Holding Power of Variable Pitch Screws in Osteoporotic, Osteopenic and Normal Bone: Are All Screws Created Equal?

R. Ramsawamy\textsuperscript{2,3}, S. Evans\textsuperscript{3}, Y. Kosashvili\textsuperscript{1}

\textsuperscript{1}Orthopedic Surgery, Arthroplasty, Assaf Harofeh Medical Center, Zerifin, Israel, \textsuperscript{2}Orthopedic Surgery, Arthroplasty, Holland Orthopaedic and Arthritic Campus, Toronto, Ontario, \textsuperscript{3}Department of Engineering, Cardiff University, Cardiff, United Kingdom

**Introduction:** Biomechanical properties of 4 different commercially available small fragment cannulated screws (Twin fix (Stryker, Freiburg, Germany), Herbert, (Zimmer, Warsaw, USA), Omnitech (Unomedical, Torino, Italy), Barouk (Depuy, Warsaw, USA)), with variable pitch, used for fracture fixation were compared.

**Materials and Methods:** Polyurethane foam blocks of three different densities with mechanical properties similar to osteoporotic, osteopenic and normal bones were used to conduct the tests. Each screw was tested for pushout and pullout holding power after a primary insertion and for pullout after a repeated insertion into the respective foam blocks.

**Results:** The mean pullout and pushout strengths of all screws correlated to the foam density, and were significantly ($p < 0.001$, $p<0.001$, respectively) better in foam with higher density. The mean pullout strength of each screw was consistently lower after reinsertion into the osteoporotic, osteopenic and normal bone densities by 4% to 30%, when compared to the index insertion (figure 3b). Yet, this difference was not found to be statistically significant ($p=0.23$). The Barouk screw performed significantly ($p < 0.0001$) better than the other screws in all three different densities of foam for both for pushout and pullout after index insertion as well as for pullout tests after reinsertion.

**Conclusion**

The holding power of screws is directly correlated to bone density, thread design and number of threads engaging the bone. Reinsertion through the same hole could reduce the ultimate pullout strength. The surgeon should consider the advantages and disadvantages of each implant, depending on the clinical situation and choose accordingly.
Ameliorative Effects of Chitosan Gel for the Prevention of Knee Osteoarthritis Following Medial Meniscectomy and Ligament Injuries in a Rat Model

D. Robinson¹,³, S. Patchornik³, S. Sagiv², N. Ben Shalom³, Z. Nevo³

¹Foot and Ankle, Orthopedics, Hasharon Hospital, Petah Tikva, Israel, ²Mor Yissum Mehhkarim Ltd, ³Chi2Gel Ltd

Introduction: Osteoarthritis is reliably induced in rats, by partial medial meniscectomy and resection of the medial collateral ligaments (there are two in a rat) and anterior cruciate ligament. The combined injury leads to joint instability and progressive osteoarthritis. This model is the typical one used to assess effectiveness of pharmacologic interventions in a rat model. The current study has been performed in order to evaluate the possible effectiveness of chitosan gel that degrades into glucosamine as a substance capable of delaying osteoarthritis progression.

Methods: 20 Lewis rats were used in the study. Bilateral procedures were performed in the rats' knees. In all rats the right knee was injected with 200 microliters of chitosan gel, while 200 microliters of saline were injected into the left knee in half the animals, in the other half hyaluronate (BTG Ltd. Israel) was injected. Rats were assessed using an Incapacitance tester to assess weight bearing on the affected limb, stress radiography after 6 weeks to assess ligament healing and radiographic and histological analysis of osteoarthritis at three months post op.

Results: The rats in both groups demonstrated preference of weight bearing on the chitosan treated knee. This indicates that this knee is less painful for the animal. Stress radiography indicates statistically significant improvement of knee stability in the chitosan treated leg as compared to the contralateral leg. Radiographic analysis indicates improved joint space, less subchondral sclerosis and less osteohyptse production in the chitosan treated knee. Chitosan was significantly superior to both saline injection and hyaluronate injection. Histological analysis again demonstrated significantly improved Mankin score in the chitosan treated knee.

Discussion: The chitosan treatment appears to protect knees from osteoarthritis induction after acute trauma. This protective effect has previously been shown to occur in osteochondral defects in animals as well as humans. However, this is the first study to demonstrate that the effect is generalized to the entire joint and not only to the site of osteochondral defects. The mechanism of action appears to involve better stem cell support, a scaffolding effect for mesenchymal cells, discharge of glucosamine that is a cartilage differentiation and matrix production inducer, as well as mechanical effects due to reduction of knee cartilage friction.
Inflammatory and Anti-Inflammatory Cytokine Profile in Mild, Moderate and Severely Traumatized Patients

G. Volpin\textsuperscript{1}, T. Meir\textsuperscript{3}, M. Asaf\textsuperscript{1}, M. Cohen\textsuperscript{3}, R. Katz\textsuperscript{1}, S. Pollack\textsuperscript{2}

\textsuperscript{1}Orthopaedic Surgery, Western Galilee Hospital, Nahariya, \textsuperscript{2}Immunology, Ramabm Medical Center, \textsuperscript{3}Immunology, Faculty of Medicine, Haifa, Israel

**Background:** Recently, an increasing research interest has been focused on the issue of cytokines and their role as a marker of immune reactivity in trauma patients. Cytokines appear to have the most potential in predicting the clinical course and outcome in trauma patients and much research is being conducted in order to understand the immunoinflammatory response system in traumatized patients.

**Objective:** to examine the concentration of different cytokines in serum and mononuclear cell cultures of patients with mild, moderate and severe trauma, in the acute, subacute and late phase after the initial injury.

**Methods:** We conducted a double blind prospective study with traumatized orthopedic patients and categorized them into three groups: In the first group we had 27 patients with severe trauma injury. In the second group 31 patients with a moderate injury and in the third one 12 patients with mild trauma injury. Patients were categorized according to a standard scale and 30 ml heparinized blood were drawn from each one a few hours after the injury and three and six months later. Serum levels and cell culture supernatant cytokine concentrations were measured by commercial ELISA kits. Cytokine levels were correlated with the severity of injury.

**Results:** High levels of inflammatory cytokines, mainly IL-6, IL-8 and Inf-gamma, were found in all traumatized patients. During a follow up of six months, a significant decrease of these cytokines was observed whereas no increase in other cytokines could be found. However, LPS- induced secretion of cytokines revealed high level of inflammatory and regulatory cytokines mainly β-IL6 ;IL8 ; TNF in patients with major trauma and much lower levels in patients with mild or moderate trauma.

**Conclusions:** Secretion of large amounts of inflammatory cytokines during the acute phase of trauma may tend to the development of systemic inflammatory response syndrome (SIRS). This may lead to life threatening conditions in polytraumatic patients.
The Regulation of Energy Demand Balance in Human Osteoblast by Synthetic and Endogenous Ligands of 18 kDa Translocator Protein (TSPO)

N. Rosenberg¹, O. Rosenberg², M. Soudry¹, A. Weizman², M. Gavish²

¹Orthopaedics A, Musculoskeletal Research Laboratory, Rambam - Health Care Campus, Haifa, Israel
²Molecular Pharmacology, Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel

Control of cell metabolism in connective tissue is crucial for human locomotor system maintenance. When taking into consideration the skeletal part of this system, the treatment of conditions such as fractures in bones in particular and osteopenia in general can be improved if extra cellular matrix elaboration, by osteoblasts and osteocytes, could be manipulated on the cellular level. Therefore further understanding of the cellular signaling pathways, that are involved in metabolic stimulation of bone producing cells, i.e. osteoblasts, may provide an important insight for the future development of additional effective therapeutic tools for the maintenance of bone mass. The mitochondrial permeability transition pore (MPTP) regulates the cellular energetic homeostasis and therefore we hypothesise it might be a target for pharmacological regulation of the human osteoblast metabolism. Accordingly the TSPO (18 kDa Translocator protein), which is one of the MPTP components and that was previously shown to have an important role in mesenchymal cells’ metabolism, might be a specific target for this purpose. Therefore our intention in this study was to identify the potential role of TSPO in the physiology of human osteoblast-like cells.

We investigated the functional importance of TSPO in proliferation, energy consumption and production, in human osteoblasts in vitro, by using specific TSPO ligands, synthetic (PK11195, Ro5-4864 and FGIN-1-27) and endogenous (protoporphyrin IX) in order to determine the role of TSPO in the regulation of the cell cycle of human osteoblast-like cells and the role of TSPO ligands in the human osteoblast-like cell apoptosis and necrosis induction. We also assessed the possible interaction between TSPO and hexokinase 2 in osteoblast energy consumption (glucose incorporation), energy production (ATP generation) and interactions of TSPO ligands with other MPTP components (VDAC, ANT, hexokinase 2), especially in relation to the later’s gene expression and net cellular content.

We show that all TSPO ligands, synthetic and endogenous, cause a shifting of the cell cycle of human osteoblast-like cells to a lower energy demand state while preventing cell death by different cellular pathways which are characteristic to the each of studied ligands. We suggest that this ability reveals a protective fine tuning mechanism of these cells adaptation for a lower energy supply, that might be otherwise cell death inductive. These results may indicate on existence of a currently unrecognized cellular pathway that is involved in energy supply-demand regulation in human osteoblast and could be a target for the future development of therapeutic agents effective in regulation of osteoblast metabolic induction.
Efficacy of Linezolid Alone or in Combination with Gentamycin and Vancomycin Impregnated in Acrylic Bone Cement

N. Snir, S. Meron-Sudai, I. Ofek, S. Dekel

1 Department of Orthopaedic Surgery 'B', Tel Aviv Sourasky Medical Center, 2 Department of Clinical Microbiology and Immunology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

The use of acrylic bone cement impregnated with antibiotics has been widely used in primary joint replacement and in the treatment of osteomyelitis or infected arthroplasties. However, the emergence of resistant strains of bacteria to a wide variety of antibiotic agents has presented a serious problem and a drawback in treatment. The clinical efficacy of bone cement impregnated with antibiotics for the prophylaxis and treatment of infections is dependent on the elution characteristics of the specific antibiotic agent, the bactericidal and broad spectrum affect at low concentrations of that agent and the biomechanical strength and fatigue life of the acrylic bone cement. Linezolid is a synthetic antibiotic of the Oxazolidinone class that inhibits protein synthesis. It is active against most gram-positive bacteria and acquired resistant has been scarce. It is used mostly intravenous. In the present study we sought to determine efficacy of linezolid impregnated in bone cement as prophylaxis and treatment against bacterial infections.

Materials and methods: Acrylic bone cement beads impregnated with linezolid, vancomycin or garamycin and in combination were prepared to reach 2.5% (w/w). The latter did not affect the biomechanical properties in accordance to the ISO 5833. Growth inhibitory time was determined by placing a bead of cement in a well followed by adding a suspension of the following bacteria: Vancomycin resistant enterococci (VRE), Meticillin resistant Staphylococcus aureus (MRSA), Klebsiella pneumonia, Escherichiae coli and Staphylococcus epidermidis). The beads were transferred each day to a fresh bacterial suspension and the number of days elapsed until positive growth appears was recorded and designated as the growth inhibitory time (GIT). The minimal inhibitory concentrations of each of the antibiotics against the test bacteria was determined and used to estimate the concentration of the test antibiotics leaching out from the beads as well as to compare the efficacy of the antibiotic GITs.

Results: The GIT of linezolid was significantly longer than that of vancomycin and gentamycin (21±7, 8±5, 0±0, respectively) for MRSA. Similar results were noted for the other two gram + bacteria (VRE and S.epidermidis). Significantly, VRE which relatively resistant to both vancomycin and gentamycin was sensitive to linezolid for as long as 15±5 GIT. Although the gram(-) bacteria E.coli and K. pneumonia were relatively resistant to linezolid (MIC of 250 and GIT value of 0), the combination of linezolid and gentamycin markedly increased the GIT of both of the gram(+) and gram(-) bacteria by a magnitude of 2-3 times that of linezolid or gentamycin alone. For example the increase in GIT of linezolid to linezolid and gentamycin for MRSA and VRE was 21±7 to >45 and 15±4 to 32, respectively; and that of gentamycin to gentamycin and linezolid for E.coli and K.pneumonia was 16±2 to 40±5 and 10±2 to >45, respectively. No such increase in GIT was noted for the combination of Linezolid and vancomycin except for S. epidermidis where the GIT increased from 19±1 for vancomycin or 29±1 for linezolid alone to >45 for the combination of vancomycin and linezolid.

Conclusion: The data suggest that linezolid alone impregnated in bone cement may be considered as the drug of choice to protect and or treat against gram + bacteria to the same efficacy as gentamycin for gram- bacteria. However, the combination of linezolid and gentamycin impregnated into acryl bone cement to 2.5% (w/w) does not affect the biomechanical properties of the cement but provide protection against infection of both gram(-) and gram(+) bacteria for a markedly longer length of time than each of the antibiotics alone.
Use of Reference Management Solutions among Orthopaedic Surgery Trainees

S. Badarudeen, A.I. Spitzer

Surgery, Orthopaedic Surgery, Cedars-Sinai Medical Center, Los Angeles, USA

Background: Manuscript guidelines for Orthopaedic journals are not uniform. Software based reference management solutions aid researchers in complying with these guidelines when formatting their manuscripts. To our knowledge, no studies have been published on the usage pattern and effectiveness of reference managers among orthopaedic surgery trainees.

Methods: 131 Orthopaedic Surgery residency programs were electronically solicited to email to their residents and fellows an anonymous web-based survey assessing whether they used reference managers. The hypothesis was that usage amongst trainees would be low, and that use of a reference manager could facilitate and improve compliance with journal manuscript guidelines.

Results: 76% of potential responders (591 trainees, 91% residents, 9% fellows) completed the survey. 49% (292) had never used a reference manager. Of the 299 using a reference manager, 87% (257) used Endnote, 12% (37) RefWorks, and 4% (13) RefMan. The perceived difficulty in following journal guidelines amongst experienced users was significantly less (p<0.0001) than non-users and novices, who were 2.6 times more likely (p=0.001) to find journal guidelines difficult to follow, and were 2.6 times more likely (p=0.0411) to spend more than 30% of their time formatting manuscripts.

Conclusions: Use of reference managers amongst Orthopaedic trainees is surprisingly very low. Endnote is the most commonly used reference manager. Formal training in the use of reference managers could significantly improve the ease of compliance with journal guidelines and reduce the time spent formatting manuscripts according to these guidelines.
Pulsed Low Intensity Electromagnetic Field Affects Cell Cycle of Human Osteoblast in Vitro

N. Rosenberg, M. Soudry

Orthopaedics A, Laboratory of Musculoskeletal Research, Rambam - Health Care Campus, Ruth and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

Pulsed electromagnetic fields (PEMF) are in a clinical use for treatment of deficient bone lesions in order to stimulate new bone formation. The mechanism of the increased bone formation by the PEMF is attributed to the osteoblast stimulation and to suppression of osteoclast bone resorption function by effecting, among others, osteoblast induced osteoclast stimulation. There is evidence that specific PEMF parameters are essential for stimulation of osteoblast proliferation and differentiation and there are not identical in different studies. In general basic high frequency electromagnetic field in the range of 4 - 33 kHz given in low frequency bursts of 7-15 Hz are found to be efficient in stimulating osteoblast proliferation and differentiation in vitro. The mechanism of the osteoblast stimulation is based on the accumulation of cytosolic Ca" but its overall effect on cell cycle is not known. We hypothesize that osteoblast cell cycle is changed following the stimulatory PEMF. For this purpose we studied the cell cycle profile of cultured human osteoblast-like cells following exposure to low intensity PEMF. Primary explants cultures of human osteoblast-like cells were used for the experiments. The cultures were subjected to sine shaped low frequency (10-30 Hz) and high frequency (4-30 kHz) electromagnetic fields and to PEMF (4-30 kHz basic frequency in pulses of 10-30 Hz). We used a specially designed system for delivery of electromagnetic field to cells in culture in 24 well plate, by placing a coil under each well. The exposure of the cultured cells to different electromagnetic fields was done in two hours periods with 1 hour interval once in 24 hours. We repeated this procedure in four consecutive days. Eight hours after the last exposure to the electromagnetic field the cultures were assayed for the cellular alkaline phosphatase activity and for LDH activity in the culture medium. The results were normalized to the cell number in each sample, which was estimated from direct cell count in a low power microscopic field. Cell cycle cytometric analysis (FACS) was applied to the cultured cell samples which were exposed to the 10-30 Hz electromagnetic field and to 4-30 kHz/10-30Hz PEMF. Then the results were compared to control cultures unexposed to magnetic fields. We found that number of cells increased following exposure to 4-30 kHz basic electromagnetic frequency (p<0.05). Additionally when 4-30 kHz electromagnetic field was delivered in pulses of 10-30 Hz a highest increase in cell number was observed. Cellular alkaline phosphatase and medium LDH activities decreased following exposure to 4-30 kHz electromagnetic field and PEMF. When a 10-30 Hz frequency electromagnetic field was applied to the cultured cells no change in cell number, cellular alkaline phosphatase activity and medium LDH activity was found. Flow cytometric analysis (FACS) of the cells exposed to the 10-30 Hz frequency electromagnetic field showed no difference in the cell cycle comparing to the controls. The PEMF stimulation increased the proportion of cells in the G1 phase (p<0.001) and decreased the proportion of apoptotic and necrotic cells (p<0.001). Electromagnetic field of 4-30 kHz frequency delivered in 10-30 Hz pulses shifted the cultured human osteoblast-like cells into G1 phase on the expense of the proportion of necrotic and apoptotic cells. This decrease of cell death caused an increase of cell number in the culture. Therefore the increase of cell number following the PEMF shouldn't be attributed to a mitogenic activity, because the S and G2/M phases of the cell cycle were not altered by the PEMF. This observation of the decreased cell death rate following PEMF is supported by lower activity of LDH in culture media which is not observed following 10-30 Hz electromagnetic stimulation. In parallel to the decrease of cell death PEMF caused a suppression of osteoblast maturation, which is expressed by a lower alkaline phosphatase activity. This phenomenon also wasn't observed following 10-30 Hz stimulation. Therefore by using PEMF a method of increase of osteoblast pool in clinical environment might be developed, which should provide higher number of cells that will further mature, following PEMF cease, and might generate more bone matrix.
Bias in Second-Opinion Consultations of Orthopaedic Surgeons

G. Vashitz¹, N. Davidovitch¹, Y. Kosashvili³, Y. Parmet¹, S. Wientrob², J.S. Pliskin¹

¹Department of Health Systems Management, Division of Public Health, Faculty of Health Sciences, Ben Gurion University, Beer-Sheva, ²Orthopedic Department, Dana Children's Hospital, Tel Aviv Sourasky Medical Center, Tel-Aviv, ³Orthopedic Department, Assaf Harofeh Medical Center, Zerifin, ⁴Department of Industrial Engineering and Management, Ben Gurion University, Beer-Sheva, Israel

Background: Legitimate discrepancies in diagnosis, treatment or prognosis, may emerge among different physicians. A known decision-making bias is the tendency to shift personal opinion either towards or away from previous opinion. Hence, physicians giving second opinions might unintentionally shift their decisions, following a previous opinion.

Objective: To evaluate physicians' bias towards previous opinions in second-opinion consultations.

Methods: A questionnaire was administrated to orthopedic physicians in a nationwide, multicenter survey. The questionnaire included eight controversial orthopedic scenarios followed by different treatment options with no clear-cut preference. Four scenarios were presented under one of three second-opinion contexts and the other 4 scenarios were used as control (no second opinion). The physicians' responses were coded according to the level of intervention, from conservative to invasive). We used Chi² and Kruskal-Wallis tests to compare the overall responses in the various second-opinion contexts, and repeated measures ANOVA to compare the individual intervention scores in the three second-opinion contexts.

Results: 172 questionnaires were collected (105 seniors and 67 juniors). Overall, when the first opinion was given to the physician, there was a tendency to shift towards the more invasive treatment, which was recommended by the first opinion. When a first opinion was already given, there was a shift towards more invasive treatment, whereas when the patient intended to seek a second opinion, there was a shift into towards a conservative treatment. There was no effect of seniority on the chosen treatment.

Conclusion: The presence of a first opinion may affect physicians' choices compared to their choices without a first opinion. This bias mainly tends towards a more invasive treatment. Due to the immense impact of any decision on the patient's health, further research should address such biases and develop tools to avoid them.