

P229

Evaluation of the biology of matrix associated autologous chondrocyte transplantation (MACT) in an equine model: results of a pilot study

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Purpose: To assess the biology and effectiveness of the matrix associated autologous cartilage transplantation (MACT) as a treatment for full thickness cartilage defects in a large animal model.

Methods and Materials: In a pilot study 200 mgs cartilage were harvested arthroscopically out of the fetlock joints of four mare horses. After 4 weeks of cell cultivation, three scaffolds, – a collagen I /III membrane, a hyaluronan membrane and a combined scaffold (collagen and hyaluronan), containing autologous chondrocytes, were reimplanted in a standardized cartilage defect created in the equine lateral patellafemoral joint in 3 horses. An untreated defect of the fourth horse was used as a control. Three months after implantation the horses were euthanised and the transplants were analysed with histology, electronmicroscopy and molecularbiology.

Results: All defects showed a complete filling with cartilage like tissue. Histology revealed fibrocartilage tissue well integrated in the surrounding native cartilage. At the basis of the transplants hyalinelike cartilage could be detected. The Real time PCR revealed a reduced expression of collagen II and an increase of collagen I compared to native cartilage. Electronmicroscopy shows that differentiation starts at the border of the defect, the appearance of extracellular matrix and collagen II fibrils.

Conclusions: The equine model is an appropriate animal model for the MACT and a study including a larger number of subjects is justified and already designed. The created regenerative tissue showed significant similarities to native cartilage therefore MACT is an applicable method for the treatment of full thickness cartilage defects.

P230

3D HR micro-MRI to quantify the medial tibial cartilage thickness progression in a rabbit Model of experimental osteoarthritis

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Purpose: Objective: to develop a 3 D High Resolution (HR) micro-MR imaging method to measure quantitatively in vivo and non-invasively medial tibial cartilage thickness (MTCTh) in both normal and Anterior Cruciate Ligament Transection (ACLT) rabbit osteoarthritis (OA) model.

Methods and Materials: Methods: left knee of the 40 ACLT rabbits were imaged in vivo with a 7 Tesla micro-MRI system at 3 and 5 months after surgery and 10 normal rabbits were used as control at both imaging time points. Macroscopic and histological MTCTh evaluations were compared to final MR measurements.

Results: OA gross macroscopic score was significantly higher ($p = 0.001$) in the OA rabbits than in the control group. A 3D-FLASH fat-suppressed MRI protocol was implemented leading to a 44 μ m³ isotropic spatial resolution. MTCTh varied longitudinally and differently depending on the measured area. The thinnest MTCTh was measured in the minimum interbone distance area. and was the most sensitive to change in the OA group. It correlated well with histological measurements ($p < 0.05$ and $r = 0.68$) and was significantly lower in OA rabbits than in control ($p < 0.0001$).

Conclusions: MTCTh obtained with a 7T micro MRI allowed longitudinal quantitative evaluation of MTCTh destruction in different areas in normal and diseased MTC. As the MTCT resulting from the semi-automatic measurement correlated positively well with histological results we concluded this MTCTh was sufficient to measure OA progression.

P231

Radiographic Atlas of the Individual Features of Osteoarthritis of the Knee Joint in the Rabbit Experimental Model

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Purpose: To create a radiographic atlas for grading knee joint osteoarthritis (OA) in the rabbit ACLT experimental model of OA and compare the radiographic and the macroscopic grades.

Methods and Materials: In vivo digital radiographs of the left knee of 10 control and 40 operated rabbits were performed at 5 months. Two blinded observers graded the osteophytes with a 4 grade scale for the medial femoro-tibial compartment and a 3 grade scale for the femoral trochlea. Joint space narrowing and subchondral cysts were graded with a 3 grade scale. Radiography and final macroscopy were compared.

Results: A "rabbit bed" was customised to standardize the extended postero-anterior radiographic view. A radiographic atlas of OA lesions was created and compiled in a power point presentation. Mean (SD) Radiographic scores Osteophytes JSN (0-2) Subchondral cysts (0-2) Medial FTC (0-3) Femoral trochlea (0-2) Medial Lateral Medial Lateral Control group N=10 0.3 (0.4) 0.7 (0.35) 0.4 (0.4) 0 (0) 0 (0) 0.1 (0.3) Operated group N= 40 1.8 (0.7) *** 1.2 (0.5) *** 1.2 (0.4) *** 0.9(0.7) *** 0.4 (0.6) *** 1.3 (0.8) *** **Significance level $p < 0.001$, Student's paired t test. All radiographic scores were significantly higher in the operated group compared to the control group ($p < 0.001$). Macroscopic and radiographic osteophytes grading were well correlated ($r = 0.64$, $p < 0.001$). JSN and meniscal lesions were correlated ($r = 0.68$, $p < 0.001$). Tibial cartilage lesions were correlated with JSN ($r = 0.58$, $p < 0.001$).

Conclusions: This radiographic atlas of OA individual features allowed non-invasive in vivo grading and was well correlated with final macroscopic evaluation.

P232

In vivo ultrasonography and meniscal injuries evaluation in the ACLT rabbit model of osteoarthritis

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Purpose: To develop a protocol for knee joint ultrasonography (US) of the Anterior Cruciate Ligament Transection (ACLT) rabbit model of osteoarthritis(OA); to evaluate the correlation between US and macroscopic medial and lateral meniscal injuries (MMI and LMI), depending on the age and weight when the ACLT is performed.

Methods and Materials: One group of skeletally mature White New Zealand Rabbits and one adolescent group were used for the study. Clinical examination, goniometry, in vivo US and final macroscopy were compared 5 months after ACLT. MMI and LMI were graded semi-quantitatively. Medial and lateral tibial cartilage damage was scored quantitatively with the EVA score (Visual Analogical Evaluation).

Results: The ACLT rabbit knee joint US protocol was standardized. ACLT could be directly or indirectly assessed with US. US detection of the transected ACL was 100% specific and 85.7% sensible. Normal and abnormal meniscal US appearances were described. US MMI were slightly higher (1.8 +/-0.6) than US LMI (1.5 +/-0.5). Positive correlation was found between US and macroscopic MMI ($p = 10^{-3}$, $r = 0.79$) and LMI ($p = 0.001$, $r = 0.63$). US MI predictive positive value was 92.3% and predictive negative value 81.25%, compared with macroscopy.

Conclusions: Significant relationships between macroscopic and US MI grading and between tibial cartilage lesions and MI were observed. US was relevant and effective in detecting meniscal lesions and we propose US as a non invasive, in vivo imaging technique for preclinical studies in the ACLT rabbit OA model. Further studies are needed to qualify US MI to provide similar US and arthroscopic or macroscopic MI grading scales