

NERVE GROWTH FACTOR ADMINISTRATION ON CULTURED HUMAN LIGAMENTOCYTES: AN *IN VITRO* PILOT STUDY

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Nerve growth factor (NGF) is involved in several joint pathologies. It has been demonstrated that its concentration increases in synovial fluid and tissue from arthritis. However, its role in joint homeostasis and pathophysiology still remain to be clarified. This study analyzed the effect of 200 ng/ml on cultured human ligamentocytes by evaluating cell proliferation, cell phenotype and gene expression. The MTT test excluded an influence on cell viability at 7 and 14 days. Regarding cell phenotype, we observed that NGF might promote the synthesis of COL1A1. On the other hand, real time PCR showed that NGF did not influence gene expression of COL3A1, FGF-BETA, IGF1, MMP2, MMP3, MMP9 and MMP13. However, COL1A1 gene was significantly upregulated in treated cell at 14 days. Our results suggest that NGF may have an anabolic effect on ligament. Additional investigations are necessary to determine how NGF may influence ligamentocytes.

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MULTI-OMICS ANALYSIS OF SYNOVIAL FLUID: A PROMISING APPROACH IN THE STUDY OF OSTEOARTHRITIS

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Osteoarthritis (OA), affecting 250 million individuals worldwide, is a significant social health problem. Therefore, the search for synovial fluid (SF) biomarkers that could anticipate the diagnosis of OA is gaining increasing importance in orthopaedics. This review summarizes the recent progresses performed in the multi-omics approach to OA, mainly focusing on proteome and metabolome analysis of SF. Proteomics of the SF has shown the up-regulation of several components of the classic complement pathway in OA samples, including C1, C2, C3, C4A, C4B, C5 and C4 C4BPA, thus depicting that complement is involved in the pathogenesis of OA. Moreover, proteomics has displayed that some pro-inflammatory cytokines, namely IL-6, IL-8 and IL-18, have a role in OA. The metabolomic profiling of the SF in OA has identified some metabolites as potential biomarkers of OA and has shown the existence of metabolically different OA subgroups. However, further studies with larger samples sizes and matched-control groups are needed to identify SF biomarkers that could be useful in the diagnosis, treatment and follow-up of OA.

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NEW INSIGHTS INTO THE TREATMENT OF NON-HEALING DIABETIC FOOT ULCERS

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Diabetic foot ulcers (DFUs) are one of the most serious and devastating complication of diabetes mellitus, affecting about 15% of diabetic patients. This review describes the innovative treatment options currently available in the treatment of non-healing DFUs. The use of Platelet-Rich-Plasma (PRP) is a safe and valid approach in the treatment of DFUs. However, the methods used to obtain and prepare autologous PRP vary between the studies, thus further evidences are eagerly awaited. Adipose tissue-derived mesenchymal stem cells (ADSCs) are a promising tool in the treatment of DFUs, but additional largescale and long-term follow-up clinical trials are needed. Bone marrow mesenchymal stem cells (BM-MSCs) transplantation, on the other hand, revealed effective in reducing incidents and improving the quality of life of patients with amputations. Autologous Peripheral Blood Mononuclear Cells (A-PBMNCs) showed a good efficacy in the treatment of diabetic patients with CLI, but further RCTs are awaited to best investigate this new therapeutic approach. Photobiomodulation (PBM) therapy revealed effective in the treatment of DFUs in two RCTs, but a standardization of therapeutic protocols as well as level-I studies are needed.

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BIOPHYSICAL STIMULATION OF THE KNEE WITH PEMFs: FROM BENCH TO BEDSIDE

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Clinical biophysics investigates the relationship between non-ionizing physical energy and the human body. Although several types of electrical stimulation devices have received US FDA approval for orthopaedic application, the use of Pulsed Electromagnetic Field (PEMFs) play a central role in joint biophysics. This narrative review aims to summarize the current evidences on the efficacy of PEMF-therapy in the treatment of knee articular diseases. Preclinical studies have assessed the effects of PEMFs on chondrocytes, synoviocytes, articular cartilage explants and animal models, showing positive effects of PEMF-therapy on cells proliferation, extracellular matrix (ECM) production, chondrocytes apoptosis and inflammatory cytokines down-regulation. Currently, PEMF-therapy is a valid option in the conservative management of several knee articular diseases, including early OA, patellofemoral pain syndrome and SONK. PEMFs could be also used as an adjunct after an arthroscopic knee procedure or TKA implantation, in order to control the joint post-operative inflammatory state.

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TANTALUM MONOBLOCK CUPS IN TOTAL HIP ARTHROPLASTY: CLINICAL RESULTS AND OUTCOME PREDICTORS

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This study aims to report the minimum 2-year follow-up results of the tantalum monoblock cup in primary THA and to identify possible outcome predictors. Eighty-eight porous tantalum monoblock acetabular cup in primary THA were reviewed. The Harris Hip Score (HHS) and the Short Form-36 Health Survey (SF-36) were used for the evaluation of outcomes. Radiographic evaluation included acetabular component orientation, presence of bone gaps, radiolucent lines, new bone formation and heterotopic ossifications. After a mean follow-up of 55.4±19.5 months, no component revision was noted. The HHS improved from 43.6±14.6 to 88.3±8.4 ($P<0.001$). The mean physical domain of the SF-36 did not significantly differ from that of age-matched, healthy subjects ($P=0.072$); the mean mental component of the SF-36 was significantly higher than that of age-matched, healthy subjects ($P<0.001$). Negative determinants of postoperative HHS (total adjusted $R^2=0.328$) using tantalum monoblock cups were age at surgery ($R^2=0.164$, $P<0.001$), female sex ($R^2=0.103$, $P<0.001$), and acetabular inclination ($R^2=0.084$, $P=0.003$).

HOW CARTILAGE STATUS CAN BE RELATED TO JOINT LOADS IN ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: A PRELIMINARY ANALYSIS INCLUDING MRI T2 MAPPING AND JOINT BIOMECHANICS

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The knee is the largest and most complex joint in the human body. Traumatic events, such as anterior cruciate ligament (ACL) tear, can lead to an alteration of joint tissues homeostasis. Literature reports an evident correlation between abnormal joint biomechanics and the status of articular tissues. These alterations, due to a sub-optimal ACL reconstruction, may result in an increasing risk of developing degenerative pathologies, such as osteoarthritis. Thus, the identification of the optimal surgical technique is a highly demanding issue in ACL reconstruction. The aim of this study was to analyze the correlation between joint cartilage conditions and knee biomechanics in ACL reconstructions, by integrating MRI T2 mapping investigations, radiostereophotogrammetry-based gait analysis and subject-specific musculoskeletal modelling.

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BIOMATERIALS AND BIOPHYSICAL STIMULI FOR BONE REGENERATION

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First, we review basic concepts of Tissue Engineering, that is, how the tensegrity is able to modulate the cell behavior. Then, we review our experimental results regarding the bone tissue engineering via biomaterials and bioreactors.

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SINGLE DOSE CEFAZOLIN IS SAFE AND EFFECTIVE FOR PRE-OPERATIVE PROPHYLAXIS IN ORTHOPAEDIC ONCOLOGY

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Surgical site infections (SSI) are a common potentially preventable complication after surgical procedures. A standardized antibiotic prophylaxis in elective orthopaedic surgery plays a major role in lowering SSI. At present, there is little published evidence regarding standardized antibiotic prophylaxis in orthopaedic oncological surgery. We introduced a prophylactic antibiotic protocol for orthopaedic oncological surgery in our hospital. The proposed protocol consists in “one-shot” intravenous administration of Cefazolin 2g, 30 min before surgery. In our setting, this preoperative antibiotic prophylaxis regimen was associated with a markedly lower rate of SSI’s. There is no current evidence in favour of greater effectiveness of prophylaxis beyond 24/48 h after surgery compared to our pre-surgical “one-shot” administration; by contrast, prolonged post-surgical prophylaxis is likely to undermine the patient’s bacterial flora and select resistant pathogens. These results are preliminary and should be used to start planning a standardised prophylactic protocol to prevent SSI’s after orthopaedic oncological surgery.

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BIOMARKERS AND INFECTIONS IN ORTHOPEDICS: OUR EXPERIENCE AND LITERATURE REVIEW

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The issue of infections in Orthopedics is rising in importance day by day. In management of Periprosthetic Joint Infection (PJI), classical biomarkers involved in diagnosis process are C-reactive protein (CRP) and Erythrocyte Serum Rate (ESR). Although wide use in PJI diagnosis process, CRP and ESR are not sensitive and specific enough for a correct diagnosis. Orthopedic surgeons, Microbiologists and Infectivologists are very interested in research about new (or rediscovered) biomarkers that can help in the diagnosis of orthopedics infections. In our Institution, a rigid protocol is applied to face suspicious PJI, implemented with LE testing routinely. In our retrospective observational study, we has compared reliability of LE test in relation ICM criteria and the comparison with other diagnostic tests or exams. Our results show that LE is a reliable method especially for intra-operatively PJI diagnosis.

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A LOCAL ANESTHESIA WITHOUT TOURNIQUET FOR DISTAL FIBULA HARDWARE REMOVAL AFTER OPEN REDUCTION AND INTERNAL FIXATION: THE SAFE USE OF EPINEPHRINE IN THE FOOT. A RANDOMIZED CLINICAL STUDY

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Hardware removal after surgical treatment fracture is one of the most common procedures in orthopaedic daily activity. A percentage from 14.5 to 21 of total removal involves the ankle joint. Trying to reduce the important socio-economic impact of this surgical procedure, we thought to perform it using the Wide Awake Local Anaesthesia Without Tourniquet (WALANT), a particular technique presented by D. Lalonde that associated a local anaesthetic drug with epinephrine in order to obtain an effective haemostatic effect despite the lack of a tourniquet. Nowadays, the WALANT efficiency and safety in hand surgery is widely demonstrated in literature but there are no data about its use in lower limb extremity surgeries. Authors performed a randomized study with 60 patients whom underwent distal fibula hardware removal between 2014 and 2016; they were divided into two groups: Group A under loco-regional anaesthesia with tourniquet and Group B under WALANT. We did not find significant differences in term of maximum pain level felt during the anaesthesiologic and surgical procedure. However, the use of WALANT significantly reduced post-operative pain levels. The WALANT procedures also reduced the number of hospitalization days. No differences in term of post-operative complication rates were found. In conclusion, the WALANT can be considered as a suitable option for distal fibula hardware removal in selected patients; it shows important clinical and economic advantages compared to the traditional loco-regional anaesthesia with tourniquet. This study also lays the foundation for the use of the WALANT beyond the field of hand surgery only.

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CRYOTHERAPY EFFICACY AND SAFETY AS LOCAL THERAPY IN SURGICAL TREATMENT OF MUSCULOSKELETAL TUMOURS. A RETROSPECTIVE CASE SERIES OF 143 PATIENTS

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Cryotherapy, also called Cryoablation (CA), is a technique that provides a local treatment to various pathological conditions. In Musculoskeletal tumours management, Cryoablation is well accepted and validated as a treatment in palliative cures for metastatic patients. Recently, CA has been proposed also as an alternative to radiofrequency ablation in osteoid osteoma and other benign tumour treatment with promising results. Cryotherapy with argon ice-balls as local adjuvant in open surgery is a tool that can provide enlargement of surgical margins if used properly. There is still not enough evidence supporting use of cryotherapy as local adjuvant in Musculoskeletal open surgery as the series cited above are very small and there is no comparative RCT between local adjuvant therapies including CA. One-hundred-and-eighty-three patients were treated with Cryoablation from 2000 and 2018 in the Musculoskeletal Tumours Surgery Unit of Careggi (Florence) and the University 2nd Clinic of Pisa. In our study group, 38 patients (26.6%) were affected by bone metastasis, 16 patients (11.1%) by aneurismal bone cysts or angiomas, 22 patients (15.4%) by low-grade malignant musculoskeletal tumours, 2 patients (1.4%) by fibromatosis, 63 patients (44.1%) by benign musculoskeletal tumours (principally Giant Cell Tumours-GCT) and 2 patients (1.4%) by Osteosarcomas. In 125 cases (87.4%), CA has been used as an adjuvant therapy, in 12 cases (8.4%) as a percutaneous ablation therapy and in 6 cases (4.2%) as adjuvant to remove tumoral lesions 'en bloc' or as a 'poor technique' for its sterilizing effect on previously resected bones. Mean follow-up was 10 years. Twenty-three patients (16%) were classified as Alive with Disease (AWD) due to local recurrence or tumour progression (14 metastases, 5 low-grade malignant bone tumours, 4 Giant Cell Tumours). Eight patients died due to the disease (6 metastases, 2 osteosarcomas), while 1 died from leukaemia. One-hundred-and-eleven patients (78%) were classified as Continues Disease Free (CDF). All patients reported decrease in pain-related symptoms after surgery and all surgeons reported better control of blood loss. Three cases (2%) of local skin necrosis or wound dehiscence were reported. No local recurrences were reported after fibromatosis ablation. Our results confirm that CA could be considered as a safe and effective technique to treat various conditions as adjuvant and palliative therapy. In particular, in open surgery, cryotherapy as an adjuvant treatment could lead to very low rates of recurrence in locally aggressive tumours like Giant Cell Tumours. These results could be generalized but a better understanding about indications and outcomes can be reached studying CA in specific populations with comparison to other adjuvant techniques.

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POLYMETHYLMETHACRYLATE-AUGMENTED FENESTRETED PEDICLE-SCREW FIXATION IN LOW BONE QUALITY PATIENTS: A CASE SERIES AND LITERATURE REVIEW

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The use of pedicle screws in low bone quality patients implicates risks of secondary implant loosening for grip lack. In fact, the result is a reduced mechanical stability at bone-screw interface and consequently an increased chance of pullout and hardware failure. Augmentation techniques have been described for many years and fenestrated screws that allow cement injection is one of them. This is a retrospective observational study of patients treated at our department with polymethylmethacrylate- (PMMA) augmented fenestrated screws. Indications for posterior instrumentation were traumatic fracture in osteoporotic spine, oncological disease, post-traumatic deformity, degenerative disease, revision surgery and sickle cell disease fractures. Implant stability was evaluated with X-Rays and CT scan performed 3 days after surgery and every 3 months during the follow-up. Accuracy of screw placement was evaluated with Heary classification. Fifty-three surgical treatments in 52 patients were performed and 247 PMMA augmented fenestrated screws were placed. According to the Heary classification, 96.21% resulted Grade I, 1.8% Grade II, 2% Grade IV. A total of 17 complications occurred. Fenestrated screw augmentation should be performed in selected patients in whom the bone quality is insufficient to guarantee implant stability. These screws may result useful in complex cases as revision surgeries, osteoporosis and tumour affections where bone quality is highly compromised.

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A RARE CASE OF HOFFA'S FAT PAD HERNIATION IN A YOUNG PATIENT: DYNAMIC ULTRASOUND AND MRI DIAGNOSIS

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Abstract Hoffa's fat pad (HFP) is part of the knee structure interposed between the joint capsule and the synovium. Recent studies have classified infrapatellar fat pad (IFP) disorders on a pathogenesis-based classification: traumatic disorders, post-traumatic disorders, lesions secondary to adjacent disorders. Masses or pseudo-masses may also be found within the IFP, however these alterations are much less frequent. Diagnostic imaging plays an important role in the diagnosis of masses and pseudo-masses of IFP and the first choice exam is a dynamic ultrasound study. We presented a rare case of Hoffa's fat pad herniation through the joint capsule, in a young child without history of knee injuries that has never been described before in the literature.

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MUSCULOSKELETAL HYDATID DISEASE: REPORT OF A RARE CASE WITH PRIMARY AND EXCLUSIVE LOCALIZATION IN RIGHT HEMI-PELVIS AND FEMUR

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Hydatid Disease (HD), also called *Echinococcosis* or *Hydatidosis*, is a parasitic infection caused by the larval stage of the tapeworm *Echinococcus*: *E. granulosus* or *E. multilocularis*. HD occur most frequently in liver or lungs, rarely in brain, skeletal muscles, bones, kidneys, spleen. Bone infestation of *Echinococcosis hydatid* cysts occurs respectively by haematogenous seeding and progressive invasion into bone by lesions in the adjacent soft tissues. Patients with musculoskeletal HD clinically show the disease in adulthood because the lesions develop very slowly. In some cases, HD is an uncommon cause of soft tissue mass, pain and neurovascular symptoms due to compression or to secondary infection. Diagnostic imaging plays an important role in the diagnosis of HD and in the differential diagnosis with soft tissue tumors. We present a rare case of male patient of 42 year-old with diagnosis of HD with primary and exclusive localization in right hemi-pelvis and femur.

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COMPARISON OF EARLY FUNCTIONAL OUTCOMES BETWEEN TWO DIFFERENT SURGICAL APPROACHES FOR TOTAL HIP ARTHROPLASTY

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Total Hip Arthroplasty (THA) is considered the most successful treatment for advanced hip osteoarthritis. Different surgical approaches for THA are available and they have shown excellent outcomes in the long-term follow-ups. However, few studies have analyzed the functional outcomes in the first days after a THA surgery. The purpose of this study was to compare the early functional outcomes between two different surgical techniques: a minimally invasive direct anterior approach (mini-DAA) and a postero-lateral approach (PL). Twelve patients for each group were analyzed. Pre- and postoperative (3, 10, 30 and 90 days after surgery) Patient-Reported Outcome Measures (PROMs) were administered: HOOS, HHS, VAS and SF-12-v2 scores. Moreover, comparison between surgical operation time and blood loss were examined. PROMs showed a significant improvement in the SF-12-v2 in the mini-DAA group compared to the PL group at 3 days after surgery: this difference was maintained also after 10 and 30 days. In addition, HOOS and HHS were significantly ameliorated in the mini-DAA group starting 10 days from surgery. In both groups, a physiological pain reduction was observed in the first days after surgery; comparing it to the pre-surgical VAS values, we found a significant improvement in the scores for the mini-DAA group after 30 days. Moreover, we demonstrated a significant reduction in blood loss for the mini-DAA group. Surgical operation times were similar in the two groups; however, the duration of the mini-DAA procedure was shorter compared with the known literature. In this preliminary study, we demonstrated that the minimally invasive direct anterior approach for THA may lead to benefits in the early postoperative time, as it allows for an improvement in functional outcomes, a reduction of postoperative pain, a reduction of hospitalization time and consequent reduction of postoperative complications; therefore, this surgical approach may consent an early return to work and daily activities.

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CHARACTERIZATION OF DIFFERENT *IN VITRO* CULTURE CONDITIONS TO INDUCE A FIBRO-CHONDROGENIC DIFFERENTIATION OF SWINE ADIPOSE-DERIVED STEM CELLS

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Meniscus repair is still a challenge for orthopaedic surgeons as this tissue has a scarce healing potential due to the limited vascularization and to the lack of progenitor cells. Lately, several tissue engineering strategies combining cells and scaffolds have been developed. Adipose-derived stem cells (ASCs) represent a novel cell source for meniscus repair as they are easy to harvest, and they possess an intrinsic chondrogenic potential. The aim of our study was to analyze and compare the chondrogenic differentiation of swine ASCs cultured *in vitro* with different supplemented media. We isolated ASCs from swine adipose tissue and we placed in pellet cultures supplemented with either Bone Morphogenetic Protein (BMP)-2 and Transforming Growth Factor (TGF)- β 3 or with Bone Morphogenetic Protein (BMP)-7 and Transforming Growth Factor (TGF)- β 1. Samples were analyzed after 7, 14 or 21 days of culture by biochemical, histological and gene expression analysis. Our preliminary results show that BMP-2 and TGF- β 3 are stronger inducers of chondrogenesis.

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ANIMAL MODELS FOR CARTILAGE REPAIR

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Cartilage lesions still represent an unsolved problem: despite the efforts of the basic and translational research, the regeneration of this tissue is far from being reached (1-3). Articular cartilage lesions can be divided in two main groups: superficial or partial defects and full-thickness defects (4, 5). Partial lesions are not able to self-heal because multipotent cells from the bone marrow cannot reach the area leading to a progressive degeneration of the tissue (6). Conversely, full-thickness injuries possess greater chances to heal because subchondral bone involvement allows for the migration of mesenchymal cells, which fill the damaged area (7, 8). However, healing occurs through the formation of a fibrocartilaginous tissue, which has different biomechanical and biological properties (9). Native hyaline cartilage has indeed specific biomechanical properties, which confer resistance to compressive and shear stresses; the reparative fibrocartilaginous tissue lacks these abilities, therefore, the surrounding healthy cartilage progressively degenerates. In the past years, several therapeutic strategies have been developed to restore the damaged cartilage, bone marrow stimulation (chondroabrasion, drilling, micro- or nano-fractures) and more recently, tissue engineering approaches (10-14). Some of these latter procedures have already been applied in clinical practice such as matrix-induced autologous chondrocyte implantation (MACI) (15) or osteochondral scaffold implantation (16). Generally, tissue engineering approaches are based on the combination of three main elements: cells (i.e. primary chondrocytes or multipotent mesenchymal cells), biocompatible scaffolds (i.e. polymers, composites, ceramics) and signaling molecules (i.e. growth factors). Moreover, several culture conditions (i.e. static or dynamic cultures) and biomechanical stimuli can be applied during the *in vitro* culture to promote tissue maturation (17-19). However, an *in vivo* culture is mandatory to validate a new engineered construct as the *in vitro* phase lacks the essential *in vivo* environmental stimuli and because the *in vivo* culture allows for the testing of the biocompatibility and safety of a new material (18, 19). Moreover, preclinical animal models are crucial to understand the molecular mechanisms of cartilage lesions favoring the development of new regenerative strategies (20, 21). *In vivo* studies on animal models should focus on the analysis of the cellular component, analyzing the maintenance of the cellular phenotype and the tumorigenicity; on the evaluation of the biocompatibility, toxicity and degradation of the biomaterial and on the assessment of the engineered construct. In this manuscript, we will review the most common preclinical animal models, which are used to understand cartilage biology and therefore to develop new tissue engineering strategies. We will focus on both small and large animal models highlighting their peculiarities, advantages and drawbacks.

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EXTERNAL FIXATION VERSUS TITANIUM ENDOMEDULLARY NAIL IN THE TREATMENT OF DIAPHYSEAL FRACTURES OF THE LOWER LIMB IN PEDIATRIC AGE: OUR EXPERIENCE

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In the past, the use of external fixation technique (FE) in children was limited, as the patient's compliance to the treatment was scarce due to an important visual impact for the little patient. With the evolution of the surgical approach and the technology of fixators, we have been able to considerably implement the treatment possibilities, thus allowing for an immediate load bearing of the operated limb and for the early mobilization of the joints. The FE technique does not represent an overcoming of classical synthesis techniques by internal fixation with elastic intramedullary nails, but it simply offers a valid treatment alternative to selected cases. In this work, we radiologically and clinically evaluated pediatric patients treated with FE for diaphyseal fractures of the lower limb and we compared them with patients treated with standard Titanium Endomedullary Nail (TEN) techniques. Our results confirmed that FE is a valid alternative treatment for these types of fractures.

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REINFUSION-DRAINS REDUCE BLOOD TRANSFUSIONS IN TOTAL JOINT ARTHROPLASTY

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This study aims to evaluate the effect of postoperative blood recovery with reinfusion drains on hematologic parameters and blood transfusion rate in patients undergoing total joint arthroplasty. Three-hundred-and-forty-four patient records were reviewed and 271 patients were included in the study; 56.8% of patients were treated with postoperative cell salvage procedure using reinfusion drains (PCS) and 43.2% had closed-suction drain (CSD) postoperatively. In comparison to the CSD group, the PCS group showed higher hemoglobin (Hb) levels on the first and second days postoperatively but no statistical differences were noted at the day of discharge. 75.2% and 37.7% of patients required blood transfusions in the CSD and PCS groups, respectively. The PCS group had a lower number of blood transfusions than the CSD group. At multivariate analysis, Hb loss rate was related to preoperative Hb values, total amount of drained blood and chronic antiplatelet therapy. The number of blood transfusions was related to preoperative Hb values, closed-suction drains, preoperative platelet count, TKA surgery and BMI. This study supports the use of PCS with reinfusion drains after THA and TKA at least for the short-term.

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AGGRESSIVE HEMANGIOMA STARTING FROM L5 BODY, TREATED WITH MASS EMBOLIZATION AND RADIATION THERAPY WITH PROTONS: A CASE REPORT

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A hemangioma is a benign tumor of endothelial cells, multiplying into the medullary spaces of the cancellous bone. This tumor is in most cases not symptomatic, and in this case, they do not require any specific treatment. Pain and neurological symptoms derived from hemangiomas as shown in 2-11% of the cases. The 55% of these cases presents low back pain, while the 45% presents neurological deficit from compression of the spinal cord, peripheral nerves or both. We present a clinical case report of a young woman, affected by aggressive L5 hemangioma causing a spinal canal stenosis with associated sciatalgic symptoms. We performed a review of the current literature on the treatment options, giving the rationale of our treatment choice (mass embolization and radiation therapy with protons).

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PRIMARY TOTAL KNEE REPLACEMENT IN HEMOPHILIACS: EXPERIENCE OF A SINGLE INSTITUTION OVER FOURTEEN YEARS OF SURGICAL PROCEDURES

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This retrospective study reports clinical and functional orthopedic outcomes and complications after 14 primary total knee replacement (TKR) performed between 2000 and 2014. The mean age at surgery was 42 years (range 26-59), with a removal-free survival of 100% at the end of follow-up (months 109.85). The KSS score was 49.64 pre-operatively (range 31-63) and 78.14 at final follow-up (range 45-90), the KSS function score was 64.64 pre-operatively (range 35-80) and 84.57 at final follow-up (range 45-100). According to this study, there are three main factors that can influence long-term and early surgical outcomes: post-operative fibrosis, a previous synovectomy and presence of inhibitors. Even if our results are slightly suboptimal compared to those obtained in non-hemophilic patients, this study shows that TKR is an effective surgical procedure in hemophiliacs.

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SECONDARY FEMUR FRACTURE FOLLOWING TREATMENT WITH ANTEROGRADE NAILING: THE STATE OF THE ART

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Cephalomedullary nailing (CMN) currently represents the best surgical technique for the treatment of intertrochanteric hip fractures. Although the success of CMN in terms of functional recovery and fracture healing, in clinical practice there are many complications. Later femur fracture following treatment of trochanteric fracture with CMN is not a very frequent complication but, when it occurs, its treatment is the most complex, because of the increase of peri-operative mortality. There are studies in literature, which have demonstrated that the incidence of this complication is about 0.5-3%. Diagnosis and classification are made with standard radiographs, using the AO classification and the modified Vancouver classification. In the actual literature, to determinate the predisposing factor to the secondary fractures, the authors focused their attention on patient-related and surgical related risk factors. The treatment is variable and it depends on the type and characteristics of fracture and device. Outcomes analyzed in literature were mortality and bone healing. The aim of this manuscript is to provide an overview of this topic and to describe the state of the art of the secondary fracture after surgical treatment with intramedullary nailing.

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MUELLER-WEISS DISEASE: REVIEW OF THE LITERATURE

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Müller-Weiss (MW) disease is a spontaneous osteonecrosis of the tarsal navicular bone in adults. It is a rare cause of chronic medial midfoot pain and deformity characterized by the collapse of the dorso-lateral part of the navicular, progressive navicular fragmentation and talonavicular joint destruction. This study provides a review of the literature about the epidemiology, etio-pathogenesis, clinical, radiological findings and therapeutic alternatives.

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TRANSILIOSACRAL FIXATION USING THE O-ARM2® AND STEALTHSTATION® NAVIGATION SYSTEM

F. LIUZZA¹, L. CAPASSO¹, M. FLORIO¹, F. MOCINI¹, G. MASCI¹, G. CAZZATO¹,
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Pelvic fractures are quite uncommon, they represent only 2-8% of all fractures. Osteosynthesis with percutaneous trans-Iliosacral screw is recognized as one of the standard procedures for the treatment of unstable posterior pelvic ring lesions. Because of the high number of complications associated with the conservative treatment of these kind of lesions such as pain, limb heterometry, difficulty in walking and sexual disability, percutaneous fixation with trans-iliosacral screw has found wide use and has become very popular among orthopedic surgeons. This technique is indicated for the treatment of dislocations of the sacro-iliac joint, some types of sacral and iliac fractures or combinations of these lesions.

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THE BIOMOLECULAR INTERACTIONS BETWEEN ENDOTHELIUM AND BONE CELLS: AN OVERVIEW

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Bone turnover is a complex set of different molecules pathways and it is strictly connected with bone vasculature. It includes every bone process concerning bone modelling and remodelling such as skeletal growth and healing process. A fundamental component of this bone architecture is played by the endothelium, that acts in a paracrine fashion on other bone stromal cells via humoral factors, growth factors and chemokines/cytokines. The alteration of those biochemical interactions between endothelium, vasculature and bone tissue may cause various pathological manifestations. Understanding the bases of the interaction between those different pathways could provide novel therapeutic strategies for bone disease. The Authors present an updated overview of the most common communication biomolecules between bone cells and endothelium and their interactions both in healthy and pathological conditions. Furthermore, focusing on gene and related therapies, possible future therapeutic strategies for bone vasculature/metabolic diseases are presented.

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HOW TO OBTAIN BETTER RESULTS, CHOICE OF IMPLANT OR SURGICAL TECHNIQUE? A NEW SURGICAL TECHNIQUE WITH AN EXTRAMEDULLARY REFERENCED CUTTING GUIDE AND A BLENDED ALIGNMENT METHOD

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Measured resection and ligament balancing techniques are the most used in TKA; both require, in the majority of knee arthroplasty systems, a femoral intramedullary canal referencing for the distal femoral cut. Fat embolism, activation of coagulation and bleeding may occur from the reamed canal; this can be avoided with different solutions such as navigation, patient specific instruments or the use of an extramedullary device. The FuZion™ tensor was created as a blended method with the purpose to overcome the downsides of both techniques by fusing them. The aim of our study is to present the technique and the preliminary results of a cohort of patients where this instrument was customized and used as an extramedullary cutting guide for the distal femur, matching the distal femoral cut with the proximal tibial cut in order to obtain a guided, kinematically adjusted, alignment and a reduction of post-op blood loss.

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HYDATID CYST IN THE SPINE. THE ALLIANCE BETWEEN SURGEON AND INFECTIOLOGIST IS WINNING: A CASE REPORT.

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Hydatid Cyst is a protozoal disease, whose spinal localization may be cause of pain and severe inability due to neurological symptoms and instability. Treatment combines the difficulties to eradicate the cyst with the spine regional constraints. The case of a 45-year-old woman is reported, affected by hydatid cyst in the spine, submitted to combination of medical treatment and surgery (double approach gross total excision and reconstruction) and followed up for 6 years. The treatment strategy allowed an excellent quality of life without pain and neurological symptoms at the latest follow-up. This case supports the validity to combine anthelmintic medical treatment and excisional surgery in the treatment of hydatid cyst of the spine. The medical treatment makes surgery more effective maintaining the result over long term. Subtotal or total excision of the cysts can be performed, including decompression of neural structures and adequate spine reconstruction.

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EVALUATION OF THE USE OF AUTOLOGOUS MICRO-FRAGMENTED ADIPOSE TISSUE IN THE TREATMENT OF KNEE OSTEOARTHRITIS: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Articular cartilage injuries are still unsolved due to the limited intrinsic healing potential of this tissue. Unlike other tissues, inflammation in the synovial joint causes perpetual damage and progressively leads to the development of osteoarthritis. Previous *in vitro* and *in vivo* studies have demonstrated the efficacy of mesenchymal stem cells isolated from adipose tissue in modulating inflammation. In this study, we analyzed the role of these cells in modifying the pathological microenvironment present in knee osteoarthritis. This is an interventional, prospective, randomized, controlled study. Starting from June 2017, 39 patients with grade III and IV knee osteoarthritis of Kellgren-Lawrence were enrolled, aged between 45 and 75 years, with pain greater than or equal to 6 according to the VAS scale, without ligament instability, with an axial deviation not greater than 10° and with a BMI between 18 and 30. The control group underwent an arthroscopic debridement, while the experimental group underwent an arthroscopic debridement and a subsequent intra-articular injection of autologous micro-fragmented adipose tissue. Patients were evaluated before surgery and at 6 months after the procedure, by radiological analysis (MRI) and functional outcome measures. The main purpose of the study is to evaluate the symptomatic improvement by comparing the functional outcome scores between the two groups. At 6 months after treatment, preliminary results on 39 patients showed pain reduction and functional improvements in the experimental group without a significant difference due to the low number of patients. The radiological and biochemical analyses are still ongoing. To date, the study has not revealed any side effects. These preliminary results demonstrate an encouraging positive trend in the experimental group. Patient recruitment is still ongoing to finalize the statistical analyses and to confirm our hypothesis.

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TOTAL HIP ARTHROPLASTY IN RAPIDLY PROGRESSIVE OSTEOARTHRITIS OF THE HIP: CLINICAL AND RADIOLOGICAL OUTCOME OF A CONSECUTIVE SERIES OF PATIENTS

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Rapidly progressive osteoarthritis (RPOA) is an uncommon subset of osteoarthritis (OA) characterized by rapid joint degeneration and destruction. The treatment of choice for these patients has traditionally been total hip arthroplasty (THA) because nonoperative treatments modalities are not effective. RPOA can lead to acetabular bone loss and consequently intraoperative technical difficulties making joint reconstruction in such patients a challenge for the surgeon. The purpose of this study was to determine the clinical and radiological results of patients suffering from RPOA and treated with hybrid or cementless THA at a single institution. We retrospectively review of all patients who underwent THA for RPOA from January 2011 to December 2016. Twenty-three hips in twenty-one patients were included in this study, with a mean age at surgery of 74 years (range, 41-82) and a mean follow-up of 30 months (range, 24-60). In all patients an uncemented cup, either plasma-spray or trabecular titanium, was implanted. In eighteen cases a cemented femoral stem was used. In eight cases autologous bone graft was used to replace the acetabular defect. Radiographic and clinical follow-up was performed at six months postoperatively, twelve months and yearly thereafter. At radiographic follow-up, no signs of prosthetic loosening or migration were seen. Harris Hip Score improved from 65.3 preoperatively to 89.2 at latest follow-up. The use of both hybrid and uncemented THA in the treatment of RPOA was found to be successful in our patients with a mean 30 months follow-up. Hemispherical cementless cups with both plasma spray and high porosity outer surface (used in the worse cases) were effective in getting primary stability and bone ingrowth.

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TREATMENT OF VANCOUVER B1, C PERIPROSTHETIC HIP FRACTURES WITH PERIPROSTHETIC POLYAXIAL LOCKING PLATE SYSTEM: A 3-YEAR FOLLOW-UP

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The incidence of periprosthetic fractures after primary knee and hip arthroplasty is around 2.5% and is increasing after revision surgery up to 4%. Management of these fractures is often particularly demanding and expensive. The primary aim of the presented study is to describe our experience in using a precontoured periarticular polyaxial standard plating system in a cohort of patients with homogeneous fracture type (Vancouver B1, C), comparing our experience with other surgical solutions. In stable implants, the primary strategies aim for fracture stabilization, leaving the original prosthesis in place. The results of conventional non-locking implants have been mostly poor with complication rates up to 53%. Therefore, today, monoaxial locking plates are strongly recommended. From May 2013 to December 2014, 30 “non-contact bridging plate” (NCB-PP®) were implanted. All fractures were periprosthetic Vancouver B1 or C fractures. In 24 patients, NCB-PP® plating was performed after periprosthetic femoral fracture as primary treatment, in 6 patients, it was performed as secondary fracture treatment after primary plating failure. All surgeons performed lateral femoral approach with ORIF. Average follow up was 36 months. Bony consolidation was confirmed in all patients, bar one, in an average time of 4 months; none of the patients bar one developed mechanical failure or implant breakage. The GOS at 52 weeks was back to the preoperative level in 18 patients and it did not improve at 24 months. The Harris Hip Score at 52 weeks showed a mean score of 80.14 points. Full weight bearing was allowed at mean time of 100 days. None of the patients developed complications that needed subsequent surgery. The use of NCBPP plates has given excellent results in our clinical practice, allowing early postoperative mobilization and recovery.

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TARGETING VEGF-A IN CARTILAGE REPAIR AND REGENERATION: STATE OF THE ART AND PERSPECTIVES

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Osteoarthritis (OA) is the most common joint disorders in western populations, and is characterized by a progressive degradation of articular cartilage (AC) leading to loss of joint function. Methods to cure, delay or prevent the onset of OA and/or improve AC repair strategies have high clinical and socioeconomic impact. Possible innovative strategies envisioned for early OA treatments or cartilage repair include the implantation/injection of mesenchymal progenitors (MPs)-based constructs or cell-free bioactive scaffolds/hydrogel coupled with the controlled recruitment and instruction of resident MPs or AC. However, these tissue engineering-based strategies still suffer from unreliable outcomes with poor fibro-cartilaginous repair and blood vessel invasion. In such conditions Vascular Endothelial Growth Factor (VEGF) family has been shown to play a key role in controlling AC catabolism on one hand and angiogenesis on the other as a crucial step for endochondral ossification of MPs, ultimately leading to progressive breakdown of the neo-formed matrix. This review aims to provide a summary of relevant relationships between impaired angiogenesis, OA and cartilage regeneration highlighting how VEGF might play a paramount role in the pathophysiology of cartilage aging or degeneration as well as in cartilage repair.

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