakers: no treatment of the cervical/thoracic/lumbar spine and shoulders;
- Cancer patients in the region of the primary lesion, if in remission for less than 5 years;
- Patients with bacterial infections of the joints.

EPILOGUE

Musculoskeletal (MS) conditions are a major burden, not only on individuals, but also on health and social care systems.[1] There are four major MS conditions that are particularly burdensome, namely OA, rheumatoid arthritis (RA), OP and low back pain. In general, the prevalence of MS conditions is higher among women, increases with age, and is the main cause of pain and disability within the older age group.[36] According to a revised report in 2002 from the United Nations Population Division regarding world population prospects, the world population is growing at a rate of 1.2% annually, implying a net addition of 77 million people per year.[37] It seems that six countries account for half of this annual increment: India 21%; China 12%; Pakistan 5%; Bangladesh, Nigeria and the US, 4% each.[37] Worldwide estimates indicate that OA affects 9.6% of men and 18% of women, over the age of 60, and RA affects 0.3–1.0% of the global population.[38] The number of hip fractures (the most detrimental fracture) associated with OP is constantly on the rise, and is predicted to be 6.3 million worldwide by 2050. In addition, it appears that the Asian populations will be most likely affected, since more than half of the hip fractures are predicted to occur in Asia by 2050.[39] Low back pain is the most prevalent MS condition and affects 4–33% of the population at any point in time.[1]

With increases in life expectancy and ageing populations, it is predicted that OA will be the fourth leading cause of disability by 2020.[1] OA is, in general, more prevalent in Europe and the US than in other parts of the world. African-American women are more prone to OA of the knee than white women,[40] but not of the hip.[41] OA of the hip is more prevalent among European whites than Jamaican blacks,[42] African blacks[43] or Chinese.[44] Most people burdened by OA are on daily medication, generally known as NSAIDs, not only associated with gastrointestinal bleeding, but liver disease, cardiovascular effects, thrombosis and other complications. Surgical and various experimental approaches are expensive and often do not provide long-term benefits. As statistics continuously escalate, efforts to develop improved therapeutic modalities to preserve function and reduce arthritis related disabilities, hospitalizations, complications related to therapy, in addition to adverse effects, are being sought.

In the era before Christ, the words 'magnetism' and 'electrical', were already associated with modalities used for the treatment of (daily) ailments, including wound healing. Today, many scientists are still lost in classical,

mechanistic, exclusively chemical treatment beliefs, failing to recognize how fundamental electromagnetic energy parameters relate to biology and life. Many believe that only chemical processes are involved in regulating growth and the healing processes. In fact, in a world dominated by the pharmaceutical industry, this enchants many physicians too. Understanding how specific biological signals carried on electromagnetic fields (EMFs) specifically affect life processes, requires a new paradigm in the understanding of the forces that regulate life itself. With increased interest in energy and electromagnetism as therapeutic modalities, much research has focused on understanding how EMFs and electrical stimuli interact with cells to elicit biochemical processes. However, to monitor the trillions of interrelated and carefully balanced biochemical enzymatic processes, even occurring within a single cell, which is a complex organism on its own, has proven to be rather challenging.

In a world dominated by power and wealth, the pharmaceutical industry reigns as the forerunner in offering diverse medication for numerous medical conditions and disorders. As time unfolds, more side-effects are being reported. Recently in Bordeaux France, a presentation by Dr David J. Graham, from the US Food and Drug Administration Office of Drug Safety, demonstrated that high-dose rofecoxib (Vioxx, Merck & Co) triples the risk of heart attack and sudden cardiac death compared with the risk in control groups not taking coxibs or other NSAIDs.[45] Such was the impact of these study results, that an article was featured in *San Jose Mercury News* via NewsEdge Corporation, dated 30 August, 2004, reporting these study results, with the headline: 'Arthritis drug linked to higher heart risks. KAISER, OTHER INSURERS TO RECONSIDER ITS USE', and had the opening statement: 'California health care giant Kaiser Permanente is likely to advise its doctors not to prescribe the popular arthritis drug Vioxx after a medical study of Kaiser members found the medicine may increase the risk of life-threatening heart problems'. Similar study results and reports have urged scientists to continue in their endeavour to seek alternative treatment modalities and continue in their efforts to further understand the biomolecular aspects of life.

Much research with EMFs has been conducted with promising results. There are many questions still left unanswered, but many hypotheses have been proposed. EMFs as treatment modalities is a growing market. Ergo, one needs to be aware of 'alternative therapies', claiming to be effective and therapeutic, but having no scientific basis for their 'therapy'. Medical certification, documented studies, and approval by recognized legal bodies of the particular therapy, are essential. PST™ has all of these attributes – and more!

PST™ is an effective treatment alternative and requires only one course of treatment to provide sustained pain relief and restoration of normal mobility. Follow-up studies have constantly demonstrated its sustained, long-term, therapeutic benefits in OA, tinnitus, for which no satisfactory treatment is available; periodontal disease, an established risk-factor for heart attacks and stroke; temporomandibular joint pain; other types of joint disorders and particularly trauma resulting from sports injuries and accidents.[16] Its effectiveness has been supported by strict scientific research, including *in vitro*, *in vivo* and imaging studies, conducted across the globe. In addition, PST™-documented success has received worldwide recognition, through publications in international scientific journals, as well as invitations to present PST™ technology at world congresses. In May of 2004, PST™ was presented at the International Osteoporosis Foundation (IOF) World Congress, in Rio de Janeiro, Brazil (14–18 May); and is scheduled to be presented at the Singapore International Scientific Meeting on Arthritis and Rheumatology, 2004 (11–14 November) as a State of the Art Lecture, organized by the National Arthritis Foundation; and also at the Osteoarthritis Research Society International OARSI 9th World Congress (2–5 December). PST™ is a unique treatment modality, that aids the body in restoring its natural rhythm, such that continued therapy is often not warranted. Its role as a safe and effective therapeutic modality has been rather well established and with the coming years, its therapeutic success in other medical disorders, will undoubtedly be recognized and supported by *in vitro* and *in vivo* scientific research studies.

It remains our challenge to understand how PST™ interacts with cells at the biomolecular level, to trigger biochemical processes and elicit the observed clinical response. In doing so, we endeavour to eventually elucidate its biomolecular mechanism of action . . .

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