Pulsed Signal Therapy® (PST™)

A Non-Invasive Treatment for Osteoarthritis and other Musculoskeletal Disorders

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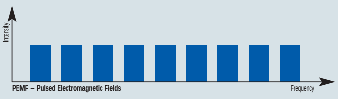
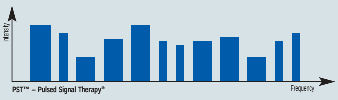
Introduction

Pulsed Signal Therapy® (PST™) is a unique, patented, form of therapy, for the treatment of diverse musculoskeletal disorders, most notably osteoarthritis. PST™ was initiated more than three decades ago following clinical evidence that pulsed electromagnetic fields (PEMF) could promote the healing of bone fractures (Bassett *et al*). Since then PST™ has undergone rigorous clinical trials over, 15 years, consistently demonstrating both long-term pain relief in osteoarthritis and traumatic joint injury, as well as a return to functionality.

Unlike conventional therapeutic devices, which deliver alternating current, or at times, direct current at a specific intensity and constant frequency, PST™ delivers changing pulsed electromagnetic signals in an alternating fashion that mimic signals generated in the body. In so doing, cartilage cell (chondrocyte) activity is stimulated in the affected area. **These findings have been patented and can be viewed in our Scientific Information CD (available upon request).**



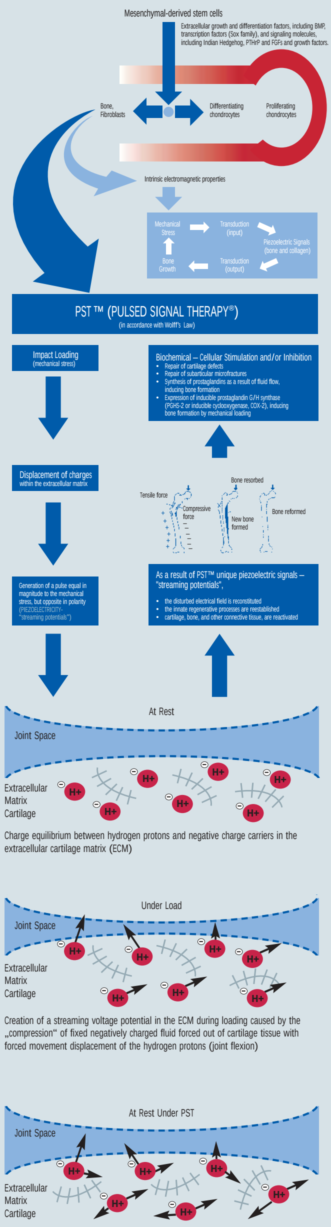
PEMF – Pulsed Electromagnetic Fields



PST™ – Pulsed Signal Therapy®

Device Parameter	Magnetic Field Therapy	PST™
Electromagnetic properties	Piezoelectric	Biological signal
Energy form	Alternating current	Direct current
Frequency	44-77Hz	1-30Hz
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

Mechanism of Action

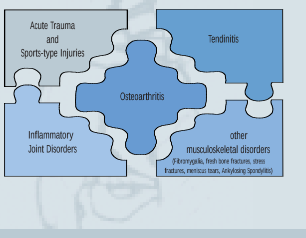


Charge equilibrium between hydrogen protons and negative charge carriers in the extracellular cartilage matrix (ECM)

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“ in the joint caused by the forced movement of hydrogen protons in the ECM through alternating PST signals as stimulation of chondrocytes in the connective tissue matrix

General Medical Applications



Clinical & *in vitro* studies

Double-blind clinical trials and other open label prospective studies have been conducted and published over a fifteen year period in the USA, Canada, France, Italy, Germany, and Asia, to verify the effectiveness of PST™ proprietary pulsed electromagnetic induction therapy, for the treatment of osteoarthritis and other musculoskeletal disorders of the knee, hip, lower back and cervical spine.

Completed Clinical Studies

DB-1 to DB-4 below are all prospective, randomized double-blind placebo-controlled studies using Extremely Low Frequency Electromagnetic Induction Therapy in the treatment of patients with Inflammatory and Non-Inflammatory Arthritis.

Nature and Duration of Study	Institution where study was conducted & publication(s) (where applicable)	Success rate (%)	Comments
DB-1 & DB-2 (Pilot Studies) A Double-Blind trial of the clinical effects of Pulsed Electromagnetic Fields in Osteoarthritis. 1990 – 1991	Yale University, Connecticut. Journal of Rheumatology. 1993; 20(3):456-460.	Approx. 70%	• The difference in means between treated and placebo groups was evaluated by two-tailed t-tests. • 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. 1991 – 1992	Three Trial Centers under a protocol from Yale University, Connecticut	Approx. 70%	• The difference in means between the treated and placebo groups was evaluated by two-tailed t-tests. • Good to very good results, with high statistical significance
DB-4 The effect of Pulsed Electromagnetic Fields in the treatment of Osteoarthritis of the Cervical Spine. 1991 – 1993	Journal of Rheumatology. 1994; 21:1903-1911.		
Open Initial Trial A Prospective Study Using Extremely Low Frequency Electromagnetic Induction Therapy in the Treatment of Patients with Inflammatory and Non-Inflammatory Arthritis. 1990 – 1991	Yale University, Connecticut.	Approx. 70%	• The difference in means between the treated and placebo groups was evaluated by two-tailed t-tests. • 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. 1990 – 1991	Yale University, Connecticut.	Approx. 70%	• Good to very good results, with high statistical significance • PST may be effective for treating various joints affected by osteoarthritis, as well as other types of arthritis, and/or other joint-related conditions.
Open Trial 2 A Prospective Study Using Extremely Low Frequency Electromagnetic Induction Therapy in the Treatment of Patients with Inflammatory and Non-Inflammatory Arthritis. 1991 – 1993	Three Trial Centers under a protocol from Yale University, Connecticut.	Approx. 70%	• Good to very good results, with high statistical significance • PST may be effective for treating various joints affected by osteoarthritis, as well as other types of arthritis, and/or other joint-related conditions.
Pulsed Signal Therapy: Treatment Of Chronic Pain Due To Traumatic Soft Tissue Injury. 1997 – 1998	McGill University, Vancouver, Canada. International Medical Journal. 1999; 6(3):167-173.	72.5%	• Statistically significant improvement in both groups - matched pair t-test analysis of pre- and post-treatment data • PST is as effective for the treatment of STI, as it is for OA.
Etude de vérification de l'efficacité antalgique des champs électromagnetiques pulsés (PST) dans la gonarthrose. [Efficacy of pulsed electromagnetic therapy (PST) in painful knee osteoarthritis.] (A placebo-controlled double-blind study) 1997 – 1998	Cochin Hospital, Paris, France • American College of Rheumatology Presentation, Nov 1998 • Arthritis Rheum. 1998; 41(3) (suppl): S.357. • arthritis + rheuma. 2002; 22(2): 101-104.	76.9% - three months post-treatment	• Statistical significance was obtained after the 9th PST treatment and 3 months thereafter - VAS (p<0.01) and Lequesne index (p<0.05). • Good to very good results, with high statistical significance
La PST (Terapia a segnale pulsante): proposta di condroprotezione con metodiche fisiche. [PST (Pulsed Signal Therapy): A Proposal for a Chondro-Protection with Physical Methods.] (A prospective clinical study of gonarthrosis and non-disc lower back pain.) 1998	Niguarda Hospital, Milano, Italy. La Riabilitazione - Revista di Medicina Fisca e Riabilitazione. April-June, 1998; 31(2): 51-59.	Knee pain: 17.8% to 68.4% increase in function. Lower back pain: 50.5% decrease in pain at 6 weeks post.	• Significant improvement post-treatment • PST long-term effects • PST is effective in pain management, and in intervening in the pathogenesis of the painful symptoms.
Impiego della Terapia a Segnale Pulsante (PST) nell'artrosi della mano. [The Use of Pulsed Signal Therapy (PST) in the treatment of arthritis of the Hand.] 1999 – 2000	Niguarda Hospital, Milano, Italy. La Riabilitazione - Revista di Medicina Fisca e Riabilitazione. September 2000; 33(3): 109-114.	76,1% to 80.95% of cases showed success.	• Successful results in 76.19% of cases according to VAS, and in 80.95% according to the algo-functional index. • A significant improvement in a follow-up control, 6 months post-treatment • PST long-term effects
Impiego della Terapia a Segnale Pulsante (PST) nell'artrosi del ginocchio [The Use of Pulsed Signal Therapy (PST) in Osteoarthritis of the Knee.] 2000 – 2001	Niguarda Hospital, Milano, Italy. La Riabilitazione - Revista di Medicina Fisca e Riabilitazione, December, 2001; 34(4):213-218.	71.4% to 87% cases showed success.	• Successful results were obtained in 71,4% of cases according to VAS, and in 87% of cases according to the algofunctional index. • High statistical significance
Procedural proposal for patients suffering with osteoarthritis of the knee by means of PST vs. placebo. 1999 – 2002	University of Siena, Siena.	Success in more than 50% of the cases.	• A statistically significant difference was found between both treatment groups.
Risultati preliminari nel trattamento di lesioni osteo-condrali di ginocchio trattate con Pulsed Signal Therapy (PST). [Preliminary results of the treatment) of osteochondral knee injuries, with Pulsed Signal Therapy (PST).] 2001	Università degli Studi di Catania	50% improvement after the first week of treatment; 100% 3 months post-treatment	• A median value of 2.5, 3 months after treatment, was obtained for subjective pain using VAS. • An overall decrease in pain and improved quality of life • High statistical significance
Risultati a lungo termine della terapia a segnale pulsante (PST). [Long-term results achieved by Pulsed Signal Therapy (PST).] 1998 – 1999	Niguarda Hospital, Milano, Italy. La Riabilitazione - Revista di Medicina Fisca e Riabilitazione. January-March, 1999; 32(1): 11-15.	85.26%, improvement in functionality, one year post- treatment.	• 85.26% was the average obtained, following assessment based on 10 tests of functionality. • PST long-term effects decreased pain intensity and improved functionality, 1 year post-treatment
Prospective, clinical verification study of PST in Gonarthrosis, Coxarthrosis and degenerative disorders of the lumbar spine. 1997	PST Treatment Center Munich, TU Munich • Medycyna Sportowa. December 1998; XIV(89):31-34. • Presentation Norddeutsche Orthopädenvereinigung e.V. 48.Jahrestagung in Münster, June 1999. • Poster Presentation - 14. GOTS, June 1999, München.	73.9%	• A reduction in the original complaints, with regard to all four investigation parameters, in 73.9%, according to VAS. • High statistical significance
Ergebnisse einer multi-zentrischen Untersuchung zur Wirksamkeit der Pulsierenden Signal Therapie (PST) Arthrosen im Kniegelenk (Gonarthrose, Stadium II und III nach Kellgren). [Results of a multicenter study of the clinical effect of Pulsed Signal Therapy in Arthrosis of the knee (Gonarthrosis, grade II and III, according to Kellgren.)] 1999 – 2001	Ludwig-Maximilians-Universität, Munich. Orthopädische Praxis. 2001; 37(11): 701-709.	73% of patients responded positively to PST™.	• Unpaired and paired results for the Lequesne Knee Arthritis Index pre-PST™ and 6 months after PST™, using Mann-Whitney U and Wilcoxon tests (p<0.0001 and p<0.001, respectively) (asymp. 2-tailed) • Both unpaired and paired results for VAS responses, pre-PST™ and 6 months after PST™, showed p<0.0001 (2-tailed). • Both unpaired and paired results for responses to daily activities (DA), pre-PST™ and 6 months after PST™, showed p<0.0001 (2-tailed). • High statistical significance
Permanent Prospective Study (VITAL) 1996 – 2001	Ludwig-Maximilians-Universität, Munich	73% responded positively to PST™.	• The results were based on the Lequesne index and VAS. • High statistical significance
Therapie der anterioren Diskusverlagerung ohne Reposition mit Pulsierender Signal-Therapie (PST). [Pulsed Signal Therapy in the treatment of anterior disk displacement without reduction.] (An observational study) Ended 1998	Humboldt-Universität, Berlin. Deutsche Zahnärztliche Zeitschrift mit Deutsche Zahn-, Mund- und Kieferheilkunde. April 1999; 54(4):284-287.	73%	• SPSS software and Friedman test were used for statistical evaluation of the recorded data (p<0.05). • Post-treatment, 58% of patients could successfully open their jaws to within 37.0 – 40.5 mm. • Significant reduction in pain
Pulsierende Signaltherapie zur Behandlung von Arthropathien des Kiefergelenks – vorläufige Ergebnisse einer Doppelblindstudie. [Pulsed Signal Therapy for the treatment of temporomandibular arthropathy – preliminary results of a double-blind study.] 1997 – 1998	Humboldt Universität, Berlin	Significant success	• Measurements were made using VAS (0-100%). • Significant reduction in pain • Improvement in moving and opening the lower jaw
Morbus Tinnitus (A pilot study) 1999 – 2000	ENT Medical Centre	At 12 weeks 52% were significantly improved and 22%, symptom free.	• Definite and significant improvement in 52% of patients (Goebel-Hiller) • PST™ long-term effect
Chronischer Mobus Tinnitus (A pilot study) 1999 – 2001	Medical Centre		• A definite improvement was found 3 months post-treatment. • PST long-term effect
Tinnitus Randomized Multicenter Double-Blind Clinical Study. 1999 – 2002	Clinics and Medical Practices. Presentation at the HNO Congress in Dresden, Germany, 27-05-2003.		• A significant decrease in the Tinnitus grade (severity), post the 12-day treatment, at 6 weeks and 3 months thereafter (p>0.05). • PST long-term effect
Three Prospective Clinical Trials conducted in Berlin, Nuremberg and Munich, Germany, on Chronic Tinnitus (Grades, II, III, or IV). 1997 – 2000	Clinics and Medical Practices		• Significant improvement in 52% of the patients • Trend in improvement post-treatment and 6 weeks later, in an additional 25% of patients. • No adverse side effects

VAS – Visual Analog Scale

Completed *in vitro* studies

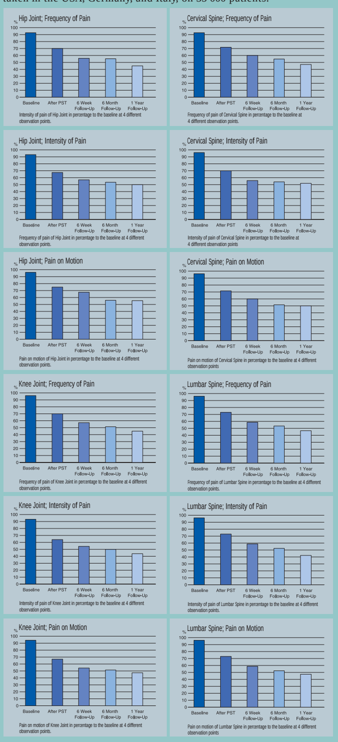
Nature of Study	Institution where the study was conducted & publication(s) (where applicable)	Published in	Comments
The stimulation of chondrocyte metabolism by pulsed magnetic fields.	North Shore University Hospital, New York (affiliated with Cornell University), USA	• Manuscript, 1992.	• Sulphate incorporation (p<0.05) following PST exposure to *in vitro* cartilage explants, maintained in organ culture • Increase proteoglycan levels - evidence for repair and/or relief in osteoarthritis
Pulsed Signal Therapy (PST) enhances the proteoglycans concentration in human chondrocyte cultures.	Institute of Rheumatology, University of Siena, Siena, Italy	• Bioelectromagnetics Society [BEMS] Twenty-Second Annual Meeting Abstract Book, Munich, Germany, June 11-16, 2000: 48. • Ann Rheum Dis. 2002; 61:1032-1033	• Stimulation of IL-β treated chondrocytes with PST™ resulted in restoration of cell structures and proteoglycan synthesis (p<0.05). • No significant differences in cell cultures subjected to pressure cycles • Enhanced cartilage repair, increased [³H]-thymidine incorporation, and [³⁵SO₄] uptake (glycosaminoglycan production) observed by transmission electron microscopy (TEM) and scanning electron microscopy (SEM), of PST™-treated cells.
Pulsed Signal Therapy (PST™) Stimulates Mitosis of Human Chondrocytes in Culture.	Praxis für Orthopädie und Sportstraumatologie, Cologne, Germany	• Singapore Humanitas Press, In Proceedings: Tenth International Conference on Biomedical Engineering, Singapore, December 2000; 473-474.	• Statistically significant higher mitosis rates in human chondrocyte cell cultures exposed to PST™.
Der Einfluss der Pulsierende Signale Therapie auf die Synthese der Extracelluaren Matrix in 3-Dimension Human Chondrozyten. [The PST Effect on 3-Dimensional Chondrocyte Culture: An *in vitro* study].	University Center, Charité, Humboldt University, Berlin, Germany	• Presentation at the Deutsches PST Symposium [PST Symposium], Salzburg, Austria; May 19, 2001 • Presentation at the 1st Biennial Meeting of the Tissue Engineering Society ETES -2001 Symposium of the International Cartilage Repair Society (ICRS) - Freiburg, Germany, Nov. 7-10, 2001.	• Biochemical analysis showed increased deposition of collageneous matrix components, in meniscal and arthritic chondrocyte cultures, treated with PST™. • Articular chondrocyte cultures showed a marginal enhancement of collagen synthesis. • Meniscal chondrocyte cultures showed significant long-term, matrix formation (up to 6 months), post-PST™ stimulation.
Study of the clinical effect of PST™ with trials of the synovial liquid in gonarthrosis.	Auguste-Victoria-Hospital Berlin, University of Erlangen	• Conducted 1998 – 2001 and to be submitted for publication.	• Statistically significant difference in MMP-1 and 9 levels, between pre- and post-PST™ treatment - two-tailed t-tests • Increased MMP-1 and 9 levels suggest PST™ may ensure the rapid onset of restoration of damaged tissue – CATABOLISM (p<0.05). • Statistically significant difference in pain intensity, pre- and post-treatment, with a decrease over time – PST™ long-term effect (p<0.05)

Current Clinical Studies

Nature of Study	Institution conducting the study	Year started	Year expected to end	Comments
Chronic Tinnitus	Medical Practice	1997	Indefinite	Study in progress. As of 22 August 2003, 194 patients have either completed, or are currently undergoing treatment.
Studie zum Nachweis der Wirksamkeit der PST™ bei Patienten mit gesicherter Osteoporose. [Verification study of the effect of PST™ in patients with established osteoporosis].	Infomed – Institut für Innovative Medizin, München, Germany	2002	Approx. 70%	Pending final approval – expected this fall.
Definitive Tinnitus Double-Blind Clinical Trial.	Johannes Gutenberg, University of Mainz, Germany	2003	2004	• June 2003 - in a written memo, Prof.Dr.Dr.h.c. W. Mann agreed to undertake the study, as Principal Investigator. • August 2003 – preparation of documents for the Ethics Committee • September 2003: first draft protocol by Prof. Mann *et al.*

Results: Prospective Multicenter Study (pooled data)

Controlled Double-Blind and Prospective Open Label Studies undertaken in the USA, Germany, and Italy, on 35 000 patients.



Intensity of pain of Hip Joint in percentage to the baseline at 4 different observation points.
Frequency of pain of Cervical Spine in percentage to the baseline at 4 different observation points.
Frequency of pain of Hip Joint in percentage to the baseline at 4 different observation points.
Intensity of pain of Cervical Spine in percentage to the baseline at 4 different observation points
Pain on motion of Hip Joint in percentage to the baseline at 4 different observation points.
Pain on motion of Cervical Spine in percentage to the baseline at 4 different observation points
Frequency of pain of Knee Joint in percentage to the baseline at 4 different observation points.
Frequency of pain of Lumbar Spine in percentage to the baseline at 4 different observation points.
Intensity of pain of Knee Joint in percentage to the baseline at 4 different observation points.
Intensity of pain of Lumbar Spine in percentage to the baseline at 4 different observation points
Pain on motion of Knee Joint in percentage to the baseline at 4 different observation points.
Pain on motion of Lumbar Spine in percentage to the baseline at 4 different observation points

In all investigated groups the improvement in pain (intensity, frequency, in motion) is significant to the baseline with p< 0.0001 and leads to a pain reduction between 40 and 50% after 1 year follow–up. Discussion: In previous studies it has been shown that the changes in the placebo patients had less significance at the end of treatment, and had lost significance for most variables at the one month follow up. The open label analysis and these data were consistent with the double-blind results. Conclusion: These studies provide continuing evidence for the use of PST in obtaining improved functionality along with effective and safe relief from chronic pain associated with Osteoarthritis.

Results: Multicenter Clinical Study – Gonarthrosis - Germany

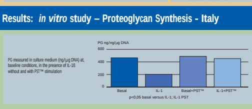
Frequency distribution of the Lequesne Knee Arthritis Index before PST™ treatment in percent.

Frequency distribution of the Lequesne Knee Arthritis Index 6 months after PST™ treatment in percent.

Representation of the averages of four pain parameters in percent. The inclusion conditions before the PST™ treatment were set respectively as basis value to 100%.

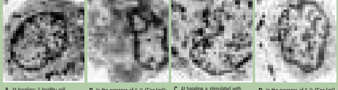
Representation of the averages of six Daily Activities (DA) trouble parameters in percent. The entrance condition before the PST™ treatment was set respectively as a basis value to 100%.

Results: *in vitro* study – Proteoglycan Synthesis - Italy



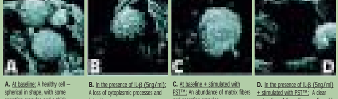
In the presence of IL-β (5ng/ml), proteoglycan (PG) levels decreased significantly (p<0.05), but were subsequently restored when chondrocytes were stimulated with PST™ (p<0.05).

TEM of chondrocytes cultured *in vitro* for 72 hours (N=nucleus; V=vacuole; RER=rough endoplasmic reticulum)



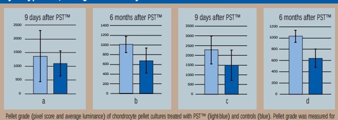
A. At baseline: A healthy cell - euchromatic nucleus, abundance of RER and lipid droplets (arrow), in the surrounding cytoplasm (x9000) **B.** In the presence of IL-β (5ng/ml): A vacuolated cytoplasm, devoid of cell organelles (x9000) **C.** At baseline + stimulated with PST™: A healthy cell - as for (A) (x10 000) **D.** In the presence of IL-β (5ng/ml) + stimulated with PST™: Cell is restored to a healthy state (x9000)

SEM of chondrocytes cultured *in vitro*

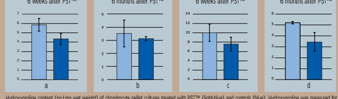


A. At baseline: A healthy cell – spherical in shape, with some secretion granules and a thick network of collagen fibrils. **B.** In the presence of IL-β (5ng/ml): A loss of cytoplasmic processes and integrity. **C.** At baseline + stimulated with PST™: An abundance of matrix fibers and secretion granules. **D.** In the presence of IL-β (5ng/ml) + stimulated with PST™: A clear restoration of the cell, as confirmed by the presence of several surface granules.

Results: *in vitro* study – PST effects on a 3-D chondrocyte culture – Proteoglycan, Hydoxyproline, Collagen - Germany



Pellet grade (pixel score and average luminance) of chondrocyte pellet cultures treated with PST™ (light-blue) and controls (blue). Pellet grade was measured for articular chondrocytes after 9 days (a) and 6 months (b) of PST™ treatment and for mensical chondrocytes after 9 days (c) and 6 months (d) after treatment.



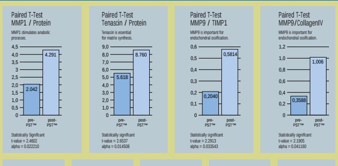
Hydroxyproline content (ng/mg wet weight) of chondrocyte pellet cultures treated with PST™ (light-blue) and controls (blue). Hydroxyproline was measured for articular chondrocytes after 6 weeks (a) and 6 months (b) of PST™ treatment and for mensical chondrocytes after 6 weeks (c) and 6 months (d) after treatment.

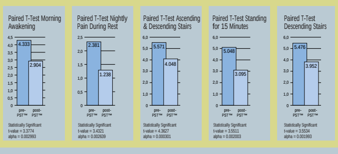
Cell Distribution **Cell Distribution**

Hematoxylin-Eosin staining of meniscal chondrocytes stimulated with PST™(M+) and controls (M-)

Alcian blue staining of proteoglycan pellet cultures of human articular (G), and human meniscal, chondrocytes (M).

Results: *in vitro* study – Matrix Metalloproteinases in Synovial Fluid – Germany





Discussion

Pulsed Signal Therapy® (PST™) is a viable, and reliable, form of therapy that has demonstrated efficacy in the treatment of osteoarthritis, and other musculoskeletal disorders, over the past 20 years. PST™ has undergone strict scientific research, including clinical trials in diverse sectors of the globe, has been certified and accepted, and is currently available in over 600 PST clinics worldwide. More than 200 000 patients worldwide have been treated – many for whom conventional therapies have failed. PST™ is non-invasive, painless, and, to date, no known adverse effects have been reported. These, and other PST™ therapeutic benefits, have been published globally in numerous scientific and medical journals – **an integrative CD is available upon request.**

Continued extensive *in vitro* and *in vivo* studies, supported by scientific clinical and research data, seek to unravel its various therapeutic potentials in several diverse disorders, for which there are no currently available treatments, or for which conventional treatments are met with rather harsh adverse side effects. In addition, studies to unravel its mechanism of action at the biomolecular level, will enable its multifaceted, therapeutic potential in the treatment of diverse musculoskeletal disorders, to be elucidated.

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