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POSITIVE EFFECTS OF LOW INTENSITY PULSED ULTRASOUND ON HUMAN OSTEOARTHRITIC SYNOVIAL MODELS

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Purpose (the aim of the study): Synovial inflammation is a characteristic symptom of osteoarthritis (OA), that is known to be closely associated with joint pain and stiffness. Low intensity pulsed ultrasound (LIPUS) has been widely used in the treatment of fractures, soft tissue injuries and inflammatory diseases. However, the functions and mechanisms of LIPUS in OA synovial inflammation are still unknown. The development of an in vitro synovial-like system that well mimics the native pathological synovial tissue may help to test new therapies for OA. This study was designed to investigate LIPUS effects on human synovial OA inflammation by using three different in vitro models.

Methods: Human OA synovial tissue explants (characterized by Kreen score) and isolated synovial cells were used as two in vitro models for testing LIPUS effects. Both models were treated with LIPUS every 2 days until day 5 of culture. At day 0, 2 and 5 gene expression (*CD68*, *CD55*, *CD80*, *CD86*, *CD163*, *ADAMTS4*, *ADAMTS5*, *MMP13*, *S100A8*) by Real time PCR and protein expression (*CD68*, *CD55*, *CD80*, *CD86*, *CD163*) by immunohistochemistry or flow cytometry were evaluated. The master regulators of Inflammation (NFKB1 and NFKBIA) and cytokines release (IL6, CXCL8, TNF- α , CCL2, CCL4 and CCL5) were also analysed at each time point. Moreover, human CD14+ macrophages derived from buffy coat were used as positive control to confirm LIPUS effects.

Results: Moderate grade human synovial tissue explants treated with LIPUS, evidenced starting from day 2 a decrease of M1-like macrophage markers (*CD80* and *CD86*), degradative enzymes (*MMP3*, *ADAMTS4*, *ADAMTS5*, *MMP13*) and alarmin (*S100A8*) associated to an increase of M2-like macrophage markers (*CD163* and *CD206*). Moreover, we also found that NFKB1 as well as the inflammatory cytokines were decreased. By using in vitro characterized synovial cells, we obtained the same results. Interestingly, using positive human CD14+ M1-like macrophages we also confirmed the switch of these cells and the reduction of inflammation.

Conclusions: In conclusion, we have demonstrated that LIPUS are responsible for the switch from an activated M1-like to an M2-like anti-inflammatory phenotype, providing new insights into the clinical application of LIPUS as a therapeutic option for the management of synovial inflammation in OA.

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CORRELATION OF MACROSCOPIC AND MAGNETIC RESONANCE FINDINGS IN SHEEP CHONDRAL LESIONS TREATED WITH AUTOLOGOUS CHONDRAL PLATELET-RICH PLASMA MATRIX IMPLANTATION

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Purpose (the aim of the study): Injuries in articular cartilage are an important problem in humans and animals because patients can develop osteoarthritis (OA) if left untreated. This pathology causes pain, dysfunction and reduces the patients' life quality. Chondral lesions treatment is a challenge due to cartilage limited reparative and regenerative ability. One of the main limitations in the OA management is the assessment of its progression after different treatments, therefore, it is important to find non-invasive techniques that show the injury progression. Thus, the purpose of this study was to analyze the correlation between macroscopic appearance measured by the International Cartilage Repair Society (ICRS) and Goebel scale, and Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scale in sheep with stifle full-thickness cartilage defect treated with Autologous Chondral Platelet Rich Plasma Matrix Implantation (PACI), Hyaluronic acid (HA), or Ringer Lactate Solution (RL).

Methods: A full-thickness chondral defect of 8 mm diameter was created in both medial femoral condyles in 7 skeletally mature Merino sheep. The seven right stifles were treated with PACI combined with an intraarticular injection (IA) of plasma rich in growth factors (PRGF) (TRT stifles). Regarding the left stifles, 3 of them were treated with a single IA injection of Ringer Lactate Solution (RL) (RL stifles) and 4 were treated with a single IA injection of Hyaluronic Acid (HA) (HA stifles). 18 months after the surgery, Magnetic Resonance Imaging (MRI) was performed to analyze the lesions using the MOCART 2.0 Knee Score sagittal view T2-weighted. Just after the MRI, the macroscopic evaluation was performed following ICRS and Goebel scales (Image 1). The statistical study was carried out with IBM SPSS statistics 27 program for Mac, in all cases a $p < 0.05$ was considered significant. A bivariate Pearson two-tailed correlation was performed between the 3 scales.

Results: In this study, it was observed that there is a negative correlation between the macroscopic results obtained with ICRS and Goebel scales ($p < 0.001$; $r = -0.874$), there is also a negative correlation between the Goebel scale and the MRI results using MOCART 2.0 knee score ($p = 0.11$; $r = -0.353$). Although there was not a significant correlation between ICRS and MOCART scales ($p = 0.055$), the results were very similar. The correlation showed the same results regarding total score for the 3 scales and the different treatments: PACI, RL and HA (Image 2).

Conclusions: The use of MRI evaluation could be an option for analyzing chondral lesions because the results correlate with the macroscopic evaluation when using Goebel scale. However, the different results obtained for the ICRS could be due to the shortage of parameters assessed with this scale. In this study, MOCART scale have demonstrated to be an optimal tool in OA prognosis, and additionally, it is a non-invasive technique. Thus, clinically it has some advantages over other techniques as arthroscopy, being less harmful for patients.

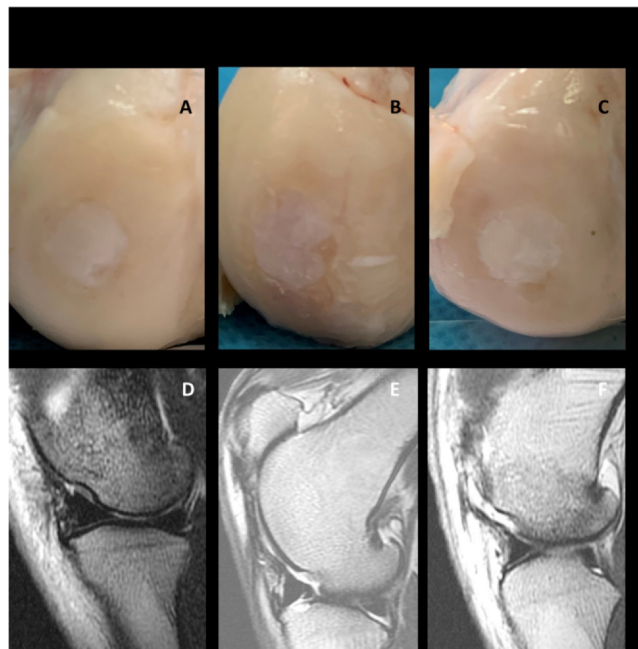


Image 1: A) Macroscopic digital photographs of chondral defects treated with PACI B) Macroscopic digital photographs of chondral defects treated with RL C) Macroscopic digital photographs of chondral defects treated with HA D) MRI T2-weighted PACI stifle E) MRI T2-weighted RL stifle F) MRI T2-weighted HA stifle. Autologous Chondral Platelet Rich Plasma Matrix Implantation (PACI), Hyaluronic acid (HA), or Ringer Lactate Solution (RL).

Image 1: A) Macroscopic digital photographs of chondral defects treated with PACI B) Macroscopic digital photographs of chondral defects treated with RL C) Macroscopic digital photographs of chondral defects treated with HA D) MRI T2-weighted PACI stifle E) MRI T2-weighted RL stifle F) MRI T2-weighted HA stifle. Autologous Chondral Platelet Rich Plasma Matrix Implantation (PACI), Hyaluronic acid (HA), or Ringer Lactate Solution (RL).