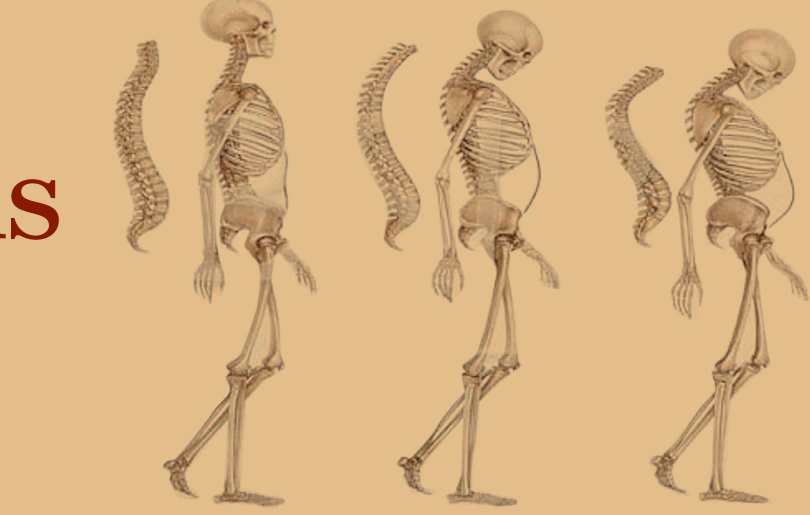


Pulsed Signal Therapy® (PST®) for the treatment of Osteoporosis – A Scientific Premise –

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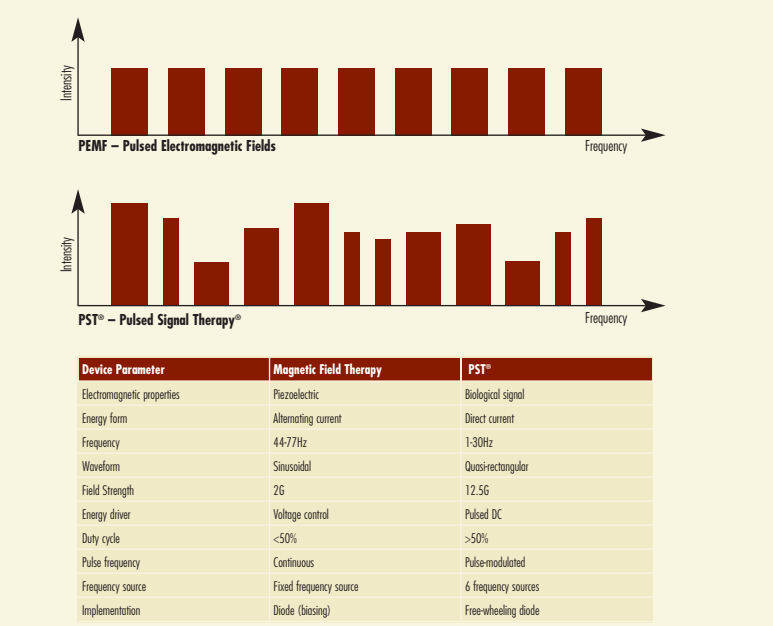


Introduction

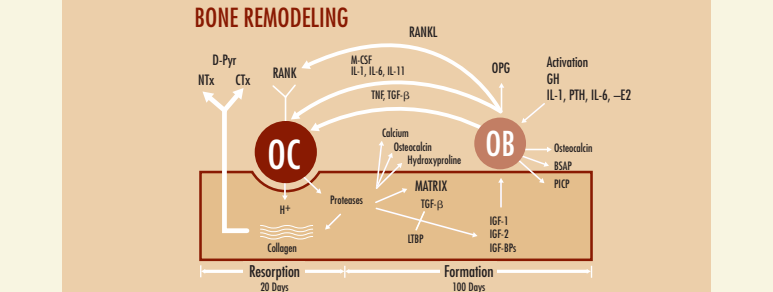
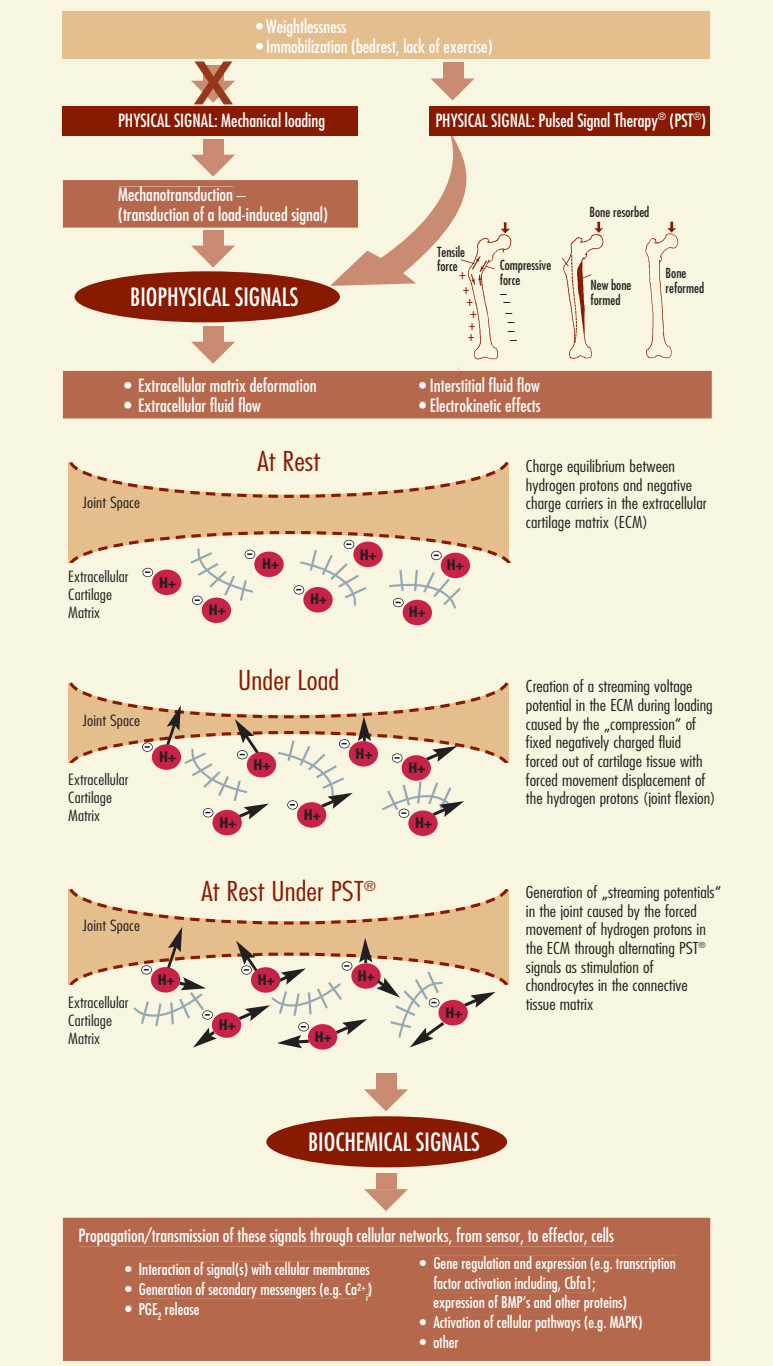
Pulsed Signal Therapy® (PST®) is a unique form of therapy, patented in the US and nineteen European countries, for the treatment of diverse connective tissue disorders, most notably osteoarthritis. PST® was initiated more than two decades ago following clinical evidence that pulsed electromagnetic fields (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. Biophysically, it has been established that PST® emulates the innate physiological and mechanical stresses evoked, and required, in bone formation. It passively induces fluid flow and ionic displacement, thereby generating a piezoelectric ("streaming potential") and eventually activating various signaling network paths – as occurs in mechanotransduction. Increased proteoglycan synthesis, and collagen synthesis, have been observed *in vitro*, following stimulation with PST® (Nerucci, Fioravanti, Krüger). A comprehensive Scientific Information CD containing studies and other relevant information regarding PST® technology, is available upon request.

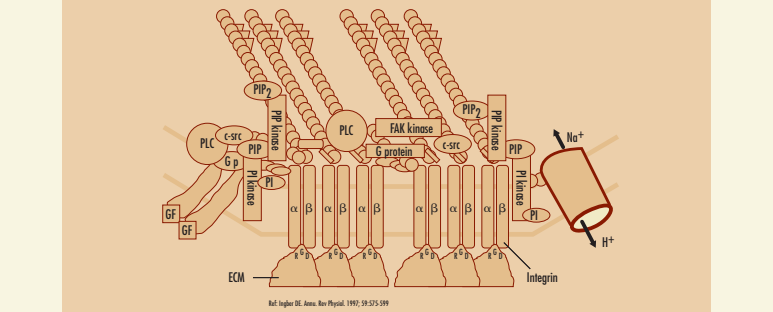
Continued scientific investigations into the medical applications of PST® for the treatment of diverse connective tissue disorders, resulted in international medical regulatory approval for the treatment of **Osteoporosis** with PST® technology, in 2003.



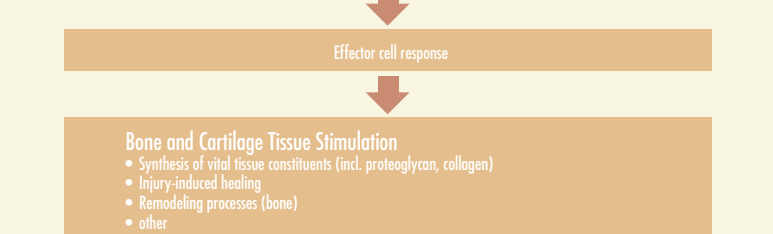
Biophysical – Biochemical Mechanism of Action



Bone Remodeling: Osteoblasts (OBs) are activated by several signalling factors, including growth hormone (GH), interleukins (IL-1, IL-6), Parathyroid hormone (PTH), and withdrawal of estrogen (E2). MSCs and RANKL are the two major OB mediated factors regulating the recruitment and differentiation of osteoclasts (OCs). Osteoprotegerin (OPG) is also synthesized by OBs and inhibits bone resorption by binding to RANKL. The RGS are released during bone resorption and serve as coupling factors to recruit new OBs to the surface. These peptides may also be important for osteoclast activity.



The cytoskeleton (CSK) framework of the focal adhesion complex, is comprised of clustered integrins and actin-associated molecules, and physically interconnects the extracellular matrix to the intracellular cell microfilaments (ends of stress fibers). Many signal transducing molecules mediate the cell's response to growth factors and ECM binding function when immobilized on the molecular framework (as shown in the figure). E.g., this may represent a major site for integration of chemical and mechanical signals (transmembrane mechanical signal transfer).



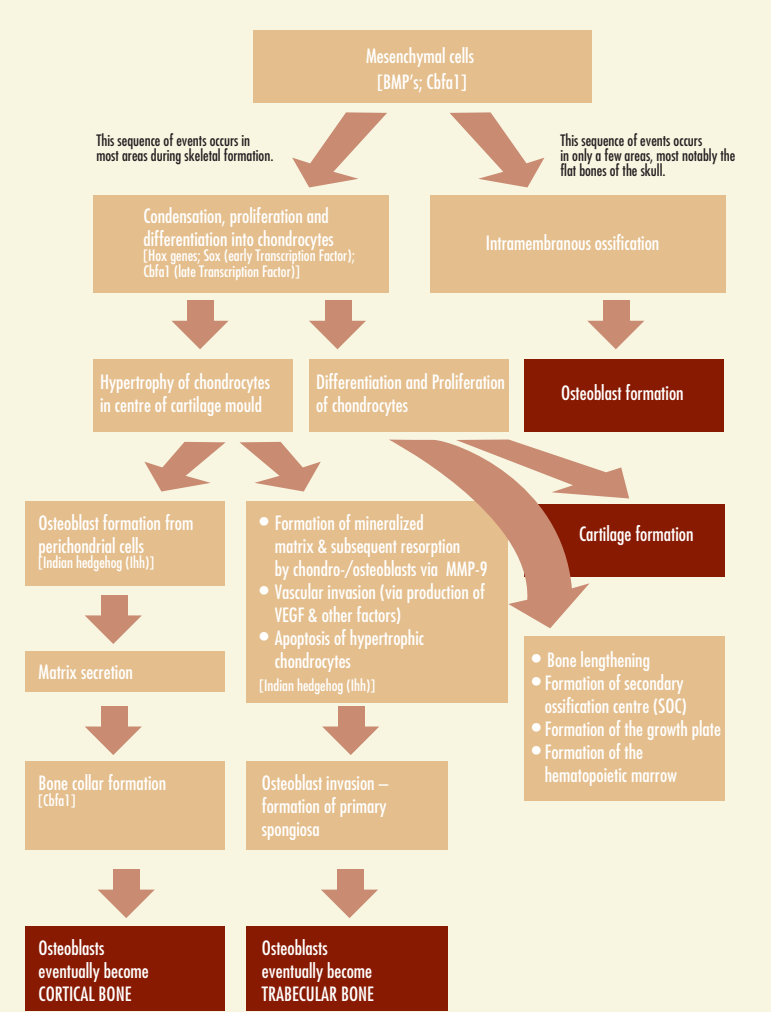
Bone and Cartilage Tissue Stimulation

- Synthesis of vital tissue constituents (incl. proteoglycan, collagen)
- Injury induced healing
- Remodeling processes (bone)
- other

Discussion and Conclusion

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 well-controlled clinical trials in diverse sectors of the globe, and has been certified and accepted in 23 countries around the globe. It is currently available in over 750 PST® clinics worldwide. PST® is noninvasive, 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

Overview: Bone and Cartilage Lineages



Pulsed Signal Therapy® for the treatment of Osteoporosis in post-menopausal women – Preliminary Data –

Aim:
To investigate the effects of Pulsed Signal Therapy® (PST®) on both Trabecular and Cortical Bone Density.

Study Design:

1. Post-menopausal women (at least 3 years)
2. Below the age of 75
3. An established Osteopenia, or onset Osteoporosis (no fractures) [Trabecular Bone Density: $-1.5SD < x < -2.5SD$]
4. No change in medication for at least 1 year
5. Voluntary, written compliance to participate in the study, after a comprehensive explanation of the study design.

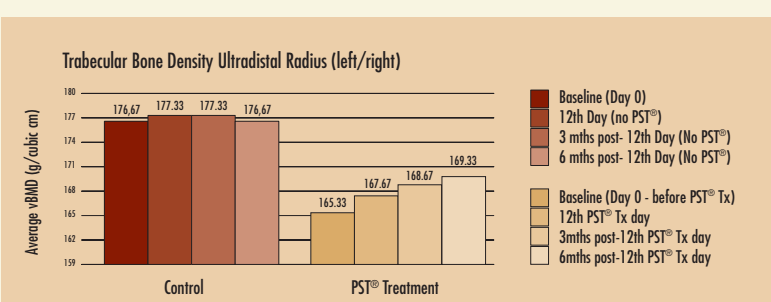
(With the exception of calcium (1000mg/day) and Vitamin D3 (800-1000 units/day), no new medication for osteoporosis was prescribed.)

- B. Exclusion criteria:**
1. A history of previous fractures
 2. Diabetes
 3. Morbus Crohn
 4. Colitis ulcerosa
 5. Hyperthyroidism
 6. Oral corticosteroids taken within the last six months
 7. New medication prescribed for osteoporosis, within the last year.
 8. Pregnancy
 9. Pace-pacemakers

Methodology:
The volumetric bone mineral density (vBMD) of both trabecular and cortical bone was measured at the ultradistal radius (wrist), using validated instruments of measurement (VIMS) warranted for wrist density measurements. Each patient served as her own control – that is, one wrist was subjected to PST® treatment and the other not (the control). Measurements were conducted and recorded for both wrists. During the entire duration of the study, patients were refrained from carrying out any form of physical training, in order to avoid inducing bone formation indirectly through mechanical loading. In this way, any increase in bone formation observed, could be attributed to PST®.

Treatment protocol: A one-hour daily treatment with PST®, for 12 days, with no treatment over the weekend. Follow-ups conducted at 3-months, 6-months and 12-months, post-PST® treatment.

Results:
These are preliminary results based on a randomized sampling from a population group of post-menopausal women. Since trabecular bone turnover rate is greater than cortical bone turnover rate, it was expected that the greatest change in vBMD measurements, would be observed when assessing trabecular bone. As early as 12 days post PST®-treatment, an increase in trabecular vBMD was observed.



Graph 1: Results of Patients Treated with PST® compared to controls
Graph 1 depicts the results of both the control (that is, the wrist NOT subjected to PST® treatment), and the wrist treated with PST®. Twelve days post connecting PST® treatment, a slight increase in trabecular vBMD, in the control group, was observed which remained constant 3-months post, and gradually decreased at 6-months post. The observed initial increase in vBMD in the control group could, in part, be attributed to the positive effects of PST®, already observed in the treated wrist at 12-days post treatment. The observed decrease at 6-months-post, in the control group, is expected due to the progression of the underlying condition, and to the fact that, in comparison to the treated wrist, the control has not been subjected directly to PST® induction effects. In the PST®-treated wrist, an increase in trabecular vBMD was observed after the 12th treatment course, and continued 3- and 6-months post. This suggests a balancing (restoration) of the resorption and formation processes, characteristic of bone remodeling, by PST®.

Conclusion:
The definite and significant increase in trabecular vBMD observed, after the 12-day PST® treatment period, clearly demonstrates PST® positive effects on bone formation. At 3- and 6-months post-PST® treatment, it would appear that the innate balance of remodeling has been restored. It is expected that PST® positive effects on cortical bone will also be observed, but at a later period, due to its innate and overall slower turnover rate. In the long-term, it is postulated that PST® will continue to stimulate bone formation, and retard bone resorption, until the innate balance between bone formation and bone resorption has been restored.

Outlook

Post-Marketing Surveillance investigations, in Berlin and München, are currently underway to verify and ascertain PST® positive effects on bone remodeling. Dual-Energy X-Ray Absorptiometry (DEXA), the most accurate and advanced test available for measuring bone mass, with the ability to determine even the earliest stages of bone loss associated with osteoporosis, will be used. Two groups will be investigated: 1. Post-menopausal women with an established osteoporosis (T-score <-2.5SD), no history of fractures and taking calcium and vitamin D. 2. Post-menopausal women with an established osteoporosis (T-score <-2.5SD), at least one fracture, and taking prescribed medication.

The whole body, principally the spine and column femoris, will be treated and bone mass measurements in the region of the lumbar spine recorded. Additionally, *in vitro* research, and analysis of biochemical markers from sera, including bone alkaline phosphatase, beta-crosslaps, calcium, BSG, Gamma-GT and Creatinine, will also be carried out. Furthermore, neuromuscular tests, using validated instruments of measurement, will serve to assess activities of daily living.

available upon request. As both *in vitro* and *in vivo* investigations continue, PST® multifaceted medical application in the treatment of diverse Connective Tissue Disorders, for which conventional treatments are often met with rather harsh adverse side effects, continues to unfold. PST® researchers have already considered and investigated its medical application in several disorders, including Fibromyalgia - a comprehensive overview is available on the gratis CD. It is anticipated, that biomolecular investigations will enable further elucidation of PST® mechanism of action, extending its therapeutic potential beyond the borders of the musculoskeletal system...

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

Nature and Duration of Study	Institution where study was conducted (where applicable)	Success rate (%)	Comments
DB-1 & DB-2 (Pilot Studies) A Double-blind at the clinical effects of Pulsed Electromagnetic Fields in Osteoarthritis. 1990 – 1991	Yale University, Connecticut Journal of Rheumatology 1993; 20(3):458-460.	Approx. 70%	• The difference in means between treated and placebo groups was evaluated by two-tailed 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 Test Centres under a protocol from Yale University, Connecticut Journal of Rheumatology 1994; 21:1903-1911.	Approx. 70%	• The difference in means between the treated and placebo groups was evaluated by two-tailed 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 – 1992	Yale University, Connecticut. Journal of Rheumatology 1994; 21:1903-1911.	Approx. 70%	• The difference in means between the treated and placebo groups was evaluated by two-tailed tests. • Good to very good results, with high statistical significance
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. Yale University, Connecticut.	Approx. 70%	• The difference in means between the treated and placebo groups was evaluated by two-tailed 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. Yale University, Connecticut.	Approx. 70%	• Good to very good results, with high statistical significance • PST® may be effective for treating various path 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 – 1992	Three Test Centres under a protocol from Yale University, Connecticut. Yale University, Connecticut.	Approx. 70%	• Good to very good results, with high statistical significance • PST® may be effective for treating various path 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; 4(3):167-173.	72.5%	• Statistically significant improvement in both groups - statistical pain Heat analysis of pre- and post-treatment data. • PST® is as effective for the treatment of SSI, as it is for OA.
Etude de validation de l'efficacité antalgique des champs électromagnétiques pulsés (PST®) dans le genou. (Efficacy of pulsed electromagnetic therapy (PST®) in painful knee osteoarthritis.) (A double-blind randomized study) 1997 – 1998	Cochin Hospital, Paris, France • Association College of Rheumatology Presentation, Nov. 1998. • Arthritis Rheum. 1998; 41(3) (Suppl): S357. • Arthritis & Rheuma 2002; 45(2):101-104.	76.9% New results post-treatment Rate pain: 17.8% to 68.4% increase in function Lowest back pain: 20.5% decrease in pain at 6 weeks post.	• Statistical significance was obtained after the 9th PST® treatment and 3 months thereafter - WS (p<0.01) and Laparase index (p<0.05). • Good to very good results, with high statistical significance
Lo PST® (Temple a Segnale Pulsante) proposito di convalidazione con metodo locale. (PST® Pulsed Signal Therapy): A Protocol for a Double-blind study in patients with Osteoarthritis of the Knee. (A prospective clinical study of genoflexion and neurotic lower back pain.) 1998	Niguarda Hospital, Milano, Italy La Rodolico - Reato di Medicina Foca a Rodolico. April June, 1998; 31(2):15-19.	76.19% to 80.95% of cases showed success.	• Significant improvement post-treatment • PST® long-term effects • PST® may be effective for treating various path affected by osteoarthritis, as well as other types of arthritis, and/or other joint-related conditions.
Impiego della Tempa a Segnale Pulsante (PST®) nel dolore del collo. (The Use of Pulsed Signal Therapy (PST®) in the treatment of arthritis of the Neck.) 1999 – 2000	Niguarda Hospital, Milano, Italy La Rodolico - Reato di Medicina Foca a Rodolico. September 2000; 33(3):109-114.	74.19% to 80.95% of cases showed success.	• Successful results in 76.19% of cases according to WS, and in 80.95% according to the algometer index. • A significant improvement in a follow-up control, 6 months post-treatment • PST® long-term effects
Impiego della Tempa a Segnale Pulsante (PST®) nel dolore della mano. (The Use of Pulsed Signal Therapy (PST®) in Osteoarthritis of the Hand.) 2001 – 2001	Niguarda Hospital, Milano, Italy La Rodolico - Reato di Medicina Foca a Rodolico. December, 2001; 34(4):192-198.	71.4% to 87% cases showed success.	• Successful results were obtained in 71.4% of cases according to WS, and in 87% of cases according to the algometer index. • High statistical significance
Procedural protocol for patients suffering with osteoarthritis of the knee by means of PST® vs. placebo. 1999 – 2002	University of Sao, Sao Paulo. University of Sao, Sao Paulo.	Success in more than 50% of the cases.	• A statistically significant difference was found between both treatment groups.
Brachial pain relief by treatment of brachial osteoarthritis with Pulsed Signal Therapy (PST®). (Long-term results achieved by Pulsed Signal Therapy (PST®).) 2001	Università degli Studi di Catania Catania, Italy.	50% improvement after the first week of treatment; 100% 3 months post-treatment.	• A median value of 2.5, three days after treatment, was obtained for subjective pain using WS. • No noted decrease in pain and improved quality of life • High statistical significance
Brachial a largo termine della tempa a segnale pulsante (PST®). (Long-term results achieved by Pulsed Signal Therapy (PST®).) 2001	Niguarda Hospital, Milano, Italy La Rodolico - Reato di Medicina Foca a Rodolico. January/March, 1999; 32(1):115.	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, double-blind validation study of PST® in Genoflexion, Cervical and degenerative disorders of the lumbar spine. 1997	PST® Treatment Center Munich, TU Munich • Medizinsprache, December 1998; 20(10):334. • Presenting: Neurologische Orthopedie und Rheumatologie a V. 48. Jahrestagung in München, June 1999. • Poster Presentation: 14. GOTS, June 1999, München.	73.9% 73% of patients responded positively to PST®.	• A reduction in the original complaints, with regard to all four investigation parameters, in 73.9%, according to WS. • High statistical significance
Esplorazione di una multicentrica valutazione per la valutazione del Pulsed Signal Therapy (PST®) Arteriosi e Kneegelenk (Genoflexion, Stadium I e II nel collo). (Results of a multicentric study of the clinical effect of Pulsed Signal Therapy in Arteriosi of the Neck (Genoflexion, grade I and II, according to Kolagen).) 1999 – 2001	Ludwig Maximilians Universität, München Orthopädische Klinik, 2001; 37(11):701-709.	73% of patients responded positively to PST®.	• Ligament and joint results for the Laparase knee Arteriosi index (p<0.001) following PST® exposure to in vitro cartilage explants, maintained in organ culture. • Increased proteoglycan levels in organ and in vitro cartilage. • Both reported and noted results for WS responses, in PST® and 6 months after PST®, showed p<0.0001 (2-tailed). • Both reported and noted results for responses to a double control: OA, post-PST® and 6 months after PST®, showed p<0.0001 (2-tailed). • High statistical significance
Permanent Prospective Study (VTD) 1996 – 2001	Ludwig Maximilians Universität, München Humboldt Universität, Berlin	72% responded positively to PST®.	• The results were based on the Laparase index and WS. • High statistical significance
Therapie der arthrosen Dislokationssyndrom nach Arteriosi am Pulsed Signal Therapy (PST®). (Pulsed Signal Therapy in the treatment of arthrosen dislokationssyndrom nach Arteriosi.) Endel 1998	Deutsche Zahnärztliche Zeitschrift mit Deutsche Zelle, Mund und Zahnheilkunde, April 1999; 54(4):284-287.	73%	• SPSS software and Friedman test were used for statistical analysis of the recorded data (p<0.05). • Both reported and noted results for WS responses, in PST® and 6 months after PST®, showed p<0.0001 (2-tailed). • High statistical significance
Pulsed Signal Therapie zur Behandlung von Arteriosi des Kneegelenks – vollständige Ergebnisse einer Doppelblindstudie. (Pulsed Signal Therapy in the treatment of Arteriosi des Kneegelenks – preliminary results of a double-blind study.) 1997 – 1998	Humboldt Universität, Berlin Humboldt Universität, Berlin	Significant success	• Measurements were made using WS (0-100%). • Significant reduction in pain • Improvement in resting and sleeping the lower jaw
Medus Tinnitus (A pilot study) 1997 – 2000	ENT Medical Centre Austria, Austria, May 19, 2001; 11(6):200-204.	At 12 weeks 57% were significantly improved and 22% operation free.	• Definite and significant improvement in 52% of patients (Statistical significance). • No significant difference in all values related to pressure cycles. • Enhanced cartilage repair, increased 1H-thymidine incorporation, and 175kD vitronectin production (production) observed by transmission electron microscopy (TEM) and scanning electron microscopy (SEM), of PST® treated cells.
Chronic Pain Medus Tinnitus (A pilot study) 1997 – 2001	Medical Centre Austria, Austria, May 19, 2001; 11(6):200-204.	At 12 weeks 57% were significantly improved and 22% operation free.	• A definite improvement was found 3 months post-treatment. • PST® long-term effect
Chronic Pain Medus Tinnitus (A pilot study) 1997 – 2001	Chronic and Medical Practices Presentation of the 18th Congress in Berlin, Germany, 27-05-2003.	Significant success	• A significant decrease in the Tinnitus grade (weekly), post the 12-day treatment, of 6 weeks and 3 months thereafter (p<0.05). • PST® long-term effect
Three Prospective Clinical Trials conducted in Berlin, Mannheim and Munich, Germany, on Chronic Tinnitus (Genoflexion, I, II, & III). 1997 – 2000	Chronic and Medical Practices Presentation of the 18th Congress in Berlin, Germany, 27-05-2003.	Significant success	• 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

Nature of Study	Institution where the study was conducted	Publication	Comments
The stimulation of chondrocyte metabolism by pulsed electromagnetic fields (PEMF) in vitro. 1997 – 2000	North Shore University Hospital, New York, USA New York University, New York, USA	• Musculoskeletal, 1997; 124:128-143.	• Soluble incorporation (p<0.05) following PST® exposure to in vitro cartilage explants, maintained in organ culture. • Increased proteoglycan levels in organ and in vitro cartilage.
Pulsed Signal Therapy (PST®) influences the proteoglycans concentration in human chondrocytes in culture. 1997 – 2000	Institute of Rheumatology, University of Sao, Sao Paulo, Brazil Journal of Rheumatology 1999; 26(10):1028-1033.	• Bioelectromagnetics Society (BEAS) Twenty-Sixth Annual Meeting Abstract Book, Munich, Germany, June 11-16, 2000; 48: 611-612.	• Stimulation of IL-6 treated chondrocytes with PST® resulted in restoration of all structures and proteoglycan synthesis (p<0.05). • No significant difference in all values related to pressure cycles. • Enhanced cartilage repair, increased 1H-thymidine incorporation, and 175kD vitronectin production (production) observed by transmission electron microscopy (TEM) and scanning electron microscopy (SEM), of PST® treated cells.
Pulsed Signal Therapy (PST®) influences the proteoglycans concentration in human chondrocytes in culture. 1997 – 2000	Pross for Orthopedics and Sportsmedicine, Cologne, Germany Pross for Orthopedics and Sportsmedicine, Cologne, Germany	• Presenting: Humerus Press, In: Proceedings, Tenth International Conference on Biomedical Engineering, September, December 2000, 473-474.	• Statistically significant higher nitrite levels in human chondrocyte cell cultures exposed to PST®.
Der Einfluss der Pulsed Signal Therapie auf die Proteoglykan-Produktion in der Synovialflüssigkeit bei Osteoarthritis. (The Effect of Pulsed Signal Therapy on the Proteoglycan Production in the Synovial Fluid in Osteoarthritis.) 1997 – 2000	University Center, Götting, Humboldt Universität, Berlin, Germany	• Presenting: Humerus Press, In: Proceedings, Tenth International Conference on Biomedical Engineering, September, December 2000, 473-474.	• Biochemical analysis showed increased degradation of collagenous matrix components, in material and articular chondrocytes, treated with PST®. • Articular chondrocyte cultures showed a marginal enhancement of collagen synthesis. • Articular chondrocyte cultures showed significant long-term, matrix formation (up to 6 months), post-PST® stimulation.
Study of the clinical effect of PST® on the effect of the synovial fluid in osteoarthritis. 1997 – 2000	Aggregat-Proteoglycan Research, 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-treatment – two-tailed tests. • Increased MMP-1 and 9 levels suggest PST® may exert the rapid effect on the degradation of the matrix. • Statistically significant difference in pain intensity, pre and post-treatment, with a decrease over time – PST® long-term effect (p<0.05).

Nature of Study	Institution where the study was conducted	Publication	Comments
Chronic Tinnitus	Medical Practice	1997	• Study in progress. • At 12 August 2003, 194 patients have either completed, or are currently undergoing treatment.
Study zum Nachweis der Wirksamkeit der PST® bei Osteoarthritis und Osteoporosis. (Validation study of the effect of PST® in patients with established osteoporosis.) 1997 – 2000	Informal – Institut für Innovative Medizin, München, Germany	2002	13 November 2002: PST®-technology was fully certified for the treatment of osteoporosis. Td and spine devices are currently available.
Definitive Tinnitus Double-Blind Clinical Trial	Informal – Institut für Innovative Medizin, München	2003	• Study in progress. • Approved from the Ethics Commission is pending.
Long-term, multicenter prospective validation study of Pulsed Signal Therapy (PST®) for the treatment of Osteoporosis	Informal – Institut für Innovative Medizin, München	2004	• Study in progress. • Approved from the Ethics Commission is pending.

Completed in vitro studies

Nature of Study	Institution where the study was conducted	Publication	Comments
The stimulation of chondrocyte metabolism by pulsed electromagnetic fields (PEMF) in vitro. 1997 – 2000	North Shore University Hospital, New York, USA New York University, New York, USA	• Musculoskeletal, 1997; 124:128-143.	• Soluble incorporation (p<0.05) following PST® exposure to in vitro cartilage explants, maintained in organ culture. • Increased proteoglycan levels in organ and in vitro cartilage.
Pulsed Signal Therapy (PST®) influences the proteoglycans concentration in human chondrocytes in culture. 1997 – 2000	Institute of Rheumatology, University of Sao, Sao Paulo, Brazil Journal of Rheumatology 1999; 26(10):1028-1033.	• Bioelectromagnetics Society (BEAS) Twenty-Sixth Annual Meeting Abstract Book, Munich, Germany, June 11-16, 2000; 48: 611-612.	• Stimulation of IL-6 treated chondrocytes with PST® resulted in restoration of all structures and proteoglycan synthesis (p<0.05). • No significant difference in all values related to pressure cycles. • Enhanced cartilage repair, increased 1H-thymidine incorporation, and 175kD vitronectin production (production) observed by transmission electron microscopy (TEM) and scanning electron microscopy (SEM), of PST® treated cells.
Pulsed Signal Therapy (PST®) influences the proteoglycans concentration in human chondrocytes in culture. 1997 – 2000	Pross for Orthopedics and Sportsmedicine, Cologne, Germany Pross for Orthopedics and Sportsmedicine, Cologne, Germany	• Presenting: Humerus Press, In: Proceedings, Tenth International Conference on Biomedical Engineering, September, December 2000, 473-474.	• Statistically significant higher nitrite levels in human chondrocyte cell cultures exposed to PST®.
Der Einfluss der Pulsed Signal Therapie auf die Proteoglykan-Produktion in der Synovialflüssigkeit bei Osteoarthritis. (The Effect of Pulsed Signal Therapy on the Proteoglycan Production in the Synovial Fluid in Osteoarthritis.) 1997 – 2000	University Center, Götting, Humboldt Universität, Berlin, Germany	• Presenting: Humerus Press, In: Proceedings, Tenth International Conference on Biomedical Engineering, September, December 2000, 473-474.	• Biochemical analysis showed increased degradation of collagenous matrix components, in material and articular chondrocytes, treated with PST®. • Articular chondrocyte cultures showed a marginal enhancement of collagen synthesis. • Articular chondrocyte cultures showed significant long-term, matrix formation (up to 6 months), post-PST® stimulation.
Study of the clinical effect of PST® on the effect of the synovial fluid in osteoarthritis. 1997 – 2000	Aggregat-Proteoglycan Research, 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-treatment – two-tailed tests. • Increased MMP-1 and 9 levels suggest PST® may exert the rapid effect on the degradation of the matrix. • 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	<ul style="list-style-type: none">• Study in progress.• As of 22 August 2003, 194 patients have either completed, or are currently undergoing treatment.
Study zum Nachweis der Wirksamkeit der PST® bei Osteoarthritis und Osteoporosis. (Validation study of the effect of PST® in patients with established osteoporosis.)	Informal – Institut für Innovative Medizin, München, Germany	2002	Approx. 2003	13 November 2003: PST®-technology was fully certified for the treatment of osteoporosis. Full spine devices are currently available.
Definitive Tinnitus Double-Blind Clinical Trial	Informal – Institut für Innovative Medizin, München, Germany	2003	2004	<ul style="list-style-type: none">• Study in progress.• Paid by D.L.G., W. Mann, from Mainz, Germany, is the Principal Investigator.• Approval from the Ethics Committee is pending.
Long-term, multicenter prospective validation study of Pulsed Signal Therapy (PST®) for the treatment of Osteoporosis	Informal – Institut für Innovative Medizin, Berlin-Wilmersdorf, Berlin-Wilmersdorf, Eastmün, Berlin-Wilmersdorf	2004	Approx. 2005	<ul style="list-style-type: none">• Study in progress.• Approved from the Ethics Committee is pending.
	Informal – Institut für Innovative Medizin, München	2004	2005	<ul style="list-style-type: none">• Study in progress.• Approved from the Ethics Committee is pending.

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