PULSED SIGNAL THERAPY FOR OSTEOARTHRITIS: CLINICAL TRIAL RESULTS IN OVER 100,000 PATIENTS WITH SUPPORTIVE *IN VITRO* METABOLIC AND IMAGING STUDIES

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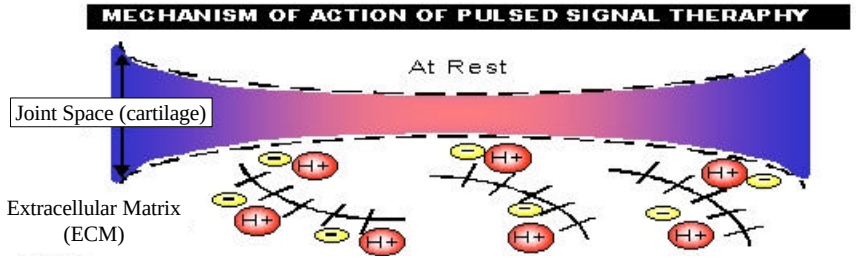
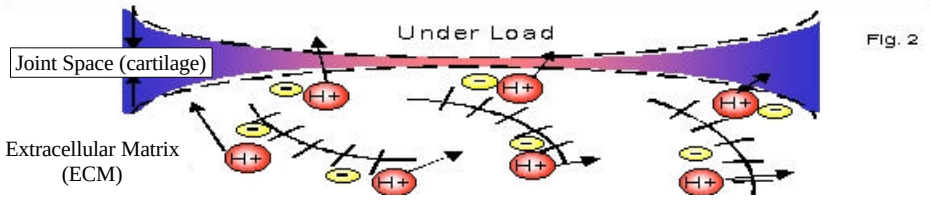
INTRODUCTION:

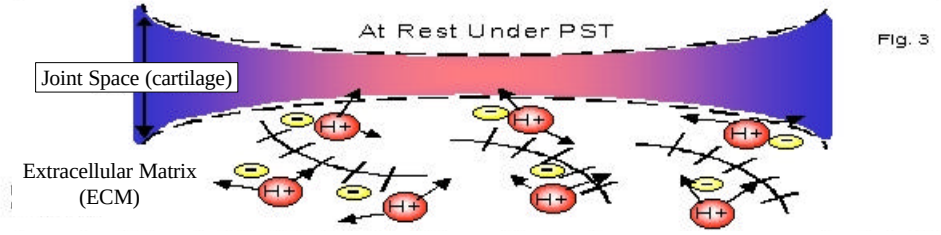
Like other tissues, bone and cartilage are constantly being built up and broken down by a variety of metabolic and physical influences. The major stimulus for bone and cartilage formation is a piezoelectric signal generated when these structures are subjected to tension or compression. This explains why bone atrophies in the absence of any significant pressure, such as weightlessness during space travel or immobilization in a cast. The transmission of this signal is also impaired following joint injury due to trauma or diseases such as osteoarthritis. Pulsed Signal Therapy (PST™) is the result of three decades of research designed to characterize and reproduce the piezoelectric signal that initiates these regenerative activities by creating a streaming potential in the extracellular matrix (ECM) when bone or cartilage are placed under a load. PST™ can recreate this streaming potential and its restorative rewards in joints impaired due to disease or trauma even though they are at rest, as illustrated in Figures 1-3 on the right.



Charge equilibrium between hydrogen protons and negative charge carriers in the extracellular cartilage matrix - no streaming potential -



Creation of a streaming voltage potential in the ECM during loading caused by the compression of fixed negative charged fluid forced out of cartilage tissue with forced influx of hydrogen protons



Generation of streaming voltage potentials flow in the joint caused by forced movement of hydrogen protons in the ECM through alternating PST signals as stimulation of chondrocytes in the ECM

MATERIALS and METHOD:

PST™ is administered via a magnetic field generator that emits a proprietary pulsed electromagnetic field by means of a connected ring-shaped applicator coil. Applicator devices with different coil sizes have been developed to treat peripheral joints (knees, shoulders and wrists or hands and elbows), the axial spine (cervical, thoracic and lumbar vertebral bodies), tinnitus and dental disorders and for veterinary applications.

As depicted in this illustration of the treatment of osteoarthritis of the knee (Figure 4), the affected joint is placed inside the applicator coil and exposed to physiological frequency/amplitude combinations that are automatically switched, so that an induction phase takes place during the first 10 minutes followed by a combination of therapeutic pulsed stimuli for the remaining 50 minutes. PST™ is typically administered for an hour a day for nine consecutive days interrupted only by a weekend. No further treatment is usually required.

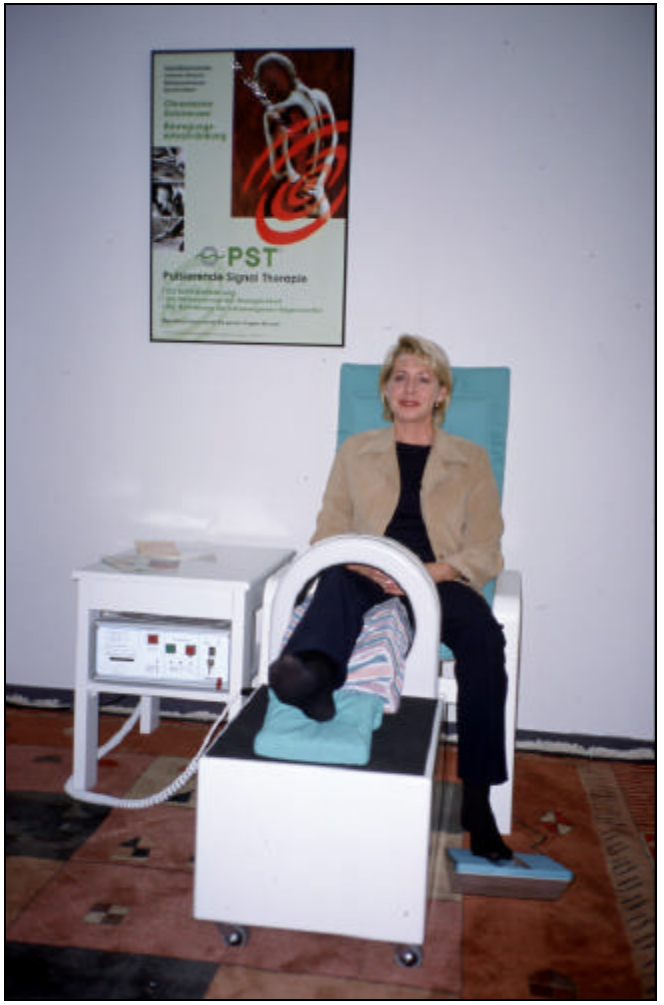


Figure 4

RESULTS:

Clinical Trials

The long term efficacy and safety of PST™ was initially established in randomized, double blind placebo controlled clinical trials conducted a decade ago that were published in a peer reviewed journal.[1,2] Since then, the ability of PST™ to reduce pain and improve functional mobility and range of motion in osteoarthritis has been confirmed in double blind and other clinical trials in over 100,000 patients.[3] Treatment is non-invasive, not associated with any adverse side effects and long term follow-up studies confirm sustained pain relief, improved mobility and complete safety.

Last year, more than 50,000 patients received PST™ in over 300 hospitals and medical clinics in sixteen countries, where it is usually reimbursed by fiscal intermediaries and governmental agencies because of its proven record of cost effectiveness and safety. PST™ is currently approved in the U.S. only for veterinary applications.

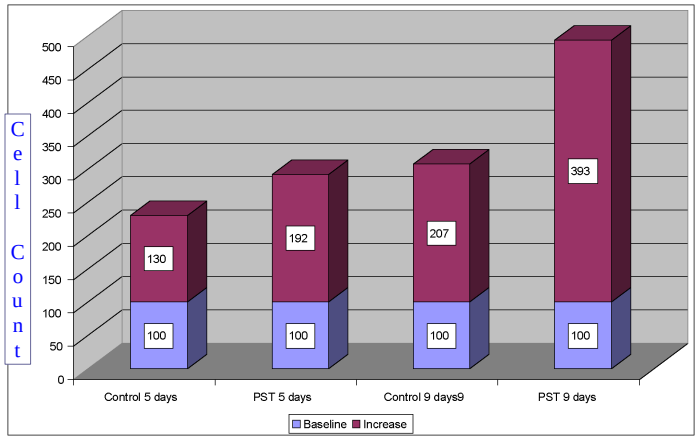


Figure 5

PST™ Stimulation Of Mitosis In Human Chondrocyte Cultures[4]

Chondrocytes obtained from the femoral condyles of six patients undergoing reconstructive surgery for osteoarthritis of the hip were cultivated following a standard protocol. The cell suspensions were divided equally into two groups, one of which received one hour of PST™ daily for 5 to nine days and the other was an untreated control group. Cell counts were obtained by light microscopy at baseline and after 5 and 9 days. As indicated in the histogram on the left (Figure 5), the treated group showed a significantly increased percentage of mitotic activity after nine days.

Enhancement Of Proteoglycans Synthesis[5]

Several mediators, such as hormones, growth factors and cytokines, regulate the dynamic balance between anabolic and catabolic bone activities. Interleukin 1β (IL-1β) is a cytokine that is involved in cartilage degradation processes and can be found in the synovial fluid of osteoarthritic subjects. This study evaluated *in vitro* effects of PST™ on cultures of human articular chondrocytes cultivated in the presence of or in the absence of IL-1β. Under these conditions, the effect of PST™ through metabolic activity was evaluated by proteoglycans (PG) levels in the culture medium and morphologic assessments carried out with a transmission electron microscope (TEM) and a scanning electron microscope (SEM).

Human articular cartilage was obtained from the femoral heads of eight OA subjects undergoing surgery for total hip prostheses. Chondrocytes were cultivated in alginate gel on Petri dishes for 72 hours with and without IL-1β (5ng/ml).

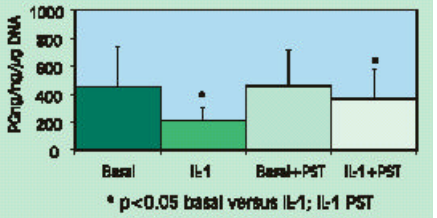


Fig. 6

Some dishes were exposed for 3 hours a day to PST™. Control cultures were maintained under identical conditions to the treated cells, but in the absence of PST™. After the culture period the medium was removed and collected for PG determination by immunoenzymatic method on microplates for the quantitative measurement of human PG. Cells in alginate gel were immediately fixed for transmission electron microscopy (TEM) and for scanning electron microscopy (SEM).

The PG concentration in the culture medium at baseline conditions, in the presence of IL-1b at a concentration of 5ng/ml without and with PST™ stimulation, is shown in Figure 6 on the left. The presence of IL-1β determines a significant decrease ($p<0.05$) in PG levels, but when the cells are cultured in the presence of IL-1β and submitted to PST™ stimulation statistically significant restoration ($p<0.05$) of PG production is observed.

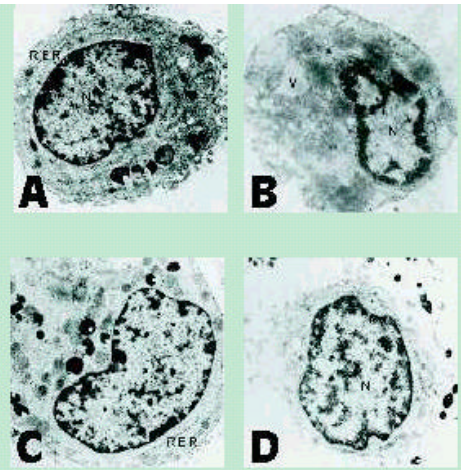


Fig. 7A, B, C, D

The results concerning metabolic production are further confirmed by the morphologic findings obtained by TEM and SEM. Figure 7 on the right shows chondrocytes photographed by TEM. Fig. 7A shows a cultured cell at basal conditions: the nucleus (N) appears euchromatic, the cytoplasm contains a fair amount of rough endoplasmic reticulum (RER) and lipid droplets. Fig. 7B shows a cell cultured in the presence of IL-1β and its damage is evident: several vacuoles (V) in the cytoplasm are devoid of typical structures. Fig. 7C shows a cell cultured in basal condition and submitted to PST™ stimulation: the cell shows a good state of health. Fig. 7D shows a cell cultured in the presence of IL-1β and submitted to PST™ stimulation; a clear restoration of the cell structures can be observed: the cytoplasm contains rough and smooth endoplasmic reticuli and lipid droplets.

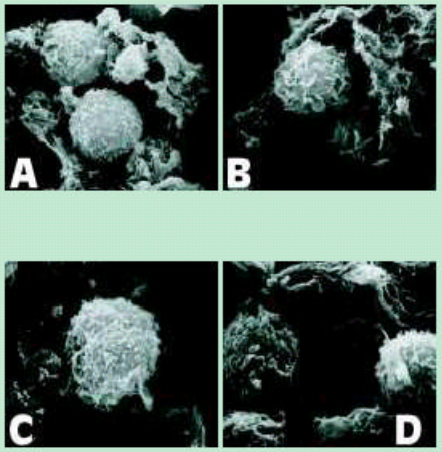


Fig. 8A, B, C, D

Fig. 8 on the left shows the SEM image of cells. Fig. 8A shows cells cultured at baseline conditions: it is interesting to observe that its spherical shape has been preserved, the presence of some secretion granules and the thick network of collagen fibrils. Fig. 8B shows a cell cultured in the presence of IL-1β: its damage is clearly evident and this is further confirmed by the loss of cytoplasmic processes and by the presence of superficial alterations. Fig. 8C shows a cell cultured at basal conditions and submitted to PST™ stimulation: its SEM image shows the presence of abundant collagen fibrils and secretion granules. Fig. 8D shows a cell cultured in the presence of IL-1β and submitted to PST™ stimulation; a clear restoration of the cell structures can be observed as confirmed by the presence of several surface granules.

CONCLUSION:

Pulsed Signal Therapy differs from other electromagnetic approaches because of its specific amplitude, frequency and repetition parameters. PST™'s patented signal (pulsed DC magnetic field 0.28 W., max. 20 gauss; 5-24 Hz; quasi-rectangular wave form) is the only electromagnetic stimulus with well documented, long term, multi-center clinical study proof of efficacy and safety in rigorously controlled trials. In sharp contrast to other devices that make similar claims, the proposed mechanisms of action of PST™ are also supported by extensive basic science *in vitro* studies, as described in the previous RESULTS SECTION.

DISCUSSION:

Arthritis affects over 43 million Americans and is the leading cause of pain and disability in the world. Costs in the U.S. of $20.2 billion last year are expected to exceed $40 billion by 2005 since senior citizens, all of whom have some degree of osteoarthritis, are the fastest growing segment of the population, particularly those over 80. Prescription and over-the-counter-drugs must be taken for a lifetime and are associated with gastrointestinal bleeding, liver disease and other complications that result in more than 100,000 hospital admissions and thousands of deaths annually. Surgical and various experimental approaches are expensive and similarly may not provide permanent benefits. Pulsed Signal Therapy (PST™) is an effective and completely safe alternative that requires only one course of treatment to provide sustained relief of pain and restoration of normal mobility as demonstrated on long term follow-up studies. PST™ has been found to be effective in tinnitus, for which there is no satisfactory treatment; periodontal disease, an established risk factor for heart attacks; TMJ syndrome; other types of joint disorders and particularly joint trauma resulting from sports injuries and accidents. As indicated, PST™ is currently approved in the United States only for veterinary applications, where it has also been demonstrated to be extremely efficacious and the likelihood of any placebo effect can be excluded.

"*There is a vast interdisciplinary gap between biophysics and medicine. We should endeavor to bridge this gap*".
C. Andrew L. Bassett

References

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