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MEETING ABSTRACTS

A1
Platelet Rich Plasma (PRP) Use in Professional Footballers
Imtiaz Ahmad
Tottenham Football Club, London, England

Background: The use of PRP in professional football has increased in recent years since the World Anti-Doping Agency removed it from their prohibited list in 2011.

Methods: Review of the evidence for safety, acceptability and efficacy of PRP in decreasing pain and improving healing and function in players with musculoskeletal injuries. A case study of post-PRP rehabilitation in professional football and qualitative data regarding players’ understanding of PRP, tolerability and effect is presented. The case study examines the rehabilitation protocol post-PRP injection of the lateral ankle ligaments following an acute ankle sprain. A player was administered with two weekly PRP injections following a Grade 2 anterior talofibular ligament (ATFL) rupture. The rehabilitation protocol with timelines is presented including use of modalities to increase healing and allow early safe progression to return to play. The use of objective markers for safe progression and feedback to avoid injury recurrences is described.

Results: Review of evidence shows good safety and a small non-significant trend favouring PRP use. The case study demonstrates a safe and accelerated return to play using objective markers. Qualitative data demonstrates a good understanding of PRP injections as well acceptability of the intervention to players, coaching and medical staff.

Conclusions: Further development in post-PRP rehabilitation is required to allow safe and quick return to play while avoiding injury recurrences.

A2
Emerging Issues in Clinical Translation of Biologies in Regenerative Medicine
Julie G. Allickson
Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC

This talk discusses the state of the field in regenerative medicine beginning with the growth in industry with more than 700 companies and the regenerative medicine space with the most mature sector being cellular therapies with more than 60 years of experience. Cells are a very important component of the field not only for direct therapy but also to build organs and tissues. As we assess replacement organs, the field weighs the pros and cons of decellularization of an organ compared to 3-D Bioprinting with the goal of identifying an inexhaustible source of organs that will not require immunosuppression nor be rejected. One new source of stem cells identified is from urine which is easy to isolate and has potential to produce a large number of multipotent cells ready to use as a source for therapeutic indications in Urology.

Translational Research begins at proof-of-concept and follows through until clinical trials commence up to Phase 2. Understanding of the appropriate regulations coupled to early discussions with regulators can accelerate therapies to the clinic.

Learning Objectives
1. Discuss emerging technology in translation.
2. Explore the general infrastructure to take a product from POC to Phase II clinical trials in academia.

3. Understand how to optimize translational and critical issues to address.

Outline

I. State of the Field of Regenerative Medicine
II. Different Subsections of Regenerative Medicine
III. Bioprinting Technology
IV. Human Urine-derived Stem cells for Urological Applications
V. Translational Research Pathway
VI. Regulatory Considerations
VII. Strategy for Accelerated Translation

A3

The Future of Platelet Rich Plasma

Jason L. Dragoo

Stanford School of Medicine, Redwood City, CA

This talk discusses the current shortcomings of PRP therapy and addressed future pathways to improve its clinical effectiveness. Techniques such as reformulation, antibody exclusion and concentration of other blood components such as alpha 2 macroglobulin are discussed.

A4

Translational Biologics: Clinical Application in the Management of Articular Cartilage Disease

Brian J. Cole

Chicago Bulls and Chicago White Sox, Chicago, IL

This talk provides an understanding of the role of growth factors, stem cells and PRP in osteoarthritis and cartilage repair. Regulatory pathways for biologics are discussed. Research demonstrating the outcomes associated with biologics and cartilage repair are covered.

A5

Adipose-derived Stem Cells Treatment of Osteoarthritis

Yong Gon Koh, Yun Jin Choi

Yonsei Sarang Hospital, Seoul, South Korea

Osteoarthritis (OA) is a degenerative process of the cartilage involving the immune system, wherein local inflammatory reactions occur through the production of proinflammatory cytokines. Currently, no treatment is available to improve or reverse the process. Mesenchymal stem cells (MSCs) have attracted attention for potential clinical use. Additionally, MSCs have been suggested for use in the cell-based treatment of cartilage lesions.

Data from five (5) published clinical studies on adipose tissue-derived stem cell therapy that were performed in our institute are presented. The first study, published in “The Knee” in 2012, includes 25 cases of knee OA treated with intra-articular injections of autologous MSCs. Autologous MSCs were separated from the infra-patellar fat pad of OA patients, isolated in vitro, and then injected into the patients’ knee joints. The short-term results were positive and showed that infra-patellar fat pad-derived MSC therapy with intra-articular injections is safe, provides assistance in reducing pain, and improves function in patients with knee OA. The second study, published in “Arthroscopy” in 2013, included clinical and MRI results collected over a longer follow-up period to indicate long-term effectiveness of the stem cell therapy. In the second study, results of both clinical assessments and MRI showed that MSC therapy, with MSCs intra-articularly injected into the knee, is an effective way to reduce pain and improve function in patients with knee OA. The third study, entitled “Clinical outcome of injection of mesenchymal stem cells with arthroscopic treatment in osteochondral lesion of the talus,” was published in the “American Journal of Sports Medicine” in 2013. In the previous two studies, patients with knee osteoarthritis were included; however, in the third study, patients with ankle cartilage lesion were included. This study concluded that in patients older than 50 years, injection of MSCs with marrow stimulation showed results that were more positive as compared to those for the marrow stimulation treatment alone.

The results of these studies propose a new option for the treatment of OA and are an important first step in
its development. Adipose-derived stem cell treatment appears to be a good option for OA treatment in elderly patients.

A6

Some Pitfalls in the Application of Autologous Platelet and Plasma Derived Products on Tissue Repair

Eduardo Anitua1, Sabino Padilla2
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2BTI Biotechnology Institute, Vancouver, Canada

Evolution has shaped the biological defense system of vertebrates consisting of several interlinked modules such as hemostasis and clotting, the innate immune system, and fibrogenesis to cope with bleeding and microbial invasion. Once tissue damage is detected, organisms mount a systemic and a local response that encompasses procoagulant and proinflammatory mechanisms with the activation of platelets, endothelial cells, tissue-resident macrophages, recruitment of circulant monocytes and neutrophils. Besides halting the bleeding process, platelets release SDF-1 and PF4 which together with the release of VEGF and fibrin adhesion cell receptors may well contribute to the resolution of inflammation.

Drawing on the regenerative potential of platelets, plasma biomolecules and fibrin matrix, several systems of producing autologous platelets-and plasma derived products (APPDPs) have been developed and aimed at triggering and enhancing the natural regenerative capacity of damaged tissues. Despite the care with which the medical staff elaborate and apply APPDPs, some pitfalls arise regarding the composition of autologous plasma and platelet derived products, the modalities of their application, and the in vitro versus in vivo evaluations, all of which can deeply influence tissue healing.

In a repair scenario, leukocytes may aggravate the tissue damage and promote a pro-inflammatory microenvironment. Much of the collateral damage inflicted by neutrophils and macrophages during the hemostatic-inflammatory period might be unnecessary to reconstruct sterile injuries such as the one found in joints or skeletal muscles. Although the TGF-β family drives fibrogenesis, and it potentially might stimulate the formation of scar tissue, the concurrent presence of TGF-β1, VEGF, and HGF in the same local environment makes leukocyte-free APPDP an antifibrotic autologous system. It has become commonplace to infiltrate APPDPs in the treatment of musculoskeletal injuries as a kind of scatter shot instead of adopting a well thought out and crafted biological approach. It is not enough to add a storm of growth factors to a tissue which for years has been undergoing a degenerative process, and, as a consequence, may have almost exhausted its healing capacity. There should also be a systematic infiltration of the healthy peripheral tissue surrounding the injury.

The efficacy of APPDPs relies on angiogenesis, innate immune system, innervation and biomechanical stimuli, whose combined presence is pivotal to recovering tissue functionality.

A7

Potential Benefits of Arthroscopy with Postoperative Bone Marrow Concentrate

Neil Ghodadra
Beverly Hills, CA

Slides & video lecture online & DVD, no abstract

A8

The Andrews Institute Experience: Biologies to Accelerate Healing

Adam Anz
Andrews Orthopaedic & Sports Medicine Center, Gulf Breeze, FL

This talk discusses the clinical experience including lessons learned regarding the use of Platelet Rich Plasma and Bone Marrow Aspirate in the treatment of athletes with degenerative knee conditions. Additionally covered are future direction, including the development of a peripheral blood stem cell processing and banking facility, as well as the initiation of two clinical studies under FDA IND direction.

Learning Objective
1. Understand success of BMA and PRP in the athletic population and factors which affect patient reported outcomes.

Outline

I. Introduction/Background
II. Experience with PRP

III. Retrospective Data on BMA

IV. Future Directions
   a. IND for Peripheral Blood Stem Cell and Cartilage
   b. IND Preparation on Adipose Cells and Osteoarthritis

A9

The Future of Biologics: Signposts from Veterinary Therapies

Robert J. Harman

Vet-Stem, Inc., Poway, CA

The veterinary profession has been able to progress regenerative therapies at a rapid pace due to more limited regulatory burden and the learning experiences from this field are relevant to human medical practice. This session outlines the current uses of stem cells, PRP and various serum products in the treatment of orthopedic conditions in animals.

Learning Objectives

1. Understand how veterinarians are using regenerative medicine to treat orthopedic conditions in animals.
2. Understand what types of cells and methods of production and delivery are being employed in veterinary regenerative therapy.
3. Learn from the mistakes and successes of clinical application of regenerative therapies in animals.

Outline

I. Introduction to veterinary regenerative medicine
II. Regulation of regenerative medicine in veterinary field
III. Equine orthopedic applications of stem cells and PRP
IV. Canine orthopedic applications of stem cells and PRP
V. Summary of learnings and application in human medicine

A10

In-situ Tissue Engineering Can Predictably Regrow Missing Parts of the Jaw

Robert E. Marx

University of Miami Miller School of Medicine, Division of Oral and Maxillofacial Surgery, Miami, FL

The concept of In-situ Tissue Engineering is the regeneration of tissue (in this presentation bone) using the components of cells-signal-matrix. This presentation shows the techniques and biology of osteoprogenitor and mesenchymal stem cells harvested from platelet rich plasma or bone marrow combined with recombinant bone morphogenetic protein and allogeneic cancellous bone to regenerate large segments of the jaw lost form tumor surgery, trauma, or infection. A randomized open label trial indicates equal results to the gold standard of an autogenous raft with far less morbidity, operating room time, and hospital course, which translate to very reduced costs and an earlier return of the patient to the home and/or work place.

Learning Objectives

1. For the participants to know the biology and time course of bone regeneration
2. To illustrate the imperative of cells in both platelet rich plasma and bone marrow aspirate concentrates
3. For the participants to learn the requirements of a successful and functional reconstruction
4. The participants to realize the reduction in morbidity, the time saving, and cost saving value of in-situ tissue engineering

Outline

I. Definition of In-situ Tissue Engineering
II. Techniques and validation of the components in platelet rich plasma and bone marrow aspirate concentrates
III. Sample cases of In-situ Tissue Engineering
IV. Randomized open label study comparing In-situ tissue engineered grafts to grafts using autogenous bone
A11

IV Nutrients and Healing: Implications in Orthobiologic Medicine

Paul S. Anderson
Anderson Medical Specialty Associates, Seattle, WA

Dr. Anderson uses his two decades experience in IV and Injection therapies to describe the role of IV therapies in improving healing outcomes in orthopedic medicine.

Learning Objectives
1. Describe the usefulness of IV nutrients in healing
2. Describe the need for nutritional augmentation beyond the oral route
3. Describe the primary micronutrients and their relationship to healing
4. List potential cautions and contraindications
5. List future training options in IV therapies

Outline
I. Is there a problem we can address?
II. Does research support a deficient patient population?
III. Can parenteral therapy assist in this arena?
IV. What interventions show most promise?
V. Minerals
VI. Vitamins
VII. Amino Acids
VIII. What risks or contraindications should we consider?
IX. How can we access appropriate training?

A12

MSCs: The New Medicine

Arnold I. Caplan
Skeletal Research Center, Cleveland, OH

Marrow derived adult Mesenchymal Stem Cells (MSCs) can be isolated and culture expanded. Although these cells are capable of differentiating into lineages that result in the fabrication of bone, cartilage, muscle, marrow stroma, tendon/ligament, fat and other connective tissues, MSCs have recently been shown to be intrinsically therapeutic. Such culture expanded adult/MSCs are immuno-modulatory especially in muting T-cells and, thus, allogeneic MSCs have been used to mute or cure graft-versus-host-disease and Crohn’s disease and are now being tested in certain autoimmune diseases. Furthermore, these allo-MSCs set-up a regenerative micro-environment which is anti-apoptotic, anti-scarring, mitotic for tissue intrinsic progenitors and angiogenic. These immuno and trophic activities result from the secretion of powerful bioactive molecules that, in combination, support localized regenerative events. The MSCs reside in every tissue of the body and function as perivascular cells (pericytes) until a focal injury occurs. At sites of injury, the pericyte is released and functions as a MSC that provides molecular assistance in activities leading to tissue regeneration. It is expected that MSCs that arise from pericytes from different tissues location or anatomical sites of injury will not be equivalent. Thus, adipose-derived and marrow-derived MSCs naturally reside as pericytes and have different functional capacities. The fact that uncultured, freshly isolated autologous “stromal vascular fraction (SVF)” from fat has been shown to be therapeutically effective in horses and dogs, strongly argues that the MSCs in the SVF are a potent multi-drug and site-specific delivery vehicle. Additionally, we have data to support the concept that the PDGF-BB in PRP not only releases the pericytes and, thus, provides activated MSCs, but also proves to be a powerful chemoattractant and mitotic agent for MSCs. There are now over 385 clinical trials listed on the clinicaltrials.gov website and these have the potential of changing the way disease and tissue injury are medically approached. This full thesis that adult MSCs are potent therapeutic agents is the theme of this lecture.

Learning Objectives
1. Define and describe MSCs
2. Show that MSCs are derived from pericytes
3. Provide details of the medicinal properties of MSCs
4. Document in both preclinical and clinical circumstances the role of MSCs
5. Discuss the current and future medical use of MSCs
6. Outline
   I. Regenerative Medicine
   II. MSCs: The Hypothesis
   III. MSCs: Today’s Mechanism
   IV. Clinical Trials
   V. Clinical Data
   VI. Innate Regenerative Potential: MSCs

A13
USG Guided Hydrodissection (HD) of Peripheral Nerves – Using Different PRPs
Stanley KH Lam
KH Lam Musculoskeletal Pain Management & Sports Injury Center, Hong Kong

Nerve entrapments or neurogenic inflammation are common in clinical practice in both acute injury and chronic pain. This problem has been largely neglected for the last century due to the lack of effective methods to diagnose and effectively release nerve entrapments.

Dr. Lam has been teaching a technique called “Ultrasound (US) Guided Hydrodissection of Peripheral Nerves in Treatment of Different Neuropathic Pain” around the world since 2013 in universities, conferences and workshops.

During the lectures and workshops, Dr. Lam reviews the biomedical science and anatomy behind neuropathic pain, nerve entrapments or neurogenic inflammation, clinical presentation, and how to effectively diagnose these common nerve pathologies with US. The common sites of entrapment of different peripheral nerves is also be discussed.

Discussion includes use of US guided peripheral nerve hydrodissection to treat neuropathic pain or nerve entrapments of different kinds. The principles and techniques of US guided peripheral nerve hydrodissection are introduced and discussed. The efficacy of different solutions, including different PRPs and stem cells, in this technique is highlighted and the pilot study of US guided peripheral nerve hydrodissection using different PRP is presented. Based on the current available data, this technique together with PRP and stem cells, seems to be a solution to many neuropathic pain conditions. Dr. Lam urges every practitioner who wants to learn and practice this technique to go to cadaver lab, e.g The Orthobiologic Institute (TOBI) Cadaver Workshop or MSKUS.com Cadaver Workshops.

A14
Lumbar Disc Bone Marrow Concentrate for Treatment of Low Back Pain
Kristin Oliver
Blue Tail Medical Group, St. Louis, MO

About 70% of people will experience pain in the lower back at some point in their lifetime. For those patients who are determined to have a herniated disc etiology to their pain, treatment options have remain limited. Conservative options that are currently accepted include: physical therapy, patient education on proper body mechanics, lumbosacral support/bracing, NSAID’s, oral corticosteroids, and epidural corticosteroid injection. Those patients who fail conservative therapy are often faced with potential surgical interventions. The presenter outlines a biological alternative to treat patients with low back pain of discogenic etiology. She has compiled a retrospective review of 35 low back pain patients with a history, physical findings and an MRI that supports a single or two level lumbar disc herniation as the source of their pain who have been treated under fluoroscopic guidance with an injection of BMC to the disc annulus. The presentation includes a literature review on the use of biocellular grafts in the treatment of herniated lumbar disc disease as well as her methods and study findings.

Learning Objectives
At the end of this session participants possess the knowledge necessary to:

1. Recognize the current most common conservative treatment measures for lumbar disc herniation
2. Understand the options for a biologic or biocellular approaches to a herniated lumbar disc.
3. Understand why the presenter chose BMC as her biologic graft of choice
4. Realize the potential BMC and other biocellular grafts in treating patients with lumbar disc herniations
5. Recognize the need for further studies looking at BMA and other biocellular graft options in the treatment of lumbar disc disease

A15

Navigating through Biologics and Regenerative Therapies for Chronic Low Back Pain

Danielle Aufero
Orthohealing Center, Los Angeles, CA

Treating chronic low back conditions can be very challenging due to the many potential pain generators (muscles, bone, nerve, disc, ligament) and their various manifestations - especially when more than one pain source is contributing to symptomatology. Clinically, dysfunction of these structures can lead to an array of commonly encountered problems including the following: Myofascial pain syndrome (MFPS), Sacroiliac Joint (SIJ) dysfunction, pain related to spondylolisthesis/spondyloysis, facet arthropathy, lumbar radiculopathy secondary to spondylosis/stenosis versus herniated nucleus pulposis (HNP), Degenerative Disc Disease (DDD), annular disc tears, instability/ligamentous laxity and neurogenic inflammation (NI). Complicating the clinical presentation even further are subclinical disease processes reported as structural abnormalities on MRI that must be teased out to help narrow the differential diagnosis list of contributing factors. Establishing all of the pain generators can be a process in more complex situations, possibly requiring diagnostic interventional spine blocks, dynamic musculoskeletal ultrasound, Neural Prolotherapy (NPT) diagnostic trial, or electrodiagnostics. A commonly encountered dilemma that arises is what to offer chronic low back patients, especially after failing traditional and sometimes even surgical measures, including Physical Therapy (PT), cortisone shots, epidurals, Radiofrequency (RF), and a slew of surgeries. Steering these patients down the alternative path of Regenerative Injection Therapies and Biologics can be facilitated by generating a logrhythm or protocol, which can minimize the shooting in the dark or shotgun approaches, especially since these procedures are considered experimental and hence patients’ finances must be utilized in a strategic manner to minimize expenses and maximize outcome in the most accurate and quickest treatment path possible. Various treatments are discussed at varying lengths within the category of biologics and alternative medicine, including prolotherapy, neural prolotherapy, prolozone, Bone Marrow Concentrate (BMC), and Platelet Rich Plasma (PRP) with emphasis on the latter. A model was presented for the complex spine patient with suggested protocols and indications for possible pain generators and their corresponding treatments, respectively. The goal is to streamline the entire work-up process which will simplify the treatment plan and increase the likelihood of successful outcome.

Learning Objectives

1. Improve ease and accuracy of properly and completely diagnosing the source(s) of patients’ spine symptoms
2. Learn how to navigate patients through a multitude of available treatment options and generate a dynamic adjustable treatment plan
3. Optimize physicians’ comfort level in recommending specific alternative treatments for specific indications in the setting of low back pain

Outline

I. Description of various pain generators in the spine
II. Clinical presentation of each pain generator acknowledgement of the significant overlap between all of them, while conversely recognizing the unique features of each
III. Diagnostic strategies to confirm the practitioner’s theory of what pain generator is causing which symptom so the treatment plan can evolve as symptoms shift and respond to the therapies
IV. Generating appropriate realistic treatment plan with specific timeline for and interplay between biologics and natural therapeutic procedures
Multiple studies confirm its value in the treatment of chronic tendinopathy especially for lateral epicondylar tendinopathy also known as tennis elbow. Future investigations will match specific PRP formulations to precise indications such as knee osteoarthritis and degenerative disc disease. Continued research and worldwide collaboration will accelerate advancements in biologic orthopedic treatment options during the next decade and beyond.

A17

Prolozone™ Cervical Injection

Frank Shallenberger

The Nevada Center of Alternative & Anti-Aging Medicine, Carson City, NV

Ozone therapy has been used for more than fifty years in Europe for various medical conditions. When injected into soft tissues ozone reacts with unsaturated fatty acids to produce various lipid soluble peroxides. These peroxides are able to penetrate and interact with cell membranes and have been shown to increase the metabolism of peripheral mononuclear blood cells. This includes stem cells and blast cells. As people age their stem and blast cells decline in their ability to function. This explains why many injuries and degenerative conditions fail to heal and become chronic as people age. By injecting ozone into these damaged areas that refuse to heal, ozone is able to stimulate healing by stimulating the healing process. The author has been successfully using this concept for over 20 years to treat chronic pain and dysfunction in the spine, joints, and soft tissues. The author has also discovered that adding in other metabolic and pain relieving substances including procaine, B-vitamins, homeopathic remedies, dextrose, sodium bicarbonate, and occasionally corticosteroids, the effects of the procedure are dramatically enhanced. The author refers to this combination approach as Prolozone Therapy. The author describes a technique he has developed for the treatment of chronic pain, dysfunction, and radiculopathy of the cervical spine.

A18

Platelet-Rich Plasma: A Decade of Clinical Experience and Future Considerations

Allan K. Mishra

Menlo Medical Clinic: Stanford Hospital, Menlo Park, CA

Platelet-rich plasma (PRP) has been used clinically now for more than a decade for a variety of disorders.
guided procedures performed in major body regions using methodological approach

a. Pertinent anatomy in each body region was demonstrated sonographically

b. Patient positioning and set-up for various procedures in each region

c. Both in plane and out of plane approaches to needle tracking will be discussed in the context of specific injections

d. Principles of sonographically guided tendon sheath/peritendinous, joint, and perineural injections were discussed as encountered during the demonstration

II. Audience participation is encouraged to ensure that procedures of interest are discussed and the set up for each demonstrated

III. Procedures are then practiced in the cadaver lab by those attending the optional cadaver lab session

A20

Early Results with Bone Marrow Concentrate & Emerging Trends in Biologics

Steven E. Sampson
Orthohealing Center, Los Angeles, CA

Incorporating orthobiologics is an appealing option to young adults to address a void in the range of treatments between hyaluronic acid (HA) and Total Joint Arthroplasty (TJA). The first generation biologic injectables of HA, have been successful in the treatment of pain for osteoarthritis (OA) of the knee. Platelet Rich Plasma (PRP) represented the second generation of biologic injectables, the first of which that is autologous. While both generations of injections have been shown to provide relief for cartilage disorders of the knee, they are ideally better suited for early intervention in active individuals. PRP has demonstrated superior results when compared to HA. There is likely a synergistic role of combining PRP with HA with their overlapping properties. However limitations of PRP may include its non-differentiated blend of anti-inflammatory, pro-inflammatory, anabolic and catabolic mediators. While the replication of the body’s natural balance of growth factors used synergistically may work best; recent studies have shown that isolating or blocking particular cytokines may be optimal for particular conditions. The third generation of patient bed-side injectables is Bone Marrow Concentration (BMC). While sufficient human safety and efficacy data is mounting; there is sparse data for the intra-articular application of same day BMC therapy in OA. Along with advanced orthobiologic therapies, MR imaging of cartilage must improve in order to demonstrate regenerative tissue quality.

This presentation provided an overview of the Orthohealing Center’s osteoarthritis treatment protocols incorporating biologics from HA, PRP, BMC, and Ozone with cutting edge adjuncts to facilitate recovery. We briefly discuss our experience with “quantitative biologics” to count platelets and monocytes from PRP and BMC in the office setting before injecting back into the patient. We believe this may shed light on post injection flares and rapid responders. Questions raised include not only variability of baseline platelet count but more importantly, why do some patients platelets concentrate well and others not? Additionally this quantitative approach may protect the physician & patient by screening for blood abnormalities (increased WBC, Platelets at baseline etc). Understanding baseline biologic profiles may explain why some patients respond favorably and others do not.

We present preliminary outcomes data for various applications of BMC from our clinic. We believe that the greatest potential of biologics in cartilage repair combines minimally invasive arthroscopic surgery (debridement, microfracture, meniscus transplant, meniscus repair, osteochondral allograft, subchondroplasty, etc.) with intra-operative and post operative cellular injections. Lastly, we present a case report of arthroscopic debridement of chondral surfaces, medial meniscectomy and Subchondroplasty (SCP) with post operative BMC injection with follow up imaging.

Further research is needed to better understand the cellular makeup of BMC including progenitor cells and exosomes. Early experimental trials of BMC have demonstrated positive results in treating OA; however, most studies are non-randomized, void of a
control group and sufficiently powered sample size. Further studies are needed to better understand the role of BMC in reducing pain and increasing function in cartilage disease. Promising adjuncts include means to improve circulation, regulate inflammation and mobilize autologous regenerative cells including Pulsed Electromagnetic Frequency (PEMF) and Hyperbaric Oxygen (HBOT).

A21

Point of Care Cellular Therapy: Growth Factors, Proteins and Bone Marrow Concentrate

Theodore Sand
Celling Biosciences, Austin, TX

The goal of the presentation is to provide an up-to-date status review of the use of bone marrow concentrate for treating patients at point-of-care with an FDA-compliant autologous cell therapy.

The following concepts are reviewed:
• Current view of the mesenchymal stem cell and its role in stem cell therapy
• The current and common approach to processing autologous bone marrow aspirate by centrifugation and the interaction of bone marrow concentrate with growth factors and proteins
• The variety of treatment areas in orthopedics to which bone marrow concentrate has been applied
• Examples of BMC-based therapy in the recent published literature, highlighting clinical lessons and procedural approaches to maximize the potential benefit to the patient
• A brief overview of the regulatory framework for the use of bone marrow concentrate

A22

Registry Data from 1,400 Patients Treated with a Unique Protocol of Same Day Bone Marrow Aspirate Concentrate

John R. Schultz
Centeno-Schultz Clinic, Broomfield, CO

Stem cell treatments for common orthopedic conditions are gaining increased attention and popularity. There are different types of stem cell treatments which include bone marrow derived and adipose. Processing of the tissue can be either same day or culture expanded. To document the safety and outcome of bone marrow derived stem cell treatments, the Centeno-Schultz Clinic created a registry tracking which has tracked 2,500 stem cell and greater than 3,000 platelet cases. The registry is being tracked by CRO quality software, several FTE’s and full time registry staff and biostatistician. The clinical outcomes in patients with knee, hip, shoulder arthritis and rotator cuff injuries are reviewed in detail.

Learning Objectives
1. Educate physicians on the use of same day bone marrow aspirate stem cell treatments in common orthopedic conditions
2. Review types of autologous stem cell procedures being used in orthopedic injuries
3. Discuss same day isolation vs. culture expansion of bone marrow and adipose tissue
4. Discuss Clinical Registry Tracking (2,500 stem cell and >3,000 platelet cases) (2005-2014)
5. Review safety profile and most common complaints
6. Review mean improvement and % of patients reporting >25% improvement in patients with knee arthritis
7. Examine whether severity of arthritis, age or BMI impact outcome
8. Examine the improved outcome after second stem cell treatment in patients with knee arthritis
9. Review outcome in patients with hip osteoarthritis
10. Identify the factors which negatively impact outcome in hip osteoarthritis
11. Review mean improvement in patients with shoulder arthritis, rotator cuff injuries and ankle arthritis

A23

Update on Intradiscal PRP

Gregory E. Lutz
Hospital for Special Surgery, New York, NY

Objective: To determine if an intradiscal injection of autologous Platelet-Rich Plasma (PRP) has
therapeutic value for chronic discogenic low back pain.

Design: Prospective, double-blind, randomized controlled study.

Setting: Outpatient Physiatric spine practice.

Patients: Adults with chronic (≥ 6 months) moderate to severe lumbar discogenic pain, unresponsive to conservative treatment.

Methods: Patients were randomized to receive intradiscal PRP or contrast agent following provocative discography. Data on pain, physical function and patient satisfaction were collected at 1 week, 4 weeks, 8 weeks, 6 months, and 1 year. Patients in the control group who did not improve at 8 weeks were offered the option to receive PRP.

Main Outcome Measures: Numeric Rating Scale (NRS) for pain, modified North American Spine Society (NASS) outcome questionnaire, Functional Rating Index (FRI), and the pain and physical function domains of the 36-item Short Form Health Survey (SF-36) were used.

Results: Forty (40) subjects were enrolled (25 in the treatment group, 15 in the control group). At 8 weeks, there were statistically significant differences between groups in FRI, NRS best and worst pain, and SF-36 pain scores. Within the PRP group, FRI, NRS worst pain, and SF-36 pain and function outcome scores maintained significant improvements from baseline at 6 months and 1 year. The treatment group reported statistically significant higher satisfaction when compared to the control group at 8 weeks (p=0.010) which was sustained in the majority of patients beyond 1 year with satisfaction rates of 57% (8/14) and 100% (6/6) at 1 year and 2 years, respectively. No adverse events were reported following injection.

Conclusion: Compared to controls, patients who received intradiscal PRP showed significant improvements in pain, function, and satisfaction at 8 weeks. The study was limited by sample size and use of PRP grafts standardized by complete blood count and a common centrifuge system, only. Further studies are needed to define the subset of patients most likely to respond to biologic intradiscal treatment and the ideal cellular characteristics of intradiscal PRP grafts.

A24
Cardiac and Orthopedic Regenerative Cell Therapy: 6 Month Preliminary Data

Kristin Comella
Bioheart, Inc & Stem Cell Training, Sunrise, FL

Late-Breaking Clinical Trials sessions are innovative and provide the latest breakthroughs in clinical science and potentially will have a significant impact on clinical practice. The field of regenerative medicine is rapidly growing with an emphasis on stem cell therapies and the promise of cures for everything from acute injuries to chronic degenerative diseases. The list of indications is expanding as more studies are published to demonstrate safety and efficacy. Regenerative medicine is the process of replacing or regenerating human cells, tissues or organs to restore or establish normal function. The concept is that damaged tissue can be restored by using the body’s own healing mechanism to promote repair. This new branch of medicine may change the course of chronic diseases and standard clinical therapies. This session will discuss the results of the ANGEL trial studying the safety and cardiovascular effects of intramyocardial implantation of autologous adipose-derived stem cells in patients with chronic ischemic cardiomyopathy.

A25
Combined Use of Adipose Derived Stem Cells and Platelet Rich Plasma: Expanding Indications

Randy B. Miller
Cosmetic & Reconstructive Surgery, Coconut Grove, FL

Mesenchymal stem cells have been shown to stimulate tissue regeneration and angiogenesis while minimizing fibrosis. Recent studies demonstrate a 2000 fold increase in the number of mesenchymal stem cells in adipose tissue compared with bone marrow. Because of the large number of stem cells, ease of harvest, the lack of donor site morbidity and tissue banking for future use, adipose is becoming a donor tissue of choice for the harvest and utilization of adult mesenchymal stem cells. Over the past five years, the number of basic science and clinical trials related to adipose derived stem cells has increased exponentially throughout the world. The outcomes of these studies have shown great promise. Platelet Rich Plasma (PRP) contains many growth factors and is
well known to have very potent anti-inflammatory and antimicrobial properties.

Treatments utilizing a combination of platelet rich plasma (PRP) and bone marrow derived stem cells are well established with proven safety and efficacy. The recent use of adipose derived stem cells in combination with PRP represents a paradigm shift and another tool in the field of regenerative medicine.

All cases in this presentation utilized a specified combination of PRP and adipose tissue containing stem cells and stromal vascular fraction (SVF). All treatments were autologous and performed at the point of care. Cell culture expansion was not used in any of these cases. Conditions treated include wound care, dermatologic eczema, breast reconstruction, craniofacial reconstruction, scar tissue, burn fibrosis and contracture, hair restoration, gingival recession, cosmetic hand rejuvenation and cosmetic facial rejuvenation. All procedures were performed on an outpatient basis. Treatment details and clinical outcomes are included.

The combined use of PRP, adipose stem cells and stromal vascular fraction is an emerging trend in biotherapeutics. The safety of this treatment modality has been demonstrated. Efficacy data is positive and encouraging. There is a great need for basic science research to better understand the mechanism of action. Refinements in clinical technique will also help to maximize efficacy and safety.

Learning Objectives

1. To compare and contrast the benefits of adipose stem cells in comparison to bone marrow derived stem cells
2. To understand the physiology and rationale behind the combined treatment of adipose stem cells and platelet rich plasma (PRP)
3. To outline the expanding clinical indications for the combined use of adipose derived stem cells and platelet rich plasma (PRP)
4. To detail specific treatment regimens for the combined use of adipose derived stem cells and platelet rich plasma (PRP) for each clinical indication
5. To highlight pearls for harvest, processing and treatment of each clinical condition with adipose derived stem cells combined with platelet rich plasma (PRP)

6. To present outcome data related to the combined use of adipose stem cells and platelet rich plasma (PRP)
7. To outline future areas of research related to the combined utilization of adipose stem cells and platelet rich plasma (PRP)
8. To refine treatment protocols which utilize the combination of adipose stem cells and platelet rich plasma (PRP)

A26

Cryoneurolysis for the Reduction of Knee Pain Secondary to Osteoarthritis

Luga Podesta

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Knee pain secondary to Osteoarthritis (OA) affects millions of Americans. Though a variety of pain management techniques exist most common nonsurgical options provide slow-acting and/or short-term relief. Therefore, a long-lasting minimally invasive approach to eliminate pain associated with osteoarthritis is desirable.

Purpose: To assess the safety and effectiveness of cryoneurolysis for temporary relief of knee pain secondary to osteoarthritis.

Study Design: Prospective case series.

Methods: Thirty-three subjects (56 knees) received cryoneurolysis to the infrapatellar branch of the saphenous nerve (ISN). Pain was measured using the VAS scale at baseline, immediately post-treatment and 7 and 30 days post-treatment. Treatment outcome was measured using the WOMAC scale at baseline and 7 days post-treatment. Treatment duration was assessed and a subject questionnaire completed at 7, 30 and 56 days post-treatment.

Results: At 7 days post-treatment, 88% of subjects demonstrated an improvement in VAS score, with an average improvement of 4.1 points (p=9.52E-12). At 30 days post-treatment 84% of subjects demonstrated continued relief with an average VAS improvement of 4.0 points (p=3.33E-10). Seventy-seven percent (77%) of subjects scored an average WOMAC improvement of ≥ 2 points per question, with an overall point improvement of 85.7 points for a 70% improvement from baseline (p=7.53E-17). Treatment duration
lasted to 56 days post-treatment for 70% of subjects, with 45% and 30% of subjects reporting relief at 84 and 112 days post-treatment, respectively. At 56 days post-treatment 84% of subjects reported they would recommend the treatment to family and would have another treatment. There were no device-related serious adverse events.

Conclusion: Subjects treated for knee pain showed significant clinical improvement, with high subject satisfaction and no serious adverse events. Based on these findings, Cryoneurolysis appears to be an effective and safe method to reduce knee pain secondary to osteoarthritis.

Learning Objectives
1. To understand the potential clinical applications of cryoneurolysis in treating knee pain
2. To be able to identify the sensory nerve innervation of the knee

PRP and Biologic Enhancement and Acceleration of Healing in Shoulder and Elbow Surgery – Now and Tomorrow

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Platelet Rich Plasma (PRP) is a fraction of autologous blood with supra-physiological concentration of platelets, upon activation, platelet-derived α granules release autologous growth factors (PDGF/ TGF/ VEGF/ EGF/ FGF/ IGF etc). PRP is thought to promote physiological wound healing and rapid tissue regeneration. Are all the PRP preparations the same? No!

The importance is in the details of the PRP composition.

Various platelet rich preparations have been described under the generic name of “PRP”. PRP preparations may contain concentration of platelets x2 to x9 and it may or may not contain white blood cells and red blood cells. It can be used activated or not. Depending on the PRP preparation it can be used as liquid, gel or fibrin clot form.

The wound healing cascade is initiated once the platelets (PLT) are activated in an area of the injury and growth factors and cytokines are released. The healing cascade has four sequential but overlapping phases: clotting, inflammation, proliferation and remodeling. Preparations of platelet rich plasma (PRP) can be used to promote healing and expedite the process bypassing the inflammatory phase and force-starting the proliferation phase, thus expediting the healing process and decreasing pain. To bypass the inflammatory phase, the polymorphonuclear white cells should be removed from the PRP preparation, however, the mononuclear cells should be retained as they contain important cytokines that enhance cell proliferation and matrix deposition as well as help in fighting infection.

In our view, the ideal platelet concentration should be between x3 and x5. The PRP should not contain Red Blood Cells (RBC) as they may decrease cell proliferation and augment apoptosis due to its cytotoxic effect. The PRP preparation should not contain White Blood Cells (WBC) due to their catabolic effect, however, in contrast, mononuclears and their cytokines enhance anabolic and healing effects and can help in fighting infection.

When using PRP, it is important that the patients will avoid using NSAID preparations at least 7-10 days prior to the PRP treatment and for at least 6 weeks post the PRP treatment.

Applications in the Shoulder and Elbow:
- Elbow epicondylitis
- Lateral epicondylitis - Tennis Elbow
- Medial epicondylitis - Golfer’s Elbow
- Shoulder Subacromial Impingement
- Patients with contraindication for op (Post Polio, co-morbidities)
- Rotator cuff tears and repairs
- Shoulder Osteoarthritis and osteochondral lesions
- Reconstruction of ligaments
- AC joint reconstruction
- Sternoclavicular joint reconstruction

We have used PRP with 90% success for the conservative treatment of elbow epicondylitis (lateral and medial). Published data also show that PRP is effective for the treatment of epicondylitis compared
Both to autologous blood and to corticosteroid injections.

Rotator cuff repair: In spite of improvements in the understanding of rotator cuff disease over the last two decades, advances in surgical treatment & instrumentation and better biomechanical repair constructs, the success of rotator cuff repairs especially re-tear rates remains a significant concern with both open and arthroscopic techniques. Rotator cuff repair retear rates range from 20% to 90%.

How can we improve this? - by improving biology. Utilizing and enhancing the natural healing capacities of the body.

Following arthroscopic rotator cuff repair (RCR) we routinely inject autologous PRP (Tropocells) into the repaired cuff to promote healing and enhance recovery. We compared 112 consecutive patients with RCR and PRP (group 1) to 116 patients with RCR without PRP (group 2) and found that group 1 was statistically significant less painful at 3 weeks post-surgery. At 3 months and 6 months the PRP group was better in pain or function, but not statistically significant. 93.6% of the PRP group stopped taking painkillers or took only occasional painkillers (paracetamol) at 3 weeks postoperative, while the 57% of the Non-PRP patients were still on the painkillers regime at 3 weeks postop. The use of PRP to promote healing after cuff tendon repair is still under investigation. Randelli et al. and several others have shown similar results to our findings that PRP improves pain and healing. Other studies seem to indicate that PRP has no effect on pain or healing of tendons, these studies used PRFM clot.

We have found autologous PRP (Tropocells) useful in the treatment of patients with subacromial impingement (SAI) especially when surgery is contraindicated or undesired.

Another application of PRP is in Acromioclavicular and Sternalclavicular joint ligament reconstruction with synthetic ligament scaffold. The PRP promotes ingrowth of host tissues into the synthetic ligament scaffold.

The experience with PRP for treatment of knee osteoarthritis (OA) led us to use it for treatment for shoulder OA in patients younger than 55 years. We perform an arthroscopic capsular release, debridement of osteophytes and arthroscopic microfracture in the humeral and glenoid chondropathic surfaces, and then inject the PRP to the joint. Early results are very encouraging as patients regained good pain relief and range of motion. They remain asymptomatic with good function one year after surgery.

Massive and irreparable cuff tears and revision cuff repair surgery may require the use of a scaffold. The ideal scaffold should rapidly and firmly attach to the cuff stump and the bone with initial strength to resist suture cut-out. It should also support ingrowth of host tissues and provide inductive and conductive stimuli for cell and vessel migration. At the same time it should cause low inflammatory and immune reaction and have a low risk of transmitting and causing infection. It should dissolve in a rate that permits tissue remodeling without compromising the strength of the repair. The cost has to be reasonable and the scaffold should be easy to use. Our results using synthetic mesh as scaffold with Tropocells PRP are encouraging. We achieved 60% successful outcome in these extreme salvage cases.

Recombinant Human type 1 collagen from tobacco leaves (Collplant) has all the pre-mentioned attributes and seems an ideal candidate for cuff scaffold. Our recent in-vitro studies using combined preparation of rhCollagen + PRP (Tropocells) showed higher proliferation rate of fibroblasts compared to Thrombin-based fibrin clot and exhibited superior shear stress compared to Thrombin-based fibrin clot. In vivo experiments using rat Achilles tendinopathy model has shown that rhCollagen (Collplant) with PRP (Tropocells) lead to decreased inflammation and improved quality repair with mature tendon tissue. It still remains to be seen if similar results can be obtained when the same combination of rhCollagen with PRP together with mesenchymal stem cells is used in vivo in humans.

A28

Orthobiologics: A New Frontier of Orthopaedics

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Results of this work were recently published in Orthopreneur

A new area of medicine, coined “Orthobiologics”, has emerged as a new frontier for disease treatment with the potential to revolutionize medicine. Although
Orthobiologic therapies have illustrated applications in a variety of medical fields [1], their use in Orthopaedics for the treatment of Osteoarthritis has exhibited an evolution unlike any other area. First generation biologics consisted of intra-articular viscosupplementation with Hyaluronic Acid, a sticky viscous glycosaminoglycan, which can provide lubrication and shock absorbency for a damaged arthritic joint [2] as well as pain reduction and functional improvements [3]. Platelet Rich Plasma (PRP) emerged as the 2nd generation of Orthobiologics, and the first Orthobiologic of the autologous form. First used in 1987 following open heart surgery [4], PRP has now been applied in a variety of medical areas [5], however recently, larger randomized controlled trials have started to emerge for orthopaedic conditions such as tendinopathies [6, 7] and knee osteoarthritis [8]. In recent years, Bone Marrow Concentrate has emerged as the 3rd generation of Orthobiologic therapy. Its potent mixture of mesenchymal stem cells, hematopoietic cells, platelets, and cytokines are hypothesized to act as the foundation for its regenerative potential [9]. Early experimental trials using BMC have illustrated positive results in Osteoarthritis patients [9, 10], as well as improved surgical results when administered postoperatively [9].


A29
Autologous Bone Marrow Concentrate: Review and Application of a Novel Intra-Articular Orthobiologic for Cartilage Disease

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Younger adults, age 65 years, increasingly present to their physicians with advanced cartilage disease or post-traumatic osteoarthritis. A number of treatments exist for lessening patient pain and improving patient function. However, many patients are becoming aware of the potential of regenerative therapies and are now seeking solutions to the impaired biology underlying their conditions rather than addressing only their symptoms. Patients do not want to merely lessen their symptoms temporarily with a surgical procedure that replaces damaged tissue, but instead seek correction and repair of the underlying biology to regenerate damaged tissue and alleviate their symptoms altogether. Current therapies for patients with cartilage disease or osteoarthritis range from non-surgical intra-articular injections with biologics, such as hyaluronic acid (HA), to total joint arthroplasty for advanced stages of disease. Total joint arthroplasty is a successful procedure for patients age 65 years; however, the limited long-term durability of implanted prostheses decreases the preference of using such methods in more active patients age 65 years. The potential of cell- based orthobiologic
injection therapies (pertaining to therapeutic injectables that aim to restore the biologic environment and/or structural components of diseased or damaged musculoskeletal tissue) is of tremendous interest for younger, more active patients, and is even more appealing in that such therapy can be delivered at point-of-care in the clinic during an office visit. Notably, the exponential rate of progress in biotechnology has allowed for immediate application of myriad novel therapies prior to clear evidence of benefit from randomized clinical trials. Orthobiologic intra-articular injection therapies include HA and platelet-rich plasma (PRP). We reported on current, available findings for a third-generation intra-articular orthobiologic injectable therapy for cartilage disease, bone marrow concentrate (BMC). Bone marrow concentrate contains mesenchymal stem cells (MSCs), hematopoietic stem cells, platelets (containing growth factors), and cytokines. The anti-inflammatory and immunomodulatory properties of bone marrow stem cells (BMSCs) can facilitate regeneration of tissue. Additionally, BMSCs enhance the quality of cartilage repair by increasing aggrecan content and tissue firmness. Following bone marrow aspiration (BMA), BMC is easily prepared using centrifugation, and is available for a same-day procedure with minimal manipulation of cells, thus complying with US Food and Drug Association (FDA) restrictions. To date, there are no published randomized controlled trials on the efficacy of use of autologous BMC intra-articular injections performed as a same-day in-office procedure for treating patients with cartilage disease; however, several publications have reported the ease of use of this method, its strong safety profile, and the fundamental science suggesting great therapeutic potential.

**A30**

**Biomarkers in Osteoarthritis**

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Osteoarthritis is the most common joint disorder in the United States, affecting 10% of men and 13% of women 60 years or older, and the numbers are expected to rise as a result of an ageing population and obesity epidemic. Due to the multi-factorial origins of Osteoarthritis, preventing the disease has proven to be quite difficult. As of current, a paucity of viable treatment options exist, primarily restricted to conservative methods, such as physical therapy and NSAIDS, or more invasive surgical options such as knee arthroplasty. Diagnosis is dependent on clinical symptoms, as well as radiographic evidence of joint space narrowing, subchondral sclerosis, and presence of osteophytes. However, clinical symptoms of the degenerative process are often present before radiographic evidence confirms the diagnosis, at which point the disease is often times more advanced. Current research is investigating the presence of biomarkers either in the blood, synovial fluid, or genome that can assist in diagnoses, assess disease severity, or determine predisposition for Osteoarthritis. As of current, biomarkers for Osteoarthritis can be classified into 3 categories: serum and urine proteomic markers, genetics, and inflammatory mediators. Identifying biomarkers for Osteoarthritis may play a large role in improving diagnostic capabilities, providing earlier diagnosis, and assessing individual risk. Furthermore, biomarkers of Osteoarthritis may provide potential specific targets for treatment methods in the future.

**A31**

**Bone Marrow Concentrate with and without Arthroscopic Repair for Rotator Cuff Tear: A Case Report**

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Traditionally, massive rotator cuff tears were treated operatively to help restore function and reduce pain. Tendon healing with or without surgical management has centered on improving the strength of the tendon and reducing pain. Recently, orthobiologics represent a new generation in treating tendon and cartilage disease. Bone marrow concentrate is a novel technique that contains mesenchymal stem cells (MSCs) to assist in regenerating damaged and diseased tissue. The healing potential of bone marrow concentrate has been attributed to the release of immunomodulators and trophic function of cytokines. The authors presented a case of a 73 year old female
with bilateral R>L rotator cuff tears. She underwent bone marrow concentrate injection with and without arthroscopic repair and had complete resolution of symptoms in both shoulders at 5 months post injection.

Conclusion: Bone Marrow Concentrate therapy demonstrates great potential for rotator cuff tendon healing with and without arthroscopic repair, however further clinical trials are warranted to better understand their role as adjuncts to operative care.

A32

Improvements on the Quality of Fibrin Scaffold Derived from Platelet-Rich Plasma by Hyaluronic Acid Microparticles

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Tissue regeneration therapy is based on three fundamental elements: scaffolds, cells and growth factors. In recent years, hyaluronic acid (HA) has been applied as an adjuvant in combination with Platelet-Rich Plasma (PRP) and Mesenchymal Stem Cells (MSCs) for tissue engineering and regenerative medicine applications. The velocity of healing process and the quality of the fibrin scaffold derived from PRP were better in HA associated than in HA alone in its fluid form. The aim of this study was to evaluate the impact of HA microparticles (HAM) on the quality of the fibrin scaffolds derived from PRP in vitro. One reason to investigate HAM is based on the properties of their dispersions, which could improve the properties of pure fibrin scaffolds such as viscoelasticity, strain hardening, release of growth factors (GFs), cell growth and migration. Therefore, the behavior of the viscoelastic and viscous parameters, the release of transforming growth factor (TGF-β1) and platelet derived growth factor (PDGF-AB) and the proliferation of human adipose-derived mesenchymal stem cells (hAdMSCs) were analyzed in pure fibrin scaffolds, in scaffolds with HAM and with fluid HA (MW 106 Da).

The results were shown that HAM improved the quality of the fibrin scaffold by suppressing the strain hardening and prolonging the release of the GFs compared with pure fibrin gels. Additionally, HAM scaffolds improved the growth of hAdMSCs compared with fluid HA scaffolds in a HAM/PRP volumetric ratio-dependent manner. These results are important for the standardization of PRP under a scientific basis, for use in clinical applications.

A33

Viscosupplementation for non-surgical glenohumeral and MTP joint arthropathy

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Rotator cuff (RTC) arthropathy, first described by Neer et al. in 1983, describes glenohumeral (GH) osteoarthritis (OA) in the setting of a complete RTC tear with progressive superior migration of the humeral head and acromion acetalubilization.1,2 The prevalence for full thickness RTC tears & arthropathy is reported to be 22-28%.2,4

Viscosupplementation has been approved for knee OA refractory to conservative treatment and intra-articular steroid injections. Many patients with RTC arthropathy have similarly failed conservative treatment, and furthermore are poor surgical candidates. Two years ago our team presented a case series of 3 patients with RTC arthropathy not responsive to conservative treatment, who underwent a series of 5 Hyalgan GH joint injections with promising results for improvement in pain visual analog score (VAS) and range of motion (ROM).

In light of the positive results, we expanded the series to include several patients with non-RTC GH joint OA, one patient from the original series who opted for a second round of Hyalgan injections, and one patient with hallux limitus/rigidus [1st metatarsalphalangeal (MTP) joint OA] seeking non-surgical treatment.4-15

Conclusions:
• Rotator cuff tears, rotator cuff arthropathy, and non-RTC GH joint OA are important causes of morbidity, especially in an ageing population.

• Athletes may experience sports-specific forces that may contribute to developing OA at an accelerated rate (e.g. ballet dancers and the MTP joint).

• Viscosupplementation is a viable treatment option for symptomatic GH or MTP joint OA that is not amenable to surgery, who decline surgery, or is refractory to traditional conservative measures.

• We expanded this case series to include patients with non-RTC GH joint OA and 1 patient with 1st MTP OA, and both patients experienced some degree of pain improvement after treatment.

• Several patients with RTC arthropathy from our prior case series continued to have some degree of pain relief, and several would opt for a repeat series of injections.

• Even if pain relief was only mild, function and ROM remained improved in several patients.

• Future studies are needed to elucidate possible mechanisms of action, enroll more patients into properly controlled trials, and explore potential combinations with other biologics and/or surgery.


### A34

**Bisphosphonate for Equine Bone Injury**

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Objective: We investigated the use of the non-nitrogen-containing bisphosphonate tiludronate, administered as a regional perfusion, to cases of equine bone injury documented by a bone scan and/or MRI.

Design: Prospective Cohort

Setting: Clinical Practice

Participants: Equine

Interventions: We administered tiludronate (50mg dose) as a regional perfusion to the affected limb(s).

Main Outcomes Measures: Return to performance

Level of Evidence: IV

Results: Two hundred five (205) horses met the criteria for inclusion in the study. The study population consisted of horses that presented for a lameness evaluation and had a bone scan (37) showing increased radiopharmaceutical (Te99m-
MDP) uptake (IRU) in the affected distal limb, an MRI (51) documenting bone injury (fluid/sclerosis/subchondral derangement) or both (117). The most common conditions treated were for those involving bone vascularity (64) and more general bone injury (51). There was a more serious injury treated in 55 cases and much less serious bone remodeling in the final 35 cases. The procedure was well tolerated with no significant complications reported. Return to previous levels of performance overall were variable depending on the condition being treated, but ranged from over 90% in horses treated for bone remodeling conditions to less than 50% in the most serious bone injuries.

Conclusions: Bisphosphonate therapy has been widely utilized for the treatment of osteoporosis, where the mechanism of action is related to inhibition of osteoclastic activity. In the equine population reported here, the non-nitrogen-containing bisphosphonate tiludronate appears to have a positive influence on clinical soundness in cases of bone injury highlighted by IRU on a bone scan or subchondral signal changes noted on MRI. Further investigation into the physiologic effects on equine bone, particularly whether there is any anabolic affect, may be needed to fully understand this mechanism of action.

A35

Biochemical Characterization of Autologous Conditioned Serum in Horses

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Objective: We analyzed the serum of horses that was processed with an Orthokine kit to determine what cytokines were induced with treatment.

Design: Prospective Cohort

Setting: Clinical Practice/laboratory

Participants: Equine

Interventions: Three aliquots of whole blood were collected from eight horses. One aliquot was treated with an Orthokine kit as described by the manufacturer. A second aliquot was immediately spun down and the serum collected, while a third aliquot was incubated overnight and then spun down 24 hours later. The three aliquots of serum were frozen at -80C for biochemical analysis. Human and mouse cytokine array blots were used to profile 45 different cytokines simultaneously. A commercial mouse IL-1ra ELISA (MRA00) was used to assay equine serum for IL-1ra levels.

Main Outcomes Measures: Cytokine array blots

Level of Evidence: II

Results: There was no significant upregulation of IL-1ra detected in the processed serum. There was, however, an increase in IL-13 levels and other chemokines such as MCP-1, Eotaxin and Plasminogen activator inhibitor-1 (PAI-1).

Conclusions: Although no significant increase in IL-1ra levels was detected in ACS treated serum, we did detect an increase in other cytokines and growth factors. IL-13 has been shown to be chondroprotective and can block collagen degradation. MCP-1 and Eotaxin are molecules that have been shown to recruit immune cells and may play a role in joint inflammation. Further studies on the other cytokines and chemokines profiled may lead to understanding the mechanism of action of ACS treatment on horses, although current clinical use results in improvement in clinical lameness scores, suggesting that there is a beneficial effect of ACS treatment.

A36

Pulsed Electromagnetic Field Therapy for Equine Lameness

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Objective: We used pulsed electromagnetic fields (PEMF) (Euipulse®) on a series of equine musculoskeletal cases to determine whether it would have a beneficial effect on the clinical signs of lameness and return athletes to the previous level of performance.

Design: Prospective Cohort

Setting: Clinical Practice

Participants: Equine

Interventions: We applied PEMF (Euipulse®) to the joint or affected body part for 5 to 30 minutes depending on location and severity of the injury.
Main Outcomes Measures: Return to performance

Level of Evidence: V

Results: 390 cases met the criteria for inclusion in the study. Treatment with PEMF was well tolerated in all horses. Of the 390 horses treated, 213 had a bone scan first to highlight the region of increased radiopharmaceutical uptake (IRU) to be treated. The other horses in the study were treated based on clinical signs alone. The most common area treated was the sacroiliac joint (206), followed by the tibiotarsal joint (198) and femorotibial joint (145). No adverse effects were noted overall and most clients reported improvement in their horse’s performance following treatment. The clients whose horse had a bone scan prior to treatment and those clients seeking periodic treatment for minor lameness reported a higher level of satisfaction.

Conclusions: Musculoskeletal soreness causing decreased performance is common in both human and equine athletes. The areas involved are often related to the insertion sites of soft tissues (entheses). In the horse, these areas are most readily identified by IRU on a bone scan and less so by direct digital palpation as in human patients. Treatment of these conditions is often difficult and fraught with initial failures or eventual recurrence of symptoms. Our experience with PEMF therapy for these conditions has been very promising, although the mechanism of action is unclear and requires further study. The therapy was well tolerated by all horses in our study and is non-invasive.

Pulsed Electromagnetic Field Therapy: Potential Clinical Applications and Cellular Mechanisms

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Pulsed electromagnetic field (PEMF) has long been researched and commonly applied in clinical settings as an adjuvant therapy for humans and animals, in promoting osteogenesis and healing nonunion fractures1,2,3,4. The current theory on how osteogenesis is being promoted through PEMF stimulation is still not clearly defined3, however, recent products5,6 that produce a weak, low-frequency PEMF, have shown regulating effects on gene expression of human mesenchymal stem cells and chondrocytes.

In recent years, regenerative medicine has been progressively incorporating PEMF as an adjunct to various conventional modalities such as shortening recovery time for muscle soreness7, regulating microcirculation8, deviating osteoarthritis progression9,11, pain analgesia12,13 and promoting joint and tissue repair14,15. Findings have shown PEMF can significantly reduce knee pain and necrosis in osteoarthritis10,16, along with improving physical function in people with knee osteoarthritis12. Moreover, low frequency PEMF has been indicated to improve microcirculation by modulating the release of nitric oxide to the blood consequently increasing the release of various signaling cascades for the healing process after a physical or chemical insult17.

The aim was to understand PEMF and its correlation to influencing human physiology18. The objective of this project was to review the benefits and potential applications of PEMF as a stand-alone treatment in sports medicine injuries or as an adjuvant to orthobiologics therapy.


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In recent years intra-articular infiltrations of Plasma Rich in Growth Factors (PRGF) have emerged as an alternative to current treatment of osteoarthritis (OA). This biological therapy uses patient’s own platelets and plasma which convey growth factors and fibrin as effectors. However, there still exist some doubts about whether this form of administration is able to reach the deeper layers of the cartilage and subchondral bone. In the light of recent studies that show the importance of subchondral bone in the pathogenesis of OA and in the cross-talking between cartilage and subchondral bone, we propose a combination of intra-articular and intraossseous injections of PRP to treat patients with severe OA, necrosis, and osteochondral lesions. The technique consists of PRGF intra-articular knee infiltrations through the mid-point of the femoropatellar region using an external approach (8mL of PRGF) and PRGF intraossseous infiltrations of both medial femoral condyle (5mL of PRGF) and medial tibial plateau (5mL of PRP) after the patient’s sedation (4-5 in Richmond Sedation Scale). The use of fluoroscope facilitates the trocar placement. After completing the infiltrations, ice is placed and the days following the surgery, patients can bear weight.

The benefits of this technique is that it stimulates the subchondral bone and mobilizes mesenchymal and chondroprogenitor cells in a gradual way for PRGF liquid turns into a viscous-gel scaffold both in the synovial membrane and subchondral bone after the infiltration. This PRGF smart scaffold releases GFs for at least 8 days, thereby restoring tissue homeostasis in both areas.

The main limitation of intraossseous infiltrations is related to patient preparation, which requires training and practice therefore the infiltration time is increased.


Slides online & DVD, no video lecture
Meniscus Reconstruction Using Scaffolds and Cells

Peter Verdonk
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Slides online & DVD, no abstract, no video lecture

A40

PRP for Cartilage Pathology

Elizaveta Kon
Rizzoli Orthopedic Institute, Bologna, Italy
Slides online & DVD, no abstract, no video lecture

A41

Subchondroplasty (SCP)® With Bone Marrow Concentrate (BMC) and Platelet-Rich Plasma (PRP); Injection In the Treatment of Knee Osteoarthritis: A Case Report

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Setting: Outpatient Clinic
Patient: Osteoarthritis (OA)

Case Description: A 71 year-old with past medical history of right knee traumatic injury resulting in anterior cruciate ligament and medial collateral ligament reconstruction and subsequent favoring of the left knee resulting in meniscal tears status post meniscal repair presents to our clinic. Patient was initially treated for his knee OA with physical therapy, bracing, visco-supplementation injections, arthrocentesis, and oral analgesics with limited success. 3T Magnetic resonance imaging (MRI) showed medial compartment cortical irregularities with cartilage thinning, patellar subchondral degenerate changes, and trabecular bone edema of the lateral femoral condyle.

Assessment/Results: Patient agreed to proceed with SCP followed by intra-articular PRP+BMC injection x 2 under ultrasound guidance. Patient subsequently demonstrated a gradual improvement in pain as well as function over the following six months. Follow-up MRI showed slightly decreased trabecular bone edema of the lateral condyle.

Discussions: Based on several well-designed studies, a new emerging theory postulates both symptoms and prognosis of knee OA have a strong correlation with the presence of subchondral bone marrow lesions. Such lesions have been observed to result in non-union type fracture in the trabecular bones which, in turn, result in collapse of part of the joint surfaces, leading to uneven loading over the cartilages to ultimately result in thinning of the cartilage. Knee joint is under constant loading, and this makes it difficult for the subchondral lesion not to progress toward non-union fracture.

Conclusions: The current case report suggests the utility of SCP and PRP+BMC for the accelerated healing of subchondral bone marrow lesions. Such healing does not only address the ongoing, painful symptom at the knee but it may halt eventual cortical irregularities by preventing non-union fracture formation thus halting further arthritic progression.

A42

A Novel Approach To Diagnosis And Treatment of Hallux Saltans: Dynamic Ultrasound Evaluation of Stenosing Tenosynovitis of Flexor Hallucis Longus Tendon at The Master Knot of Henry

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Setting: Outpatient Clinic
Patient: Hallux Saltans

Case Description: A 37 year-old otherwise healthy male presents with chief complaint of right foot pain for 2-3 months. Pain started after he had started training for a marathon, and is localized to medial plantar foot. Primary care physician has diagnosed the patient with plantar fasciitis and has been treating him with a night splint without relief. Pain is worse with great toe flexion and running. Physical examination revealed pain to deep palpation along flexor hallucis longus tendon (FHL) at medial midfoot to 1st metatarsal area. Right foot musculoskeletal ultrasound revealed a normal plantar fascia. Dynamic ultrasound examination revealed a catch of FHL tendon at master knot of henry. Comparative ultrasound of the left foot revealed normal finding and biomechanics.
Assessment/Results: Hallux Saltans was diagnosed, and ultrasound-guided corticosteroid injection with hydrodissection was performed with complete resolution of patient's symptom.

Discussions: Triggering of flexor hallucis longus tendon, or hallux saltans, is a rare diagnosis encountered in clinics. A total of less than 20 cases have been reported to date, and the great majority of such cases is diagnosed surgically and occur at the tarsal tunnel. Our case is unique because it is the first case reported to utilize dynamic ultrasound evaluation to visualize the triggering of FHL tendon and the only second case reported where triggering occurred at or near master knot of henry. Previously suggested mechanism for triggering includes fibrosis of the master knot of henry. This case also suggests safe and effective application of ultrasound-guided injection for hallux saltans at the master knot of henry.

Conclusions: Utility of ultrasound examination and ultrasound-guided injection are well established for management of patients with stenosing tenosynovitis of fingers. Our case suggests such utility of musculoskeletal ultrasound is transferable to the diagnosis and management of hallux saltans, and can be suggested as an alternative to surgical diagnosis and treatment of hallux saltans.