PASIG MONTHLY CITATION BLAST: No.29 **April 2008**

Dear PASIG members:

Spring and blossoming trees are here in the East. Planning for the CSM PASIG programming is well underway. Save the date: our next Combined Sections Meeting will be held in Las Vegas, NV, February 9 –12, 2009.

CSM abstract submission is open as of March 18th and the deadline will be here sooner than you think (June 18th). I hope many of you will consider submitting an abstract from your performing arts research. Abstract topics can include pilot and full scientific research studies, case studies, clinical topics, or special interest reports. Go to http://www.apta.org/csm for more information and to connect to Scholar One Abstract Central for electronic submission. If PASIG members would like feedback on an abstract prior to submission, please contact me and either I or someone on the PASIG Research Committee will help you or recommend you to someone knowledgeable in your area.

Don't forget, the PASIG sponsors an annual student research scholarship. This award is to recognize students, who have had an abstract accepted to CSM, for their contribution to performing arts medicine and research. We encourage you to mentor your students in PA-related research and have them apply! If the PASIG Research Committee can assist students, please contact us. For more information on the research award please check our webpage (www.orthopt.org/sig_pa.php). Students with additional questions can contact PASIG President Leigh Roberts (lar@brventures.com).

The PASIG is an important clearinghouse for information. To that end, the PASIG is developing an electronic survey to update our records and compile a comprehensive directory for our members. Please support this effort with your response! I'll keep you posted on its release.

Our topic this month is *Bone stimulation*, contributed by myself. The format is an annotated bibliography of articles on the selected topic focusing on the last decade. Each month's citations will be added to EndNote libraries available on the PASIG webpage for our members to access and download. (Information about EndNote referencing software can be found at http://www.endnote. com, including a 30-day free trial). If you'd like to suggest a topic or create one, please let me know. As always, your comments and entry contributions to these Citation Blasts are always welcome.

As always, please drop me an e-mail anytime.

Regards,
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BONE STIMULATION

Nonunion fractures and avascular necrosis can be particularly devastating for a dancer or athlete. Surgical options include excision or open surgical debridement with internal fixation and bone grafting. There are alternatives to conventional bone-graft surgery. Both electrical and low intensity ultrasound bone stimulators have demonstrated effective acceleration of bone healing. However, the majority of this research has focused on fresh fractures, arthodesis, and non-union fractures of long bones (e.g. femur, tibia, fibula, metatarsals, radius).

We have had good experiences in the treatment of two dancers using an inductive coupling bone stimulator with pulsed electromagnetic field for a nonunion lateral sesamoid fracture and for a nonunion tibial fracture.

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PASIG Research Chair

Anglen J (2003). The clinical use of bone stimulators. J South Orthop Assoc **12**(2): 46-54.

Delay or failure of healing in long bone fracture is a common clinical problem confronting the orthopaedic surgeon, and can have significant impact on the quality of life for patients who have it. One treatment option for this problem is the use of electrical or ultrasonic bone stimulation. Electrical signals can be delivered with an implantable direct current stimulator, or noninvasively using inductive or capacitive coupling to induce currents in the tissues. Low-intensity ultrasound can speed the healing of fresh fractures.

Although regarded with skepticism by many physicians, there is abundant evidence from clinical studies of the effectiveness of these treatments. In addition to dozens of retrospective reports, randomized, prospective, double-blind controlled trials have shown the efficacy of electrical stimulation for nonunion and ultrasound for speeding healing. Patients with unacceptable deformity, synovial pseudarthrosis, or large gaps are generally not good candidates for this treatment modality. This article is a review of the clinical literature regarding treatment of long bone nonunion with bone stimulators.

Brighton CT, Pollack SR (1985). Treatment of recalcitrant non-union with a capacitively coupled electrical field. A preliminary report. J Bone Joint Surg Am **67**(4): 577-85.

Twenty-two well established non-unions in twenty patients were treated with a capacitively coupled electrical signal (sine wave, sixty kilohertz, five volts peak to peak) that was applied non-invasively through stainless-steel capacitor plates placed on the skin surface overlying the approximate site of the non-union. The average age of the eleven female and nine male patients in this series was 38.4 years, and the average duration of the twenty-two non-unions was 3.3 years. Seventeen of the non-unions were labeled recalcitrant, meaning that they had failed to heal after either previous bone-grafting or another type of electrical stimulation, or both. Five of the non-unions had not been previously treated. Seventeen (77.3 per cent) of the non-unions achieved solid osseous union after an average of 22.5 weeks of treatment with capacitive coupling. The results in this small series were not affected by the non-union being recalcitrant, by the fact that one patient bore full weight on the extremity in a cast, by the presence of osteomyelitis, or by the presence of remaining metallic internal-fixation devices in the bone. Since capacitive coupling is non-invasive, involves portable equipment, allows full weight-bearing on the lower extremity in a cast, is easy to apply, and does not require precise localization of the capacitor plates, it has distinct advantages over other methods of treating non-union with electricity.

Chang WH, Sun JS, et al. (2002). Study of thermal effects of ultrasound stimulation on fracture healing. Bioelectromagnetics **23**(4): 256-63.

Low intensity ultrasound stimulation has been used as a strategy to promote fracture healing. This study investigated the mechanism of ultrasound stimulation in enhancing fracture healing. Forty-five adult New Zealand White rabbits were divided into control, microwave treated, and ultrasound stimulation groups. After anesthesia, transverse osteotomy was created at midportion of the fibula bone. Intravital staining followed by fluorescence microscopic examination of new bone formation in the osteotomy site and biomechanical tests on torsional stiffness of the osteotomy site were performed. The difference between each examination was evaluated and analyzed. After ultrasound stimulation, new bone formation in the osteotomy site of the stimulated limb was 23.1-35.8% faster than that of the sham treated limb; the torsional stiffness of the stimulated limb was 44.4-80.0% higher than that of the sham treated limb. In the group of microwave hyperthermia treatment, the new bone formation was higher than that of the sham treated limb, but the difference was not statistically significant. The difference in torsional stiffness between the microwave hyperthermia treated limbs and the sham treated limb was not quite statistically significant. We demonstrated that low intensity ultrasound stimulation could increase the new bone formation and torsional stiffness. These effects probably are not mediated via hyperthermia.

Claes, L., A. Ruter, et al. (2005). Low-intensity ultrasound enhances maturation of callus after segmental transport. Clin Orthop Relat Res(430): 189-94.

The purpose of this study was to determine whether low-intensity ultrasound can be used to enhance callus maturation. Fifteen-millimeter bone defects at the metatarsal bones of sheep were treated with a segmental bone transport for 16 days. The callus formations in the bone defects were allowed to mature for 63 days before the animals were sacrificed. Eighteen sheep were operated on and divided into two groups. One group was treated with low-intensity ultrasound for 20 minutes per day, whereas the other group served as an untreated control group. Biomechanical tests after removal of the metatarsals showed significantly higher axial compression stiffness and significantly higher indentation stiffness of callus tissue in the healing zone in the group treated with ultrasound. Also, histologic analysis of the cortical defect zone showed significantly more callus formation and more active zones of endochondral ossification in the group treated with ultrasound. Stimulation of callus maturation by ultrasound is possible, similar to stimulation of fresh fracture healing, and may be used to shorten clinical treatment times.

Divelbiss BJ, Adams BD (2001). Electrical and ultrasound stimulation for scaphoid fractures. Hand Clin **17**(4): 697-701, x-xi.

The standard treatment for delayed union or nonunion of the scaphoid is operative management. Electrical stimulation has been employed in these clinical situations in patients unable or unwilling to undergo surgical intervention. Recent interest has also focused on the use of low-intensity ultrasound as an adjunct to healing in distal radius and tibial fractures. Results with the use of ultrasound for scaphoid fractures is encouraging. A review of the mechanisms of action, clinical results, and possible indications is presented for these two nonoperative modalities.

Gebauer D, Mayr E, et al. (2005). Low-intensity pulsed ultrasound: effects on nonunions. Ultrasound Med Biol **31**(10): 1391-402.

To study the efficacy of low-intensity pulsed ultrasound (US), or LIPUS, of 85 treated nonunion cases with a minimum fracture age of 8 months, 67 cases met the study criteria. These were: no surgical intervention during 4 months before US treatment and radiographically ceased healing for 3 months before US. In a self-paired control study, the mean fracture age of the 67 patients was 39 +/- 6.2 months. After a daily 20-min US treatment at home for an average of 168 days, 85% (57 of 67) of the nonunion cases were clinically and radiographically healed. The study did not include any cases that were malaligned, grossly instable, actively infected or that had extensive bone loss. The results demonstrate that the specific US can effect heal rates similar to those achieved by surgical means, without the associated risks and complications, and to those achieved by electrical bone growth stimulation or by extracorporeal shock-wave therapy.

Gossling HR, Bernstein RA, et al. (1992). Treatment of ununited tibial fractures: A comparison of surgery and pulsed electromagnetic fields (PEMF). Orthopedics **15**(6): 711-9.

The use of pulsed electromagnetic fields (PEMF) is gaining acceptance for the treatment of ununited fractures. The results of 44 articles published in the English language literature have been compiled to assess the effectiveness of PEMF vs surgical therapy. For ununited tibial fractures, 81% of reported cases healed with PEMF vs 82% with surgery. After multiple failed surgeries, the success rate of PEMF is reported to be greater than with surgery; this discrepancy increases with additional numbers of prior surgeries. In infected nonunions, the results of surgical treatment decreased by 21% and were less than the results utilizing PEMF (69% vs 81%). In open fractures, surgical healing exceeded PEMF (89% vs 78%), whereas in closed injuries PEMF cases healed more frequently (85% vs 79%). In general, PEMF treatment of ununited fractures has proved to be more successful than noninvasive traditional management and at least as effective as surgical therapies. Given the costs and potential dangers of surgery, PEMF should be considered an effective alternative. Experience supports its role as a successful method of treatment for ununited fractures of the tibia.

Hayton MJ, Dillon JP, et al. (2005). Involvement of adenosine 5'-triphosphate in ultrasound-induced fracture repair. Ultrasound Med Biol **31**(8): 1131-8.

Ultrasound (US) accelerates fracture healing; however, the mechanism of this effect remains unclear. Adenosine 5'-triphosphate (ATP) stimulates bone remodeling and is released constitutively from intact osteoblasts; this is a process that is enhanced after mechanical stimulation. We hypothesized that ATP release from osteoblasts is increased after US stimulation and that this leads to accelerated fracture healing. US was applied to SaOS-2 human osteoblasts and the concentration of ATP in the cell culture medium was determined. Cell proliferation and gene expression were subsequently investigated. Increased concentrations of ATP were detected in the culture medium of US-treated cells and both ATP and US stimulation caused increased receptor activator of nuclear factor-kappa B ligand (RANKL), decreased osteoprotegerin expression and increased cell proliferation by SaOS-2 cells. These findings indicate that US causes ATP release by osteoblasts in vitro and that this may contribute to accelerated fracture healing by enhancing osteoblast proliferation and increasing RANKL expression and decreasing osteoprotegerin expression by osteoblasts to promote osteoclastogenesis.

Heybeli N, Yesildag A, et al. (2002). Diagnostic ultrasound treatment increases the bone fracture-healing rate in an internally fixed rat femoral osteotomy model. J Ultrasound Med **21**(12): 1357-63.

OBJECTIVE: To investigate the healing effects of diagnostic ultrasound in a standardized rat femur fracture model. METHODS: Thirty-two male rats aged 14 weeks were used, and each rat's right femur was osteotomized and stabilized under anesthesia. The rats were then divided into 4 groups. Five days after surgery, ultrasound was applied every fifth day with diagnostic sonographic equipment and a probe with a 7.5-MHz frequency and 11.8-mW/cm2 total output intensity for 10 minutes in each session. Ultrasound was applied 8 times in group A, 3 times in group B, and only once in group C. Ultrasound was not applied to sham-operated group D. Healing and callus formation of the rats' femur fractures were evaluated by radiography and dual-energy x-ray absorptiometry. RESULTS: Dual-energy x-ray absorptiometric and radiographic results showed that the ultrasound therapy accelerated the fracture healing. Radiographically, groups A and B showed better fracture healing than groups C and D. Ultrasound exposure increased both the whole-bone mineral density and the density at the fracture region, increasing in parallel with the exposure period. CONCLUSIONS: This study confirms the previously shown efficacy of low-intensity ultrasonic stimulation in acceleration of the normal fracture repair process even when performed with a diagnostic sonographic device.

Lerner A, Stein H, et al. (2004). Compound high-energy limb fractures with delayed union: our experience with adjuvant ultrasound stimulation (exogen). Ultrasonics **42**(1-9): 915-7.

The use of low intensity pulsed ultrasound accelerates cortical and cancellous bone fracture healing. Seventeen patients with eighteen high-energy fractures of the long bones were treated with low intensity pulsed ultrasound supplementation to surgical skeletal stabilization and tissue flaps. Sixteen fractures were healed within 13-52 weeks after starting ultrasound supplementation despite severe soft-tissue injuries and varying degrees of tissue loss. This method may be useful in the combined treatment of high-energy limb injuries.

Nelson FR, Brighton CT, et al. (2003). Use of physical forces in bone healing. J Am Acad Orthop Surg **11**(5): 344-54.

During the past two decades, a number of physical modalities have been approved for the management of nonunions and delayed unions. Implantable direct current stimulation is effective in managing established nonunions of the extremities and as an adjuvant in achieving spinal fusion. Pulsed electromagnetic fields and capacitive coupling induce fields through the soft tissue, resulting in low-magnitude voltage and currents at the fracture site. Pulsed electromagnetic fields may be as effective as surgery in managing extremity nonunions. Capacitive coupling appears to be effective both in extremity nonunions and lumbar fusions. Low-intensity ultrasound has been used to speed normal fracture healing and manage delayed unions. It has recently been approved for the management of nonunions. Despite the different mechanisms for stimulating bone healing, all signals result in increased intracellular calcium, thereby leading to bone formation.

Raasch WG, Hergan DJ (2006). Treatment of stress fractures: the fundamentals. Clin Sports Med **25**(1): 29-36, vii.

This article is an introduction to the fundamentals of stress fracture management. Extrinsic and intrinsic factors, that may play a role in the development of stress fractures, are discussed and incorporated as possible treatment options. Different treatment modalities including ultrasound and electromagnetic fields are addressed, with an emphasis on literature support.

Sharrard WJ (1990). A double-blind trial of pulsed electromagnetic fields for delayed union of tibial fractures. J Bone Joint Surg Br **72**(3): 347-55.

A total of 45 tibial shaft fractures, all conservatively treated and with union delayed for more than 16 but less than 32 weeks were entered in a double-blind multi-centre trial. The fractures were selected for their liability to delayed union by the presence of moderate or severe displacement, angulation or comminution or a compound lesion with moderate or severe injury to skin and soft tissues. Treatment was by plaster immobilisation in all, with active electromagnetic stimulation units in 20 patients and dummy control units in 25 patients for 12 weeks. Radiographs were assessed blindly and independently by a radiologist and an orthopaedic surgeon. Statistical analysis showed the treatment groups to be comparable except in their age distribution, but age was not found to affect the outcome and the effect of treatment was consistent for each age group. The radiologist's assessment of the active group showed radiological union in five fractures, progress to union in five but no progress to union in 10. In the control group there was union in one fracture and progress towards union in one but no progress in 23. Using Fisher's exact test, the results were very significantly in favour of the active group ($p = 0.002$). The orthopaedic surgeon's assessment showed union in nine fractures and absence of union in 11 fractures in the active group. There was union in three fractures and absence of union in 22 fractures in the control group. These results were also significantly in favour of the active group ($p = 0.02$). It was concluded that pulsed electromagnetic fields significantly influence healing in tibial fractures with delayed union.

Zorlu U, Tercan M, et al. (1998). Comparative study of the effect of ultrasound and electrostimulation on bone healing in rats. Am J Phys Med Rehabil **77**(5): 427-32.

This study was performed to compare the effects of direct current with ultrasound on fracture healing. Thirty-two rats were subjected to the experiment. Each rat's right legs were used as the experimental sample, and their left legs were used as the control. Four groups were formed, each consisting of 16 ultrasound, 16 electrostimulation, 16 ultrasound control, and 16 electrostimulation control animals. Fibular osteotome was applied to the rats under anesthesia. In the electrostimulation and electrostimulation control groups, a stainless steel cathode electrode was installed in the fractured side. In the electrostimulation group, 10 microA of direct current for 30 min, using a semi-invasive method, was given one day after fracture, for 15 days. On the control side, the aforementioned protocol was followed but sham treated. The ultrasound group was treated with 0.1 W/cm2 ultrasound for 2 min every second day for 6 days after fracture (4 times). Rats were killed on the 7th and 14th days to investigate the macroscopic, radiologic, and histopathologic parameters of fracture healing. There was a difference ($P < 0.05$) between the electrostimulation and the electrostimulation control groups on the 7th day. There was a difference ($P < 0.05$) between the ultrasound and ultrasound control groups on the 14th day. After statistical evaluation of the experimental results, it was found that in both the ultrasound and the electrostimulation groups, the fracture healing had been accelerated more so than in the control groups. There was no observed statistical difference between ultrasound and electrostimulation effects.