P157

Shock Wave Therapy Improves Cartilage & Subchondral Bone Repair

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Purpose: To determine if extracorporeal shock wave therapy (SWT) improves cartilage healing in an osteochondral defect rabbit model.
Methods and Materials: Two 3 mm diameter patellofemoral osteochondral defects were made bilaterally in 48 radult rabbits. Animals were assigned to groups: no treatment (NT), unilateral SWT-500 pulses and SWT-1500 pulses. SWT was administered immediately postoperatively in 33 animals and they were sacrificed on days 0 (n=3), 30 (n=15), and 90 (n=15). The remaining 15 rabbits received an additional SWT treatment on day 120 and were sacrificed on day 300. Outcome measures reported here include ICRS histological scoring, type II collagen immunostaining, creep indentation and biochemistry (sGAG) of cartilage as well as microCT.
Results: At 30 days matrix and cell type were improved in the SWT-1500 group and surface continuity was improved in the SWT-500 over NT controls (p=.05, Wilcoxon). By day 90 the SWT-1500 group had improved cell type (p=.06) and the SWT-500 group had improved cartilage sGAG (p=.05), cell viability, subchondral bone integrity (both p=.01), and subchondral bone mineral conentration (p=.05) . Cartilage healing was ongoing in the long term rabbits, but the SWT-500 group had better cell distribution and type, cell viability (p=.01), calcified cartilage restoration (p =.04). and subchondral bone mineral concentration (p=.01).
Conclusions: SWT has a dose dependant effect on cartilage repair and subchondral bone mineralization but additional investigations should be done to optimize timing, number of treatments and final outcome.

P158

Long-term evaluation of the resurfacing of large cartilage defects by a periosteal cell-based approach supported by BMP-2 gene transfer

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Purpose: To investigate the potential of transgene-activated periosteal cells for resurfacing large partial-thickness cartilage defects.
Methods and Materials: In miniature pigs, bone morphogenetic protein-2 (BMP-2) gene transfer using a combination of adeno-associated (AAV) and adenoviral (Ad) vectors was performed to stimulate autologous periosteal cells prior to loading the cells on a polyglycolic acid scaffold and application to chondral lesions comprising the entire medial half of the patella. The resulting repair tissue was analysed 6 and 26 weeks after transplantation by histochemical and immunohistochemical methods. The biomechanical properties of the repair tissue were characterized by nanoindentation measurements. Implants of unstimulated cells and untreated lesions served as controls.
Results: Six weeks after transplantation all grafts showed tight integration into the pre-existing cartilage. BMP-2-stimulated periosteal cells had adopted a chondrocyte-like phenotype in all layers. The newly formed repair tissue was rich in proteoglycans and type II collagen, and its contact stiffness was close to that of healthy hyaline cartilage. Unstimulated periosteal cells only formed fibrocartilaginous repair tissue with a reduced contact stiffness. However, 26 weeks following transplantation the AAV/Ad-stimulated cells in superficial layers tended to dedifferentiate into fibroblastic cells characterized by a switch from type II to type I collagen synthesis and reduced contact stiffness. In deeper zones, however, the cells retained their chondrocytic phenotype with type II collagen staining of the matrix.
Conclusions: Large partial-thickness cartilage defects can be resurfaced with hyaline-like cartilage formed by transgene-activated periosteal cells. Its long-term stability seems to depend on physico-biochemical factors provided only in deeper zones of cartilaginous tissue.

P159

A pilot study of tacrolimus (FK506) for cartilage repair

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Purpose: Tacrolimus is an immunosuppressant that can create chondroid differentiation in vitro and suppress collagen-induced arthritis in rats. Our hypothesis was that tacrolimus would improve the cartilaginous phenotype of repair tissue in acute chondral defects.
Methods and Materials: Full thickness, microfractured chondral defects (8mm) were made bilaterally in the trochlear ridge of 18 adult sheep.Three treatment groups were: no treatment (n=4), 0.03 mg/kg (n=7) and 0.1 mg/kg (n=7). Treated joints received intra-articular injections of FK506 every 14 days while the contralateral joints received 0.5% methylcellulose. Three animals in each treatment group were sacrificed at 90 days and the remaining sheep were sacrificed at 180 days postoperatively. Synovial fluid FK506 concentrations were measured to confirm delivery. India ink staining, O'Driscoll histology scoring, histomorphometry, sGAG concentration, and immunostaining for type II collagen were performed.
Results: At 90 days there was a trend for improved histology scores (12+5.1 versus 7.0+3.6 out of 29) and sGAG concentration (p<.06, T-test) in joints treated with 0.1 mg/kg. At the 180 day endpoint there were improved histological scores for the 0.03 mg/kg group over the no treatment group and contralateral joints (p<.03). Tissue fill, saffranin-O stained volume and collagen II immunostaining within the experimental defects was improved in the 0.03 mg/kg group over controls but the small group size eliminated statistical differences. Though chondral healing was improved it was incomplete in this challenging model.
Conclusions: This small pilot study indicates that FK506 can positively influence cartilage repair in microfractured full thickness lesions. Additional studies may help identify an optimized timeframe and dosing regime.

P160

Occurrence and patterns of meniscus damage following ACL transection

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Purpose: Evaluation of the frequency and pattern of meniscus damage following anterior cruciate ligament (ACL) transection
Methods and Materials: 32 NZW rabbits were used according to a protocol permitted by both, the Institutional and the Governmental Ethics Committee. All animals were male and skeletally mature as checked by standard x-ray. An open medial parapatellar approach was used of only the right knees. A complete transection of the ACL was achieved under full visualisation of the ligament. Postoperatively, rabbits were allowed full activity in their cages. At 2, 4, 8 and 12 weeks, 8 rabbits each were sacrificed. At dissection, the frequency and pattern of meniscus damage was recorded for both, medial and lateral menisci.
Results: The frequency of changes was 5/8 in the right knees at 2 weeks, 6/8 at 4 weeks, 7/8 at 8 weeks and 6/8 at 12 weeks. At 2 weeks, damages like meniscus oedema, fibrillations and minor tears of the posterior horn were observed. The tear sizes grew with time, also major fibrillations and meniscus dislocations occurred. At 8 and 12 weeks, damage to medial and lateral menisci was observed in the majority of knee joints.
Conclusions: Transection of the ACL leads to meniscus damage in rabbits, like after ACL rupture in human patients. Under full weight bearing, this meniscus damage begins very early. It seems to follow a typical pattern of increasing number and size with time. Our findings underline that damage secondary to ACL rupture is not restricted to just one (medial) compartment but is a secondary joint disease.