



THE ORTHOBIOLOGIC INSTITUTE 9TH ANNUAL PRP & REGENERATIVE MEDICINE SYMPOSIUM (TOBI 2018): COMPENDIUM OF ABSTRACTS

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ABSTRACT #1

The Evolution of Biologics into the Orthopedic Mainstream

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Orthobiologics has risen into the mainstream for orthopedic surgery, because patients are relying on biologics for success. In recent years, there has been a significant increase in publications regarding platelet-rich plasma (PRP). Further-more, The New York Times has driven much of the accelerating interest in PRP and other orthobiologics. Today there are about 10,000 references of PRP on Pubmed and the Google trends have been rising since the early 2000s. Although interest surrounding orthobiologic procedures has steadily increased, there are many issues still to address such as treatment standardization and legal questions regarding the “minimally manipulated” nature of some treatments.

Key words: Biologics, Orthopedic Surgery, PRP

ABSTRACT #2

The Future of Regenerative Medicine 2018–2028

Robin R. Young, CEO, RRY Publications LLC and PearlDriver, Inc., Wayne, PA.

The field of regenerative medicine holds vast potential for the future, with an ever-expanding innovative environment. Recently, tissue engineering products have made significant improvements in wound healing, including advancements in amniotic tissue products. However, while an innovative environment is crucial for scientific advancement, clinical relevance is often the most important requirement for success. As the field of regenerative medicine expands, identifying specific medical needs and creating applicable regenerative solutions will be essential for positive progress.

Key words: Amniotic, Regenerative Medicine, Tissue Engineering

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ABSTRACT #3

60 Years of Cartilage Research in Pittsburgh

Freddie Fu, MD, University of Pittsburgh School of Medicine, Pittsburgh, PA.

As we look at the breadth of cartilage research over time, it can be separated into two categories: biology and biomechanics. Countless researchers and pioneers in the fields of tissue engineering, stem cells, and clinical sciences have contributed to the volume of research that have led to the many gene and autologous therapies available today. The need for innovation continues in the health care field, and the burden falls on researchers and clinicians to produce high level evidence of both positive and negative outcomes.

Key words: Cartilage Research, Stem Cells, Tissue Engineering

ABSTRACT #4

The Healing Power of Fat: Plastic Surgery, Regenerative Medicine, and the Science of Adipose Derived Stem Cells

J. Peter Rubin, MD, University of Pittsburgh School of Medicine, Pittsburgh, PA.

Adipose tissue has been identified as a rich source of adult mesenchymal stem cells, and the field of plastic surgery has utilized fat grafting and adipose tissue's pool of stem cells for decades. Fat tissue is obtained by lipo-aspiration and then processed by centrifugation or other methods. The adipose tissue contains adipose stem cells which can be isolated from the connective tissue. Adipose derived mesenchymal stem cells have been shown to possess significant healing potential including the ability to reduce pro-fibrotic gene expression. They have been applied in a variety of clinical trials including craniofacial deformities and traumatic amputation sites for pain improvement and wound healing. There are many potential uses for adipose derived mesenchymal stem cells, and more clinical research is needed to investigate their efficacy and applications.

Key words: Adipose Tissue, Mesenchymal Stem Cells, Wound Healing

ABSTRACT #5

Platelet-Rich Plasma Update: What have we learned? Where are we going?

José Fábio Lana, MD, The Bone and Cartilage Institute, Indaiatuba, São Paulo, Brazil.

Platelet-Rich Plasma (PRP) holds vast potential in the field of orthopedics, however currently there is significant variability in its preparation and application, leading to decreased standardization across the field. A new classification system titled MARSPILL attempts to standardize PRP description based on the following criteria: Method of preparation, activation, presence of red blood cells, centrifuge technique, platelet concentration, image guidance, leukocyte concentration, and light activation [1]. While the MARSPILL classification is a step towards cohesion, there are significantly more cellular components to PRP that need to be analyzed as the field continues to advance, and more research will continue to emerge in this area.

Key words: Leukocyte, Orthopedics, Platelet-Rich Plasma, Classification

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ABSTRACT #6

Biology of Stem Cells

Jason L. Dragoo, MD, Stanford School of Medicine, Redwood City, CA.

Over the last decade, the growth of stem cell clinics in the United States has been unprecedented, with both positive and negative ramifications. The United States-Food and Drug Administration has started taking action against unsafe clinics that make unwarranted claims. While stem cells are a source of great potential in the medical field, it's important to understand the limitations of their application. While stem cells maintain homeostasis and respond to injury and disease, they also age and begin to lose their ability to differentiate into a wide variety of cells. They can also communicate via growth factors and exosomes. In the future of stem cell therapeutics, understanding exosomes and stem cell communication could prove to be useful in cell delivery and behavior, and is an area that deserves further investigation.

Key words: Exosomes, Stem Cells, Growth Factors, Cellular Communication

ABSTRACT #7

Advances and Barriers in Evaluating the Efficacy of Platelet-Rich Plasma Treatment for Tendinopathy

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Tendinopathy is a common problem in athletes, characterized by acute inflammation followed by degeneration of the tendon. Platelet-rich plasma (PRP) injections are a potential treatment option for tendinopathy. It has been shown to cause differentiation of tendon stem cells into active tenocytes, which are responsible for producing type I collagen. In a recent study, total collagen production from tenocytes after PRP treatment was shown to dramatically increase when compared to control. In addition, PRP was shown to suppress COX protein expression which is responsible for the symptom of pain. PRP treatment of tendon stem cells illustrates significant potential for future application of PRP for tendinopathy.

Key words: Platelet-Rich Plasma, Tendinopathy, Immunomodulation

ABSTRACT #8

Red Blood Cell (RBC) Rich Bone Marrow Concentrate for Osteo Arthritis: Friend or Foe?

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Positive outcomes with orthobiologics are dependent on a variety of factors including practitioner skill-set, type of orthobiologic, patient's cellular fitness, method of delivery, and overall degree of pathology. Each disease may require a different mixture of these factors for a successful outcome, and the recipe for treating joint osteoarthritis is currently evolving. When examining the pathophysiology of osteoarthritis,

a practitioner must consider the deleterious effects of red blood cells (RBCs) on joint homeostasis and stem cell health. Some studies on hemophilic arthropathy have illustrated negative effects of red blood cells on joint tissue [1]. It is a reasonable conclusion that eliminating RBCs from bone marrow concentrate (BMC) could improve the effects of BMC in the treatment of osteoarthritis. More basic science and clinical research is needed to investigate this area of orthobiologics.

Key words: Bone Marrow, Osteoarthritis, Red Blood Cells, BMC, Regenerative Medicine

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ABSTRACT #9

Patient Outcome Data Tracking & Registry

Kwadwo Boachie-Adjei, Regenerative SportsCare Institute, New York, NY.

With the increasing widespread use of orthobiologics, it is imperative that the medical community commit to tracking patient outcomes and identifying safety profiles and treatment algorithms. The orthopedic community as a whole has exhibited concerns over the vast amount of misinformation and false claims regarding biologic therapies. In an effort to combat the growing research gap, the American Academy of Orthopaedic Surgeons has promoted the use of electronic data registries to ensure the safety and effectiveness of emerging biologic therapies. In order to create standardization and forward progress in the field of orthobiologics, larger coordinated research efforts need to be organized, and the use of electronic data registries is a step in the right direction.

Key words: Biologic, Orthopedic, Registry, Patient Reported Outcomes, Orthobiologics

ABSTRACT #10

Federation of State Medical Boards (FSMB) Regenerative and Stem Cell Therapy Perspective

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With the stark increase in orthobiologic use in recent years, the Federation of State Medical Boards (FSMB) has investigated the current environment of regenerative and stem cell clinics. While use in the United States has vastly increased, citizens of the US have also travelled to many countries around the world to receive stem cell treatments. The FSMB found that patients with chronic medical conditions may overlook potential side effects or lack of evidence in an effort to find a cure, creating a huge risk for exploitation. As the field of orthobiologics continues to grow, the FSMB states that several factors are needed to establish legitimacy including: patient safety, patient autonomy, avoidance of patient exploitation, informed consent, and appropriate documentation. Furthermore, providing ample patient education and tracking patient outcomes are vital for creating a legitimate landscape for the future ahead.

Key words: Stem Cells, FDA, Treatment Guidelines, Stem Cells

ABSTRACT #11

FDA Guidelines for Regenerative Medicine Therapies

Amy Dow, JD, Epstein-Becker-Green, Chicago, IL.

In an effort to reform the growing stem cell industry, the United States-Food and Drug Administration (US-FDA) released a comprehensive regulatory policy for regenerative medicine titled Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P). Under the new set of guidelines several points regarding orthobiologic use and minimal manipulation are discussed. Platelet-Rich Plasma (PRP) and Bone Marrow Concentrate (BMC) products are considered “blood products” and are not enforced as human cellular tissue. Autologous use of PRP and BMC is currently permissible, but further cell culturing or addition of anti-microbial products renders the blood products as an enforceable item. In general, the FDA has listed four criteria to define an accepted Human Cellular Tissue Product including: Minimal manipulation, Homologous use, no combination with other products (except saline or preserving solutions), and no systemic effects. Furthermore, the HCT/P guidelines state that adipose tissue is technically defined as a “structural tissue” for providing support or cushioning, and any processing of adipose tissue that removes the cells, leaving a demineralized extracellular matrix is considered by FDA to be more than minimal manipulation. In addition, several high-risk routes of administration including intravenous, intraocular, or central nervous system infusion are not recommended by the FDA.

Key words: Adipose Tissue, Human Cells, Regenerative Medicine

ABSTRACT #12

Autologous Tenocyte Implantation (ATI) for Elbow Tendinopathy: Data and Clinical Results

Jeffery Hughes, MD, Sydney Shoulder Research Institute, Chatswood NSW, Australia.

Tendinopathy is a common condition that often affects manual workers and can lead to an inability to perform daily work requirements. While many treatment options exist, many cases can also be recalcitrant to some or all options. An emerging treatment option involving the injection of autologous tenocytes injection (ATI) to the common extensor tendon may provide another option. Hughes et al., performed ATI on 25 patients with chronic lateral epicondylitis for an average of 22 months, who had failed multiple conservative treatment methods. At 6 months the results showed 90% pain reduction at rest and 54% reduction with work. In addition, 88% of patients were able to return to work post procedure (average 1-3 months), while >50% of patients returned to full duty. Future studies are needed to validate this preliminary research, but ATI treatment for chronic tennis elbow could be a viable treatment option in the future.

Key words: Tendinopathy, Tenocyte, Tennis elbow, Orthobiologics, Culture Expanded, Regenerative Medicine

ABSTRACT #13

Bone Marrow Concentrate for Partial Thickness Rotator Cuff Tears: Preliminary Results

Don Buford, MD, The Dallas PRP and Stem Cell Institute, Dallas, TX.

This ongoing prospective clinical study examines the efficacy of a single injection of autologous bone marrow concentrate for partial thickness rotator cuff tears (n=25), diagnosed via magnetic resonance imaging (MRI). Patients were excluded if they had prior rotator cuff surgery, significant glenohumeral osteoarthritis, labral or biceps tendon tears, history of shoulder instability, or history of cancer/chemotherapy. The ART BMC disposable kit (Celling Biosciences, Austin, Texas, USA) was used to obtain bone marrow aspirate via ultrasound guided posterior iliac crest bone marrow aspiration (UPICA), which was then centrifuged and cell analysis performed. A single ultrasound-guided intratendinous bone marrow concentrate injection has been performed for 23 of the projected 25 patients. No infections, fractures or neurovascular injuries have been seen with the bone marrow aspirations. In addition, 15 patients are 12 months post-injection with an average Visual Analog Scale of 3 mm and significant improvements in American Shoulder and Elbow Scores. Complete analysis of results and comparison with 15-month post-injection MRI will be published soon with further conclusions regarding therapeutic efficacy.

Key words: Bone Marrow, Osteoarthritis, BMC, Ultrasound Guided, Cellular Therapy, Stem Cell

ABSTRACT #14

Multi-Center Blinded Randomized Controlled Trials Comparing Saline to Hyaluronic Acid to Amniotic Suspension Allograft for Osteoarthritis Symptom Relief: Preliminary Data

Jack Farr, MD, Knee Preservation and Cartilage Restoration Center of Indiana, Greenwood, IN.

In 2016, our research team performed a pilot study examining the effects of cryopreserved amniotic suspension allograft injection for treatment of knee osteoarthritis (n=6). The study revealed 67% improvement in SANE, 56% improvement in the International Knee Documentation Committee, and significant improvements in all Knee Osteoarthritis Outcome Score (KOOS) subscores at 12 months follow-up. The results from the pilot study led to the development of a larger multicenter randomized controlled trial involving 200 patients divided into one of three treatment arms: saline injection, viscosupplementation, or amniotic suspension allograft (ASA). Thus far, the Visual Analog Scale scores for the ASA group have shown statistically greater improvements than hyaluronic acid (HA) group at 3 months, and both the HA and saline group at 6 months. In addition, ASA group showed greater improvement in KOOS pain subscore at 3 mo when compared to HA and at 6 months compared to saline and HA groups. Also, ASA showed statistically greater improvement over baseline at 3 months compared to HA and at 6 months compared to both HA and Saline for the KOOS activities of daily living subscore. The remainder of the subscore data has yet to be calculated, and 12 month follow-up data for all 200 patients is to be expected shortly.

Key words: Amniotic, Hyaluronic, Osteoarthritis

ABSTRACT #15

Biomarkers of Early Osteoarthritis

Christian Lattermann, MD, Harvard Medical School, Boston, MA.

Osteoarthritis is a progressive disease involving anatomic, molecular and physiologic elements which leads to joint degeneration. However, changes in the joint microenvironment after injuries or trauma, can increase risk for developing osteoarthritis, called post-traumatic osteoarthritis (PTOA). Research has shown

numbers as high as 80% of combined Anterior cruciate ligament (ACL) and meniscus as well as 62% of isolated ACL patients had radiographic osteoarthritis at 10-15 years [1]. The presence of biomarkers in serum, synovium, urine and genetics may hold potential for various aspects of monitoring osteoarthritis including risk for joint osteoarthritis, inflammatory microenvironment changes, treatment effectiveness, or osteoarthritis progression. Currently, several matrix markers can be obtained in the serum and synovial fluid in patients before an ACL injury that are correlated with a future ACL injury, but as of yet are not completely predictive [2]. The area of biomarkers in orthopedics has significant potential for future applications. Larger cohort studies are needed to evaluate these biomarkers as predictors of ACL injury risk or development of PTOA.

Key words: ACL, Biomarker, Osteoarthritis

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ABSTRACT #16

Intraosseous PRP Injection with Ultrasound-Guidance

Nicolás Fiz, MD, Arthroscopic Surgery Unit, Vitoria-Gasteiz, Spain.

A growing volume of research has emerged suggesting that joint osteoarthritis is more than just wear and tear, and is correlated with distinct changes in the inflammatory microenvironment [1]. In addition, the role of subchondral bone has become a larger topic of discussion, with evidence showing a biochemical cross-talk between bone and cartilage [2]. In an effort to thwart the inflammatory changes in joint osteoarthritis (OA), our team suggests a role for mesenchymal stem cells to treat joint disease. Our research team presents a technique for treating joint disease involving intraarticular application of platelet-rich growth factors (PRGF-BTI Biotechnology Institute, Vitoria, Gastiez, Spain), followed by intraosseous application of PRGF, targeting areas of bone marrow edema in both the tibia and femur [3]. It is proposed that intraosseous injection of PRGF will help to modulate the senescent native stem cell population, and promote a more advantageous environment for healing. Typically, the intraosseous procedure is performed under fluoroscopic guidance, however our initial preliminary results (n=300) showed statistically similar patient outcomes in all Knee Osteoarthritis Outcome Score subscores performing the procedure under ultrasound guidance. New results will be published in the coming year on intraosseous applications of PRGF for hip OA.

Key words: Bone Marrow Edema, Cartilage, Platelet, Mesenchymal Stem Cells

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ABSTRACT #17

Clinical Evaluation of Autologous Micro-Fragmented Adipose Tissue as a Treatment Option for Degenerative Meniscus Tears

Gerard A. Malanga, MD, New Jersey Sports Medicine, Cedar Knolls, NJ.

The meniscus consists of two crescent shaped fibrocartilaginous wedges located between the femoral condyles and tibial plateau, acting primarily as a shock absorber of compressive loads in the knee joint. Because of the peripheral location of the peri-meniscal capillary plexus, meniscal tears involving the central portions of the menisci are increasingly susceptible to poor healing. Conservative treatment measures with therapy and anti-inflammatory medications are typically reserved for mild cases without mechanical symptoms. In more severe cases that do not respond to conservative treatment, surgical repair is the gold standard. However, in cases such as degenerative meniscal tears, much of the research fails to show long-term benefit from surgical intervention compared to exercise. We conducted a prospective clinical trial to evaluate the effectiveness of micro-fragmented adipose tissue (Lipogems, Milan, Italy) as a treatment for meniscus tears (n=20). Beneficial results were seen at 3 months and sustained through 12 months, with significant improvements in mean Numerical Pain Scale decreasing from 2.2 to 5.5, and sustained improvements in all Knee Osteoarthritis Outcome Score subscores. More research is needed to validate our preliminary findings, however microfragmented adipose tissue shows potential as a nonsurgical option for degenerative meniscal tears.

Key words: Adipose, Meniscus, Perivascular Fraction

ABSTRACT #18

Knee Treatment of Chondral Defects Using an Autologous Biological Matrix

Ramón Cugat MD, PhD, Garcia Cugat Foundation, Barcelona, Spain.

Over the past 2 decades, extensive research on cartilage and chondrogenesis have resulted in significant bounds in our understanding of knee pathology. Our research team has a particular interest in repairing chondral defects, with the use of an autologous biological matrix. The autologous matrix is constructed by first isolating a cartilaginous donor plug from the patient, then slicing the cartilage into small chips. The small cartilaginous pieces are soaked in Platelet-Rich Growth Factors (PRGF-BTI Biotechnology Institute, Vitoria, Gastiez, Spain), derived from the patient's venous blood, and overtime during the coagulative process are integrated into the matrix end product. The biologic matrix end product is constructed from both the patient's own cartilage, and the clot formed by the PRGF. The biologic matrix is then surgically implanted into the chondral defect. Preliminary case reports have shown promising results for filling of chondral lesions on second look arthroscopy, and the positive outcomes warrant further investigation with larger studies.

Key words: Arthroscopy, Biologic, Cartilage, Chondrogenesis, Matrix Grafting

ABSTRACT #19

Clinical Application of PRP/BMA Developing Surgical Applications

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

The use of biologics holds significant potential for not only nonsurgical applications, but also in surgical augmentation, to potentially improve patient outcomes or prevent the need for surgical revision. In the context of rotator cuff tears, the retear rate is significant variable ranging from 11-94%, which is also associated with poor patient outcomes. However, it is possible that the use of biologics both intraoperatively or perioperatively could benefit surgical outcomes of rotator cuff repair. But significant research is needed to evaluate the optimal cellular composition of biologics, such as leukocyte concentration and Mesenchymal Stem Cells (MSC) concentration. Anterior cruciate ligament (ACL) repair is another area of surgical augmentation that holds potential. Preliminary animal research illustrates techniques involving direct application of mesenchymal stem cells to the ACL stump or wrapping an MSC-coated carrier sheet around the ACL graft, both with initial positive results. Furthermore, a new technique involving pharmaceutically enhanced cellular mobilization with granulocyte colony stimulating factor (G-CSF), prior to removal of autologous biologic from the patient, is another area of significant interest. While many surgical augmentation techniques are emerging in the field of biologics, it is critical to understand of the cellular mechanisms involved with biologic augmentation as it is crucial for forward progress.

Key words: ACL, Biologics, Mesenchymal Stem Cells, Rotator Cuff, Articular Cartilage

ABSTRACT #20

PRP and ATI (Autologous Tenocyte Injection) in Gluteal Tendinopathy: Development of Treatment Algorithm

Ming-Hao Zheng, MD, PhD, The University of Western Australia, Perth, WA, Australia.

Gluteal tendinopathy has been cited as the most prevalent of all lower limb tendinopathies. It is a major cause of lateral hip pain or greater trochanteric pain syndrome more common in women than men (4:1) and also associated with osteoarthritis of the hip. Our treatment algorithm for gluteal tendinopathy is characterized by rest, physiotherapy, Platelet-Rich Plasma (PRP) injection, autologous tenocyte injection (ATI), and surgery correlating with worsening grades of tendinopathies. In 2017, our research team performed a double blinded, randomized clinical trial comparing corticosteroid injection (CSI) versus PRP for gluteal tendinopathy (n=80). Patients received a single injection of corticosteroid or PRP, and underwent the same post-injection rehab protocol, with 3-4 weeks of low load, followed by 6 weeks of progressive load. Findings showed that a single ultrasound-guided PRP injection provided greater improvement in pain and function in the Modified Harris Hips Score (mHHS) compared to corticosteroid injection at 12 weeks, mean score of the CSI group 67.13 (SD 16.04); Leukocyte-Rich Platelet-Rich Plasma (LR-PRP) group 74.05 (SD 13.92), $P=0.048$. The minimal clinically important difference (MCID) of a change in score of 8 points was 82.0% in the LR-PRP group and 56.7% in the CSI group ($p=0.016$). This research was followed up with a pilot study assessing the effectiveness of ATI for the treatment of chronic recalcitrant gluteal tendinopathy. The 12 patients in the study underwent tendon biopsy, which

was culture expanded for 6-8 weeks, and the expanded tenocytes injected under ultrasound guidance into the gluteal tendon. No persistent adverse reactions were noted and the patients exhibited positive clinical results at 24 months. This treatment algorithm for tendinopathy can enable better patient care by clearly delineating appropriate treatment modalities depending on the pathological stage of tendinopathy, with PRP serving as a biological enhancer and ATI functioning as a biological builder.

Key words: Corticosteroid, Platelet-Rich Plasma, Tendinopathy, Culture Expanded Tenocyte

ABSTRACT #21

Treating Tendinopathy with Laser Therapy: Equine Data

MJ Martinelli, DVM, PhD, California Equine Orthopedics, San Marcos, CA.

Photobiomodulation is defined as any form of light therapy intervention which modulates biological processes within the body. There are two well-known forms of laser therapy used today: low-level laser light therapy (LLLT) and high intensity laser therapy (HILT). Low-level laser light therapy (LLLT) uses photon absorption to elicit a tissue response which induces activation and mobilization of stem cells. The goal of LLLT is to reach a biostimulating threshold above which an anti-inflammatory and anesthetic effect is evoked while remaining below the threshold of toxicity. Low-level laser therapy has been shown to manipulate the physiologic functions of circulation, oxygenation, and cellular metabolism. The goal of HILT, also referred to as regenerative laser therapy (RLT) is to reach a threshold at which point tissue regeneration is stimulated. RLT therapy has been used for scar and adhesion reduction as well as tendon regeneration, via the agitation of the extra-cellular matrix and release of dormant growth factors on injured cells. Although photobiomodulation holds much potential, more work is to be done to determine the mechanism of action, and identify the best pathology and patient population to receive such treatment.

Key words: Low Level Light Therapy, Stem Cells, Tendon Regeneration

ABSTRACT #22

Orthobiologics and the Athlete: An Update 2018

Bert Mandelbaum, MD, Cedars-Sinai, Kerlan-Jobe Institute, Los Angeles, CA.

There are a variety of mechanistic and genomic factors which play a role in anterior cruciate ligament (ACL) injuries. Following an ACL injury, a biochemical response leads to a cascade of inflammatory cytokines which creates a catabolic cellular milieu and has been shown to increase the likelihood of knee osteoarthritis. Despite the various surgical options for ACL repair, there is a notable 15% rate of failure and 35% rate of reoperation after surgical repair. To improve function and minimize the need for ACL revision, there are several emerging areas of focus in which biologics can potentially play a role, such as creating an anabolic joint environment, improving the maturation and regeneration of graft durability and strength, improving healing of donor site, improving tunnel regeneration, and optimizing the structure and performance of the athlete. Furthermore, orthobiologics may be implemented to help with chondroprotection and chondrogenesis. Some research has shown Platelet-Rich Plasma (PRP) to increase the expression of growth factors, alter the expression of target genes and cell maturation during early graft remodeling, and accelerate graft maturation and healing

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time. However, a systematic review of ACL repair with PRP by Murray et al., demonstrated that not all studies had such encouraging results, and the volume of research at this time is mixed as to PRP's effects on ACL repair. The use of orthobiologics in sports medicine and orthopedics has an increasingly important role in recent years, but more research is needed to investigate the use of different cell types, mechanisms of action and appropriate clinical indications.

Key words: ACL, Chondrogenesis, Platelet-Rich Plasma

ABSTRACT #23

An Athlete's Perspective: Overcoming Injuries with Regenerative Medicine

Diego Lugano, Professional Footballer, Uruguay National Team and Brazilian club Sao Paolo, Canelones, Uruguay.

Moderator and Translator: Cristina Bertolotto, MD, David Geffen School of Medicine at UCLA, Los Angeles, CA.

As the captain of the Uruguayan national soccer team from 2006-2014, I have endured many injuries throughout my professional career. Starting at the age of 18, I underwent arthroscopic partial meniscectomy on my left knee. Twelve years later, I started having severe pain and swelling of my left knee, but continued to play with pain every day. During that period, I tried and failed many conservative treatments. In 2014, I continued to have more problems, suffering a left medial collateral ligament (MCL) tear with bone edema. As a result, I was forced to stop playing for quite some time. I underwent a Bone Marrow Concentrate (BMC) and Platelet-Rich Plasma (PRP) injection to my left knee. A year later, I had a follow-up treatment with arthroscopic removal of loose bodies along with another bone marrow stem cell injection. As a result of these biologic interventions, I was able to play at an elite level again, without pain, from 2014 until 2017. One of my greatest fears as a professional athlete is to suffer an injury because it can lead to losing your position within the team, decreased training, and loss of financial stability. In my own personal experience, biologics hold significant benefit for prolonging and enhancing the career of professional footballers. I urge clinicians, scientists, trainers and athletes to continue to seek out biologic interventions for relieving pain and improving healing.

Key words: Bone Marrow, Biologic, Platelet-Rich Plasma

ABSTRACT #24

Regenerative Medicine in the Department of Defense

Sean Mulvaney MD, LTC, MC, US Army (ret.), Department of Defense, Fort Meade, MD.

An important focus of the military is to couple appropriate conservative care and rehabilitation with innovative treatments to help soldiers get back out on the field. The Department of Defense is focused on applying regenerative medicine to their soldiers because it is a safe and cost-effective alternative that can help soldiers achieve optimal function. The military has started incorporating numerous regenerative treatments from prolotherapy, to Platelet-Rich Plasma, and stem cells in an effort to move away from destructive or palliative therapies which can merely provide temporary relief. One innovative treatment that our research team has

investigated is the use of a stellate ganglion block for the treatment of soldiers suffering from post-traumatic stress disorder (PTSD). From a theoretical standpoint, the ganglion block is an attempt to reset chronic dysfunctional sympathetic nervous system tone. We conducted a multicenter randomized controlled trial (n=450) with two treatment arms: Stellate ganglion block versus sub-sternocleidomastoid saline injection as placebo. The results of our preliminary study showed beneficial psychiatric effects, without any evidence of adverse events. Furthermore, this nervous system reset may reduce the barriers to therapy and help with more long-term benefits. Orthobiologics have an important role in the treatment of our military personnel, and we must continue to investigate the basic science and optimal clinical applications for such treatment.

Key words: Post-Traumatic Stress Disorder, Platelet-Rich Plasma, Stem Cells, Stellate Ganglion Block

ABSTRACT #25

Helping Veterans through Regenerative Medicine

Tom Chaby, CAPT, US Navy (ret.), Former Commanding Officer of SEAL Team FIVE, Tampa Bay, FL.

After decades of military service and many tours in war, my body has ultimately started to breakdown and pain is common place in my life today. The Injuries and surgeries to many of my joints have affected my sleep, mental health and overall quality of life. I am not alone in this feeling. The mental and physical effort required for military service takes a toll on our soldiers that return from war. It is important that they receive the treatment they need to get healthy and return to form, so they can reintegrate back to civilian life and take care of their families. Regenerative therapies have not only changed my life in a positive way, but also helped many other soldiers reduce their pain and return to optimal health. In an effort to provide this support system, I have started a not-for profit facility focused on utilizing regenerative medicine and alternative treatment options to improve mental and physical health for veterans. As we continue to support our troops, it's important to utilize all the resources at our disposal, and biologics hold vast potential for improving quality of life for our military.

Key words: Biologics, Regenerative Medicine

ABSTRACT #26

Physical Therapy Following Orthobiologics Procedures

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When designing an appropriate rehabilitation program for any patient, it is important to treat each patient individually and each condition uniquely. The rehabilitative process can be significantly different for patients who undergo nonsurgical biologics versus standard surgical techniques. In general, the best therapy approach encompasses a multifaceted technique utilizing patient education, psychological aspects, diet, sleep, appropriate rest intervals, and use of strengthening and restorative exercises. In the case of elbow ulnar collateral ligament tear treated with leucocyte-rich platelet-rich plasma (LR-PRP) the post-injection therapy protocol can be divided into multiple phases. Phase 1 (weeks 1-2) is focused on basic range of motion and restoring joint biomechanics for both the elbow and the shoulder girdle. Phase 2 (weeks 2-4) is focused on basic strengthening utilizing upper extremity

loading progressions with varying joint angles, trying to reestablish joint control throughout various ranges of motion. Phase 3 (weeks 4-8) starts to emphasize functional strengthening in multiple planes. Phase 4 (weeks 9- return to play) places focus on performance and advanced strength training, such as intervals with sport specific training in a controlled environment. Another developing area of therapy is the use of blood flow restricted (BFR) exercise. The restriction of blood flow, via circumferential cuff, to exercising muscle is hypothesized to create a physiologic response to muscle loading which increases muscle hypertrophy. Typically, BFR exercise is performed at 15-30% of 1 max rep (1RM) for each specific resistance training movement, however it can also be used with cardiovascular exercise. This type of therapy can reduce stress to joints, and may increase hypertrophic factors and growth hormone release to stimulate muscle hypertrophy. The use of blood flow restriction can hold significant value for physical therapy, in that it can potentially allow patients to improve strength without unwanted joint or tissue stress.

Key words: Biologics, Exercise, Strength Training, Regenerative Rehabilitation

ABSTRACT #27

Facial Palsy: A Novel Regenerative Approach to Treatment

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Facial palsy is a condition characterized by paralysis of the facial nerve, affecting the muscles of facial expression. It can be caused by many etiologies from a virus, neuroma, lyme disease or even many unknown causes. In the acute phase it is typically treated with high dose steroids for 72 hours along with antibiotic or antiviral therapy. Most cases have 70-85% spontaneous recovery over 3-6 months time. Various conservative measures such as mirror box therapy and biofeedback have shown positive results. A new technique involving ultrasound guided hydrodissection of the facial nerve and muscles of facial expression could be a potential treatment method in refractory cases. It is hypothesized that hydrodissection could debride fibrosis of the underlying facial muscles which have undergone fibrotic changes as a result of the facial palsy. The fibrotic changes and impaired muscle movement is known as synkinesis. By loosening up fibrosis, the muscles would allowed to move independently of each other, preventing long-term deficits in the setting of neurological recovery. Our preliminary research illustrated positive changes in Facial Grading System, Facial Disability Index, and Facial Clinimetric Evaluation Scale functional scores, with minimal adverse events. Future areas of or research will examine EMG/NCS findings, the application of biologics, and using of additional conservative measures.

Key words: Biologics, Lyme Disease, Facial Palsy

ABSTRACT #28

Intraneural and Perineural Infiltrations with PRP in Peripheral Nerve Injuries

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The use of intraneural injections has been controversial throughout the years. Several studies have shown neurotoxicity with intraneural injection of anesthetics such as lidocaine or bupivacaine, however the true mechanism of neurotoxicity is unknown and it could be secondary to mechanical pressures, anesthetic chemical effects, or location within the nerve. Preliminary research has emerged suggesting that platelet-rich

growth factors (PRGF-BTI Biotechnology Institute, Vitoria-Gasteiz, Spain) may hasten neurological recovery and prevent muscular atrophy, by facilitating axonal regrowth. Treatment techniques involving PRGF application for nerve damage utilize ultrasound guided perineural hydrodissection with PRGF in combination with intrafascicular PRGF. Small case re-reports have shown neurological benefit for peroneal neuropathy at the fibular head, carpal tunnel syndrome, sural neuropathy, lateral femoral cutaneous neuropathy, and peripheral neuropathy secondary to leprosy. Intraneural platelet-rich plasma can also be used in conjunction with surgical procedures, such as carpal tunnel release, to help with surgical outcomes and recovery. The use of PRGF to treat neurological damage holds significant potential, but larger randomized studies are needed to validate its benefits.

Key words: Carpal Tunnel Syndrome, Peripheral Neuropathy, Peroneal Neuropathy

ABSTRACT #29

Pilot Study Evaluating Intra-annular Fibrin to Treat Cervical Disc Pathology

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Cervical spine surgery for degenerative disc disease is extremely costly to the medical field and has a very high-risk of clinical failure. The use of biologics for cervical disc pathology holds vast potential. However, animal studies have shown that mesenchymal stem cells injected intradiscally illustrate significant leakage and backflow, limiting the amount of viable cells that remain inside the damaged disc. The use of an intra-annular fibrin sealants may provide better results than using biologics alone, by acting to provide structural support to damaged areas within the annulus of degenerative discs. Our research team performed a prospective study comparing intra-annular fibrin (n=39) versus intradiscal platelet-rich plasma (PRP) (n=235) for cervical degenerative disc disease. The fibrin group showed improved functional Oswestry Disability Index scores at 200 days, as well as similar improvements in Visual Analog Scale score for back and leg pain at 300 days compared to intradiscal PRP alone. In addition, both fibrin and PRP groups showed improvements in 12-Item Short-Form Survey(SF12), Veterans-RAND 12-Item Survey (VR12), and Global Mental Health scores for overall mental health and quality of life. Further research is needed to investigate intra-annular fibrin, but our preliminary research is promising.

Key words: Cervical Spine, Degenerative Disc Disease, Intradiscal

ABSTRACT #30

Ultrasound-guided Selective Nerve Root Block in the Cervical Spine with Platelet Releasate and D5W

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Cervical transforaminal epidural injections have most commonly been performed with fluoroscopic guidance using a corticosteroid injectate. However, these procedures are not without risk, and some cadaver studies have shown risk for intravascular injection or even embolic stroke from particulate steroid use. However, recent literature has shown that transforaminal cervical epidural injections can safely be performed under ultrasound guidance. In addition, some studies have illustrated positive benefits with selective nerve blocks in the cervical spine using platelet releasate and D5W. Further research is needed to evaluate the accuracy of ultrasound guided cervical transforaminal injections, as well as the efficacy of non-steroid injectates.

Key words: Epidural Injections, Platelet Lysate

ABSTRACT #31

Government-Private Partnership for Stem Cell Therapies

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Mesenchymal stem cells (MSCs) hold vast potential for treating a myriad of injuries and pathology. My research team in Chile has partnered with the Chilean government to create a regenerative medicine center, focused on research and application of stem cell therapies. One of our facility's primary goals is to investigate the use of MSCs to repair cartilage damage. One of our initial research studies has shown osteochondral lesions $> 2\text{cm}^2$ can be treated in an effective manner using a membrane seeded with autologous expanded and pre – differentiated MSCs. Furthermore, our center investigated the use of bone marrow derived mesenchymal stem cells (BM-MSCs) in combination with hip arthroscopy. Our study examined patients who had received hip arthroscopy and intraarticular BM-MSCs (n=29 hips) for cartilaginous injuries. In the study group, only 2 patients (6.8%) required total hip replacement at 27 months mean follow-up. No infections or major complications were seen in any of the treated patients. Another study in 2017, examined ex-vivo expanded BM-MSCs for treatment of hip OA. Ten patients with mild to moderate hip osteoarthritis were injected with 2.0×10^7 ex-vivo expanded BM-MSCs in 2 or 3 consecutive weekly doses. Although follow-up time varied from 7-30 months, all patients showed clinical improvement in Visual Analog Score, Harris Hip Score, Western Ontario McMaster Universities Osteoarthritis Index, and VAIL scores. There is significant potential for the use of MSCs in the treatment of a variety of pathology, including cartilage lesions. Further research is needed to validate our initial studies, and we are optimistic about new results to published in the near future.

Key words: Culture Expanded Bone Marrow Derived Mesenchymal Stem Cells, Cartilage Regeneration, Osteoarthritis