Index[1] - Comprehensive List of all PST™ Studies

[1] *NOTE: Clinical, in vitro, and ongoing studies have been listed here, in the aforementioned order. Each study pertaining to each section, has been classified according to the country in which it was conducted, and further subdivided into the study area with which it was concerned.*

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

Completed Clinical Studies / USA

1) Ortho (Osteoarthritis)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
An early "Comprehensive Report of all patients treated with Magnetic Therapy at Waterbury, from January 1990, for chronic and/or persistent, joint-disorders", was compiled, outlining the outcomes of the Pilot, Double-Blind and Open Trial, Studies, being conducted. A tabulated précis of the initial data obtained,is provided	Yale University School of Medicine Teaching Hospital, Waterbury, Connecticut Yale Clinical Presentations	1990	1991	Total=142 patients [2] • 13 in a Pilot Study {observational } • 50 in a Placebo-Controlled Double-Blind (DB) Phase I Study • 52 in a Placebo-Controlled Double-Blind (DB) phase II	• **Open Pilot Study:** 77% definite improvement • **Placebo-Controlled DB Phase I:** 87% definite improvement 25% improvement in the placebo. • **Placebo-Controlled DB Phase II:** 75% definite improvement 37%	Assessments were made using the Overall Response Ratings, based on a Final Evaluation Key (developed in conjunction with St. Mary's physicians). Assessments were made following individual patient evaluation: • Definite = Maximal therapeutic response considering stage of disease process) • Improved = Good (short of maximal therapeutic response) • Slight = Fair; minimal response • None = Absence of therapeutic response	All 142 patients received at least five evaluations: • Baseline • 2-week follow-up • 4-week follow-up • Final • 2-week post-treatment evaluation. **In general, good to very good results were obtained in all studies, with high statistical significance.** **[More specifically, in the Placebo-**

[2] From January 8 to June 12, 1990, a total of 142 patients were given magnetic therapy treatment. Initially, an observational study of 13 patients with chronic and/or persistent disease was conducted. Further, a total of 102 patients were entered into a randomized, Double-Blind placebo controlled study. This study was conducted in two phases: the first being a 50 patient-joint study, and the second, a 52 patient-joint study. Additionally, a total of 27 patients were entered into an open crossover study of non-responding patients from the double-blind controlled study. The magnetic therapy center moved, and this study continued until March 1991.

here, followed by a detailed summary of the individual studies (1-7, below), post-completion. • Open Pilot Study Markoll *et al*. 1/90-2/90 • Placebo Controlled Double –Blind (DB) Study Phase I Markoll *et al*. 1/90-4/90 • Placebo Controlled Double –Blind (DB) Study Phase II Markoll *et al*. 3/90-6/90 • Crossover Study from Double-Blind (1) Dyer *et al*. 4/90-3/91				Study • 37 in an Open Crossover Study	improvement in the placebo. • **Crossover Study from Double-Blind:** Greater than 50% definite improvement	**Open Pilot Study (n=13):** Definite= 8 (62%) Improved= 1 (8%) Slight= 3 (23%) None= 1 (8%) **Placebo-Controlled DB Phase I: (n=50):** ▪ **Active treatment:** Definite= 18 (36%) Improved= 2 (4%) Slight= 2 (4%) None= 1 (2%) SUBTOTAL= 23 Dropouts= 2 TOTAL= 25 ▪ **Placebo Treatment:** Definite= 4 (8%) Improved= 2 (4%) Slight= 3 (6%) None= 15 (30%) SUBTOTAL= 24 Dropouts= 1 TOTAL= 25 **Placebo-Controlled DB Phase II: (n = 52)** Only 36 case reports were returned for source documentation and statistical evaluation) ▪ **Active Treatment** Definite= 12 (33%) Improved= 0 Slight= 0	**Controlled DB studies:** • **Phase I:** ▪ **Active Treatment:** 20/23 (87%) ▪ **Placebo Treatment:** 6/24 (25%) Statistical evaluations were made using the Chi-square test, where X_2=18.2, with $p<0.001$ - a high statistical significance. • **Placebo-Controlled-DB Phase II:** ▪ **Active Treatment:** 12/16 = (75%) ▪ **Placebo Treatment:** 6/16 = (37%) Statistical evaluations were made using the Chi-square test, where X_2= 4.56, with p values between 0.05 and 0.01 – a high statistical significance was obtained.

						None= 4 (11%) SUBTOTAL= 16 Dropouts= 3 TOTAL= 19 ▪ **Placebo Treatment** Definite= 6 (6%) Improved= 0 Slight= 0 None= 10 (27%) SUBTOTAL= 16 Dropouts= 1 TOTAL= 17 **Open Crossover Study: (n=27)** Definite= 11 (41%) Improved= 5 (19%) Slight= 5 (19%) None= 6 (22%)	

PST – PROVEN, DOCUMENTED & CURRENT 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.

2. DB-1 (Initial Pilot) A Double-Blind trial of the clinical effects of Pulsed Electromagnetic Fields in Osteoarthritis. T.P. Greco, Richard Markoll	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut *Journal of Rheumatology* 1993; 20(3):456-460.	1990	1991	47	Approx. 70%	The difference in means between the treated and placebo groups were evaluated by two-tailed t-tests. The baseline data were analyzed for frequency distribution to ensure an approximately normal distribution.	Good to very good results, with high statistical significance
3. DB-2 (2nd Pilot) A Double-Blind Trial of the Clinical effects of Pulsed Electromagnetic Fields in Osteoarthritis. D.H. Trock, A.J. Bollet	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut *Journal of Rheumatology* 1993; 20(3):456-460.	1990	1991	42 (27 with osteoarthritis)	Approx. 70%	VAS (Visual Analog Scale) and ADL (Activities of Daily Living) were used at different time periods, before and after treatment. An average improvement of 23-61%, in clinical variables, was observed in the group receiving active treatment, while only 2-18% was observed in the placebo group.	Good to very good results, with high statistical significance

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

4. DB-3 The effect of Pulsed Electromagnetic Fields in the treatment of Osteoarthritis of the Knee. D.H. Trock, R. Roseff, M. Spiegel, E. Heller, R.M. Higley, R.H. Dyer, Jr., W.K. Miner, S.H. DeWitt	Three Trial Centers under a protocol from Yale University School of Medicine Teaching Hospital Waterbury, Connecticut. The effect of Pulsed Electromagnetic Fields in the treatment of Osteoarthritis of the Knee and Cervical Spine. Report of Randomized, Double-Blind, Placebo-Controlled Trials. *Journal of Rheumatology* 1994; 21:1903-1911.	1991	1992	86	Approx. 70%	The difference in means between the treated and placebo groups were evaluated by two-tailed t-tests. The baseline data were analyzed for frequency distribution to determine an approximately normal distribution. The difference in means was greater at the end of treatment, rather than at the midway observation, primarily because of a much greater improvement in the treated group at the end.	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.
5. DB-4 The effect of Pulsed Electromagnetic Fields in the treatment of Osteoarthritis of the Cervical Spine. D.H. Trock, R. Roseff, M. Spiegel, E. Heller, R.M. Higley, R.H. Dyer, Jr., W.K. Miner, S.H. DeWitt		1991	1993	81	Approx. 70%		

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

2) Ortho (Arthritis and Osteoarthritis)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
6. Open Initial Trial A Prospective Study Using Extremely Low Frequency Electromagnetic Induction Therapy in the Treatment of Patients with Inflammatory and Non-Inflammatory Arthritis. T.P. Greco, R. Markoll	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	1990	1991	69	Approx. 70%	The difference in means of the treated and placebo groups were evaluated by two-tailed t-tests. The baseline data were analyzed for frequency distribution to ensure an approximately normal distribution.	Good to very good results, with high statistical significance
7. Open Trial 1 A Prospective Study Using Extremely Low Frequency Electromagnetic Induction Therapy in the Treatment of Patients with Inflammatory and Non-Inflammatory	Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	1990	1991	97	Approx. 70%		Good to very good results, with high statistical significance

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

Arthritis R.H. Dryer, Jr. W.K. Miner, S.H. De Witt						The data generated from these open studies suggest that this type of therapy may be effective for different joints affected by osteoarthritis, as well as other types of arthritis, and/or other joint-related conditions.	
8. Open Trial 2 A Prospective Study Using Extremely Low Frequency Electromagnetic Induction Therapy in the Treatment of Patients with Inflammatory and Non-Inflammatory Arthritis D.H. Trock, R. Roseff, M. Spiegel, E. Heller, R.M. Higley	Three Trial Centers under a protocol from Yale University School of Medicine Teaching Hospital Waterbury, Connecticut	1991	1993	38	Approx. 70%		Good to very good results, with high statistical significance

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

3) Ortho (Traumatic Soft Tissue Injury)

Nature of study & Study Directors	Institution where study was conducted & Publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
9. Pulsed Signal Therapy: Treatment Of Chronic Pain Due To Traumatic Soft Tissue Injury. (Diagnostic Profile of Pulsed Signal Therapy Patient Population Treatment of Degenerative Joint Disease, Muscle/ ligament/tendon injuries, Disc degeneration-herniation) C. Hershler, A. Sjaus	McGill University, Vancouver, Canada *International Medical Journal.* 1999; 6(3):167-173.	1997	1998	80	72.5%	Matched pair t-test analysis of pre- and post-treatment data revealed statistically significant improvement in both groups.	High statistical significance. This study also showed that PST™ is as effective for the treatment of STI (i.e. clinical tenderness in soft tissue structures around the joint, with associated pain and limitation in function, but no diagnostic image positive for bony involvement) as it is for OA.

Completed Clinical Studies / EUROPE

A) France

A.1) Ortho (Osteoarthritis)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
10. Ètude 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) S. Perrot, M. Marty, A. Kahan, C-J. Menkés	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.	1997	1998	40 (21 in the PST™ group and 19 in the placebo group)	76.9% as assessed both by the doctor and patient at 3 months after the treatment had ended.	The most noticeable criteria to differentiate between the two treated groups was the VAS of pain in motion (statistically significant difference at day 9 and month 3, as well as in the analysis of variance in repeated measurements) ($p<0.01$) ; and the Lequesne index (statistically significant difference at day 9 and month 3, as well as in the analysis of variance in repeated measurements) ($p<0.05$).	Good to very good results, with high statistical significance

B) Italy

B.1) Ortho (Osteoarthritis)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
11. 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.] M. Cossu N. Portale	Niguarda Hospital, Milano, Italy *La Riabilitazione-Revista di Medicina Fisca e Riabilitazione,* April-June, 1998; 31(2):51-59.	1998	1998	58	<u>Knee pain</u> Function improved from 17.8% to 68.4% with the entire group reporting no pain at rest, six weeks after treatment. Of the 21 who initially reported difficulty in doing housework, this number fell to 0 at six weeks post-treatment. <u>Lower back pain</u> The pain, according to the VAS, fell from 7.92 (baseline) to 6.25 (9 Treatments) and	Pain was measured with a Scott-Huskisson Visual Analogue Scale (VAS). Apart from the VAS, use was made of a personal questionnaire, comprised of 10 questions, inquiring about the patient's functional capacities, as affected by the prevalent pain (this questionnaire was compiled by a doctor at each of the three survey times). A significant improvement was found at the end of the therapeutic cycle, and continued to	The results confirmed that this treatment has a beneficial effect at th end of therapy, but reaches its maximum effect later. This fact appears to justify the proposal of PST™, not only for pain management, but also for treatment aimed at intervening in the pathogenesis of the painful symptoms.

					3.92 (6 weeks post) with an improvement of 50.5% at 6 weeks post.	increase in subsequent weeks.	
12. 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.] M. Cossu, C. Leuci, N. Sias	Niguarda Hospital, Milano, Italy *La Riabilitazione-Revista di Medicina Fisca e Riabilitazione,* September 2000; 33(3):109-114.	1999	2000	21	Successful results were achieved in a range of 76,19% to 80.95% of cases.	Successful results have been achieved in 76.19% of cases according to VAS, and in 80.95% of cases according to the algofunctional index.	A follow-up control, conducted six months after the end of therapy, showed that the percentage of patients benefiting from treatment was significantly high according to both evaluation methods adopted: 76.19 (VAS) and 80.95 (algofunctional index).
13. Impiego della Terapia a Segnale Pulsante (PST) nell'artrosi del ginocchio [The Use of Pulsed Signal Therapy (PST) in Osteoarthritis of the Knee.] M Cossu, N. Sias, G. Devito	Niguarda Hospital, Milano, Italy *La Riabilitazione-Revista di Medicina Fisca e Riabilitazione,* December, 2001; 34(4):213-218.	2000	2001	49	Successful results were achieved in the range of 71.4% to 87% of cases.	Successful results have been achieved in 71,4% of cases according to VAS, and in 87% of cases according to the algofunctional index.	High statistical significance
14. Procedural proposal for patients suffering with	University of Siena, Siena	1999	2002		Success in more than 50% of the	A statistically significant difference	High statistical significance.

osteoarthritis of the knee by means of PST vs. placebo R. Marcolongo					cases.	was found between both treatment groups.	

B.2) Ortho (Osteochondral Knee Injury)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success rate (%)	Definition of success used in study [% showing improvement]	Notes
15. Risultati preliminary nel trattamento di lesioni osteocondrali di ginocchio trattate con Pulsed Signal Therapy (PST). [Preliminary results of the treatment) of osteochondral knee injuries, with Pulsed Signal Therapy (PST).] M. Di Martino, S. Avondo, T.C. Russo, M.G. Onesta, G. Sessa	Università degli Studi di Catania Atti del Congresso della Società Medico-Chirurgica Catanese – Novembre 2002. http://www.riabilitazioneitalia.it/ortoped4_art2.htm	2001	2001	15	Successful results were achieved 3 months post-treatment by 100% of the patients. [After the first week of treatment, 50% of the patients showed improvement.]	In terms of subjective pain measurement assessed using the VAS, a median value of 2.5 three months after treatment, with an exit value of 6.1, was achieved. A clear decline of pain symptoms, and consequently an improved quality of life, was also shown. This result was confirmed by individual patient responses, to function tests conducted.	High statistical significance.

B.3) Ortho (PST™ - Long-term Effects)

Nature of study & Study Directors	Institution where study was conducted & Publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
16. Risultati a lungo termine della terapia a segnale pulsante (PST). [Long-Term Results Achieved by Pulsed Signal Therapy (PST).] M. Cossu, C. Leuci	Niguarda Hospital, Milano, Italy *La Riabilitazione-Revista di Medicina Fisca e Riabilitazione,* January-March, 1999; 32(1):11-15.	1998	1999	34	85.26%, as an average of 10 tests of functionality, one year after treatment.	Tests of motor functionality	PST™ -effects were long-term, that is, decreased pain intensity and improved functionality, prevailed, 1 year post-treatment.

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

C) Germany

C.1) Ortho (Osteoarthritis)

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success rate (%)	Definition of success used in study [% showing improvement]	Notes
17. Prospective, clinical verification study of PST in Gonarthrosis, Coxarthrosis and degenerative disorders of the lumbar spine. S. Frhr von Gumppenberg H. Martin, M. Faensen, R. Breul	PST™ Treatment Center Munich, TU Munich • *Terapia Sygnałami Pulsującymi – Ocena Pierwszej Części Prospektywnego Badania Klinicznego Skuteczności Leczenia W Zwyrodnieniu Stawu Kolanowego.* Medycyna Sportowa, December 1998, XIV(89):31-34. • Poster Presentation: "Kann die Pulsierende Signal Therapie (PST) bei arthrosebedingten Beschwerden sinnvoll eingesetzt werden?" 14.GOTS (14. Deutsch-Österreichisch-Schweizer Kongress für Sportorthopädie und Sportstrauma-tologie, 25-27 June 1999, München • Presentation: „Pulsierenden Signaltherapie (PST) – Ein nichtinvasives Verfahren zur Behandlung von Gelenkerkrankungen" Norddeutsche Orthopäden-vereinigung e.V.	1997	1997	80	70%.	A reduction in the original complaints (> 20%), with regard to all 4 investigation parameters, was achieved in 51 of 69 patients (that, is in 73.9%), according to VAS.	High statistical significance

	48.Jahrestagung in Münster, June 17-19, 1999.						

18. Ergebnisse einer multi-zentrischen Untersuchung zur Wirksamkeit der Pulsierenden Signal Therapie (PST) Arthrosen im Kniegelenk (Gonarthrose, Stadium II and III nach Kellgren). [Multi-Center-Study of the clinical effect of Pulsed Signal Therapy in Arthrosis of the knee (Gonarthrosis, grade II and III, Kellgren.)] M. Faensen, R. Breul	Ludwig-Maximilians-Universität, Munich Orthopädische Praxis, 2001; 37(11): 701-709	1999	2001	303 patients from 40 clinics	73% of the 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, Wilcoxon $p<0.0001$ 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

19. Permanent Prospective Study (VITAL) R. Breul, F. Hahn, D. Rost	Ludwig-Maximilians-Universität, Munich	1996	2001	42 000 as of 15 March 2001	73% of the patients responded positively to PST™.	The results were based on the Lequesne index and VAS.	High statistical significance; further documentation and analysis of the patient Data.

C.2) Dental

Nature of study & Study Directors	Institution where study was conducted & publication(s) (where applicable)	Year started	Year ended	Number of patients	Success Rate (%)	Definition of success used in study [% showing improvement]	Notes
20. 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; Pilot Study to the Double-blind, below) I.Peroz, Y-H P. Chun, J-F Roulet, K-P Lange	Humboldt-Universität, Berlin *Deutsche Zahnärztliche Zeitschrift mit Deutsche Zahn-, Mund- und Kieferheilkunde,* April 1999; 54(4):284-287.		1998	21 (3 men, 18 women, 14-85 yrs of age (average: 46+/-17 yrs) Each was his/her own control. Only 3 received treatment of both mandibules.	60% success rate	SPSS software, and Friedman test, were used for statistical evaluation of the recorded data ($p<0.05$). Post- PST™ treatment, 58% of patients could successfully open their jaws to within 37-40.5mm. All reported a significant reduction in pain.	Data show PST™ as a potential and effective therapeutic modality in the treatment of anterior disk displacement without reduction.
21. Pulsierende Signaltherapie zur Behandlung von Arthropathien des Kiefergelenks – vorläufige Ergebnisse einer	Humboldt Universität, Berlin	1997	1998	78 patients (65 women & 13 men, between the ages of 18-84; average:	Patients reported a significant reduction in pain, and an	Measurements were made using VAS, Visual Analog Scale (0-100%).	The results obtained were significant, encouraging further studies.

Doppelblindstudie. [Pulsed Signal Therapy for the treatment of temporomandibular arthropathy – preliminary results of a Double-Blind Study.] G. Karageorgi, I.Peroz, Ch. Schwerin, Y-H. Chun, O. Bernhardt, J-F. Roulet, WB. Freesmeyer, G. Meyer, K-P. Lange				43.7+/-14.2 years) 1 dropout	improvement in their ability to move and open their lower jaw.		

C.3) Tinnitus

Nature of study & Study Directors	Year started	Year ended	Number of patients	Measurements and success	Conclusive Findings
22. Morbus Tinnitus (A Pilot Study) K. Pfeiffer *et al*	1999 (April)	2000 (Feb.)	43	• VAS (Visual Analog Scale) was used to assess the degree of their Tinnitus. Patients were evaluated before PST™-treatment, after the 12-day PST™-treatment period, 6 weeks thereafter, 12 weeks, and 6 months. • Final evaluation at 12 weeks: 52% were significantly improved and 22% were symptom free.	Following analysis, Goebel-Hiller Scores showed a definite and significant improvement in 52% of the patients, evaluated. This improvement was found to increase over time (long-term effect).

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

23. Chronischer Mobus Tinnitus (A Pilot Study) K. Pfeiffer, R. Markoll, R. Breul	1999	2001	78	The severity of Tinnitus was assessed using Goebel-Hiller Scores. Patients were evaluated before PST™-treatment, after the 12-day PST™-treatment period, 6 weeks thereafter, 3 months, and 6 months.	A definite improvement was found 3 months post-PST™ treatment. This improvement was found to increase over time (long-term effect).
24. Three Prospective Clinical Trials conducted in Berlin, Nuremberg and Munich, Germany, on Chronic Tinnitus (Grades, II, III, or IV). M. Dornacher, G. Buschmann, K. Pfeiffer *et al.*	1997	2000	Tot.= 199 patients [128 females and 71 males ranging in age from 17 to 78 years (mean age 57)].	Treatment consisted of 12 one-hour PST™ sessions conducted over a two-week period All patients were evaluated before and at the end of treatment, and six and 12 weeks after the treatment using validated measurement instruments (Goebel-Hiller). Data on hearing loss and other relevant parameters were also obtained.	Randomly selected patients, with long-standing Tinnitus, who failed to respond to conventional treatments, were and the population at large, chosen as the control. A gratifying and progressive trend of improvement was reported at the end of treatment and six weeks later (an additional 25% of the patients). Final evaluation 12 weeks following treatment revealed that 26% were unchanged, 52% were very significantly improved, and 22% were now completely symptom free. No adverse side effects were reported or noted. Many in the significantly improved cohort reported a loss or diminution of high frequency pitch ringing or replacement by a low frequency hum that was much less disturbing.

25. Tinnitus Randomized Multi-Center Double-Blind Clinical Study Biesinger, Guth, K. Pfeiffer *et al.* Nyhuis, Gabler, Dornacher, Sikezsdy, Hilber (Conducted at a Clinics and Medical Centres)	1999	2002 Presentation at the HNO Congress in Dresden, Germany 27-05-2003		Patients were examined and the impairment due to Tinnitus assessed and measured using the tinnitus questionnaire of Goebel-Hiller (1998). The intensity/severity of the Tinnitus was graded (classified) as low, medium, high or very high, depending on the total score obtained on the Goebel-Hiller questionnaire, for all psychometric measurements made. The data was statistically analyzed using the paired-samples T-test, pre-treatment, after the 12-day treatment period, and thereafter, at 6 weeks, 3 months, 6 months, and 1-year.	It was found that following the 12-day treatment, as well as, at 6 weeks and 3 months thereafter, there was a statistically significant difference ($p>0.05$) between the degree (grade) of tinnitus severity, compared to pre-treatment. This indicates that, with time, treatment decreases the overall severity of the tinnitus to a statistically significant degree.

C.4) Osteo

Nature of study & Study Directors	Location	Year Started	Conclusive Findings
Studie zum Nachweis der Wirksamkeit der PST bei Patienten mit gesicherter Osteoporose (Pilot Study) K. Pfeiffer* H. Radspieler** R. Markoll*	* Infinomed – Institut für Innovative Medizin, München ** Osteoporose Diagnostik- und Therapiezentrum München	2002	In the control group (the wrist not subjected to PST™), no significant changes in vBMD were observed. However, at the end of treatment, an increase in trabecular vBMD was observed in the wrist subjected to PST™, which continued increasing at 3- and 6-months post end of treatment. This increasing trend suggests a balancing (restoration) of the resorption and formation processes, characteristic of bone remodeling, by PST™. PST™ demonstrates positive effects on bone formation and restores the innate balance of the remodeling process(es). 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.

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

Completed in vitro Studies

Nature of the Study	Institution where the study was conducted & publication(s) (where applicable)	Published in	*Notes*
26. The stimulation of chondrocyte metabolism by pulsed magnetic fields D-A Grande, A.J. Bollet, R. Markoll	North Shore University Hospital, New York (affiliated with Cornell University), USA	*Draft*, 1992.	The purpose of this study was to examine the potential biostimulation of the BMTS field configuration on *in vitro* cartilage explants maintained in organ culture during exposure to the electromagnetic (EM) fields. During exposure to the EM fields, a strong effect was seen in response to sulfate incorporation that was statistically significant at the 0.05 level. This is perhaps the most significant parameter for assessment of repair or relief, as proteoglycan is one of the principle matrix molecules lost in OA.
27. Pulsed Signal Therapy (PST) enhances the proteoglycans concentration in human chondrocyte cultures. F. Nerucci, A Fioravanti C.Tofi, K. Righeschi, R. Marcolongo, R. Markoll	Institute of Rheumatology, University of Siena, Siena, Italy	• *Bioelectromagnetics Society [BEMS] Twenty-Second Annual Meeting Abstract Book,* Munich, Germany, June 11-16, 2000: 48. • Fioravanti A, Nerucci F, Collodel G, Markoll R, Marcolongo R. Biochemical and Morphological Study of Human Articular Chondrocytes cultivated in the presence of Pulsed Signal Therapy. *Ann*	This study focused on the biochemical and morphological analysis of human articular chondrocytes cultured in the presence and absence of Interleukin-β (Il-β) and subjected to PST™. The presence of large vacuoles in the cytoplasm, devoid of other cellular structures, confirmed the marked cellular damage, caused by Il-β. Stimulation of these cells by PST™ was found to restore cell structures, and so too, proteoglycan synthesis by chondrocytes. A significant ($p < 0.05$) increase in PG concentration in the culture medium of cells subjected to PST™ exposures was found, exceeding that in the control groups. No significant additional differences were found for those cell cultures subjected to pressure cycles. The increase in metabolic activity was further supported by morphologic assessments carried out with a transmission electron microscope (TEM) and a scanning electron microscope (SEM). These results collaborate with studies showing electric stimuli and PEMF enhanced cartilage repair, increased [^{3}H] Thymidine incorporation into chondrocyte DNA of chondrocytes (proliferation), as well as $^{35}SO_4$ uptake (glycosaminoglycan production). They provide evidence in

		Rheum Dis. 2002; 61:1032-1033	general support of the explanatory hypothesis, in particular, confirming the argument that PST™ exposures tend to enhance proteoglycan concentrations in challenged human cartilage tissues.
28. Pulsed Signal Therapy (PST) Stimulates Mitosis of Human Chondrocytes in Culture. H. Gierse, R. Breul, M. Faensen, R. Markoll	Praxis für Orthopädie und Sportstraumatologie, Cologne, Germany	Singapore Humanitas Press, *In Proceedings: Tenth International Conference on Biomedical Engineering.* Singapore, December 2000; 473-474.	This experiment clearly demonstrated that **human chondrocyte cell cultures exposed to the specific electromagnetic fields generated by PST™ attained statistically significant higher mitosis-rates than chondrocytes in untreated cultures.** This *in vitro* finding confirms the positive results of over twenty prospective clinical studies of patients suffering from osteoarthritis and supports one of the proposed mechanisms of action that may be responsible for these benefits.
29. 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]. I. Krüger, T. Knedel, J. Zimmermann, M. Sittinger, M. Faensen	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.	Histological analysis revealed the formation of cartilaginous extracellular matrix in PST™-treated cultures and controls. On the basis of biochemical analysis, treatment of meniscal and arthritic chondrocyte cultures resulted in an increased deposition of collageneous matrix components. For arthritic, articular chondrocytes, only a marginal enhancement of collagen synthesis was documented almost directly after stimulation of artificial cartilage cultures. For meniscal chondrocytes, PST™ demonstrated a positive effect on matrix formation in the long-term (up to 6 months post-electro-magnetic stimulation).
30. Study of the clinical effect of PST with trials of the Synovial liquid in	Auguste-Victoria-Hospital Berlin, University of Erlangen	Commenced: 1998 Terminated: 2001	In general, matrix metalloproteinases (MMP's) are responsible for the degradative (CATABOLIC) events invoked in the cartilage and bone of arthritic joints. However, some have a dual function, and are

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

gonarthrosis. D. Schuppan, M. Faensen R. Markoll		Submitted for publication	therefore also responsible for triggering events and signalling pathways, to restore and rebuild damaged tissue (ANABOLIC). Two-tailed t-tests for difference between means, showed statistically significant difference between pre- and post-PST™ treatment*, for MMP 1 and 9. The increased levels of MMP1 and MMP9 obtained, suggest that **PST™ may function to ensure rapid onset of restoration of damaged tissue**. In addition, the pain intensity, two-tailed t-tests for difference between means, showed statistically significant difference between pre- and post- PST™ treatment*. **Pain decreased significantly with time, post-PST™ treatment*.** Increased levels of bifunctional MMP's, 1 and 9 were obtained, post-PST™ treatment*, suggesting that PST™ may function to stimulate these, triggering the onset of catabolic events, and in so doing, shortening the time span to initiate anabolism ($p<0.05$). Pain intensity evaluated pre- and post-PST™ treatment*, with regards to morning awakening, at rest (night), on ascending and descending stairs, on standing for 15 minutes, and also on descending stairs, shown significantly increased decreases, in all regards, post-PST™ treatment* ($p<0.05$). Pearson Correlation showed that the clinical results and improvement in pain (assessed by VAS and ADL) obtained, correlated with the change in levels of ECM parameters measured in the joint fluid post-PST™ treatment* associated with ECM breakdown and repair.

* post-PST™ treatment = 8 weeks ±2 days

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

Current Clinical Studies

"Study"	Investigators	Location(s)
Ortho Clinical Improvement of Gonarthrosis after Pulsed Signal Therapy® (PST™), is accompanied by an increase in intrarticular Matrix Metalloproteinases and markers of regeneration.	Prof. Michael Faensen, Dr. med. Burckhardt Neise, Dr. med. (cand.) Dulce M. Da Silva Ferreira, BSc, BSc Hons Pharmacology) Harald Martin, Dr. med. (cand.) Richard Markoll, MD PhD Theresa K. Toohil, MS PhD Prof. Detlef Schuppan, Dr. med. PhD *In press*	University of Erlangen, Germany
Osteo Long-term, Multicenter Post-Marketing Surveillance Investigations of Pulsed Signal Therapy® (PST™) for the treatment of Osteoporosis.	Dr J. Semler * Dr. B. Muche* Dr M. Dornacher + D. Da Silva Ferreira** Dr H. Martin** Dr R. Markoll**	* Immanuel-Krankenhaus Rheumaklinik Berlin-Wannsee + ProGelenk Zentrum, Berlin-Wilmersdorf **Infinomed - Institute for Innovative Medicine, München Selected medical centers in Germany
Tinnitus	Dr Vitztum	Magdeburg, Germany
Dental	Dr Rotlauf	Munich, Germany

PST – PROVEN, DOCUMENTED & CURRENT STUDIES

2005 Prospective Studies

"Study"	Investigators	Location(s)
Ortho The potential role of PST™ in reversing liver fibrosis – effects on matrix remodelling.	Prof. Detlef Schuppan, Dr. med. PhD Richard Markoll, MD PhD Dulce M. Da Silva Ferreira, BSc, BSc Hons Pharmacology Theresa K. Toohil, PhD	Harvard University, Boston, Massachusetts