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Influence of stage of maturation of engineered cartilage on the outcome of osteochondral repair in a goat model

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Purpose: We investigated how the stage of development of engineered cartilaginous tissues influenced the repair outcome of large osteochondral defects in a goat model.

Methods and Materials: Engineered cartilage was generated from autologous articular chondrocytes cultured in Hyaff-11[\hat{a}] meshes (FAB) for 2 days, 2 weeks or 6 weeks and implanted on top of hydroxyapatite/Hyaff-11[\hat{a}] sponges into osteochondral defects. Experimental settings included defects that were untreated or treated with cell-free scaffolds. The repair was assessed histologically and biochemically 8 months post implantation.

Results: GAG and type II collagen contents in engineered tissues progressively increased with culture time. Implantation of the biomaterial into the subchondral compartment induced an extensive remodelling of the surrounding bone. No significant differences of GAG, type-I and -II collagen content between experimental groups were observed in the repair tissue overlying the subchondral part due to large experimental variability. Modified O'Driscoll scores indicated poor cartilage repair for untreated and cell-free treated groups (29.7 \pm 1.6, 24.3 \pm 5.8). Instead, in groups using cells, improvement in the cartilage repair process was noticed with the best scores observed for 2d and 2w preculture time (17.3 \pm 8.4, 16.3 \pm 5.8). Although the repair tissue was still fibrocartilaginous, an improvement in the architecture of surface and within the entire defect was noticed as compared to the 6w preculture time.

Conclusions: In this animal model, although the presence of precultured chondrocytes in the graft was of benefit, extensive maturation of engineered tissues did not enhance the outcome of cartilage repair.

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Meniscus loss during meniscectomy is correlated with clinical symptoms, function, and activity levels

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Purpose: No reports quantify amount of meniscus removed at meniscectomy and correlate loss with symptoms, function, and activity. We determined percent loss at partial meniscectomy and correlated loss with symptoms, function, and activity 2 years later.

Methods and Materials: 149 patients 18 to 60 years old underwent partial medial meniscectomy. Eighty-one patients had no prior meniscus surgery; 68 had 1 to 3 partial meniscectomies on involved meniscus. At index surgery, meniscus defect size was measured and percent meniscus loss calculated based on measurements. Patients were followed >2 years. At follow-ups, patients completed Lysholm and Tegner scores to assess function and activity. Meniscus remaining at index surgery was correlated with individual Lysholm scale domains. Tegner index was calculated to determine amount of lost activity regained after 2 years.

Results: Two-year data were available for 127 (85%) patients. There was significant correlation between meniscus amount remaining following index meniscectomy and 2-year Lysholm domains of squatting ($r=0.28$, $p=0.001$), stair-climbing ($r=0.25$, $p=0.004$), and swelling ($r=0.26$, $p=0.003$). Patients with >50% meniscus remaining had significantly better function than patients with <50%. Patients with worse/no improvement in pain symptoms at 2 years averaged 42% meniscus remaining; patients with improved pain averaged 51%. Tegner index for patients with <50% meniscus remaining averaged 24%; patients with >50% meniscus averaged 52% ($p=0.02$). More meniscus remaining allowed patients to regain significantly more of lost activity.

Conclusions: Amount of meniscus remaining after meniscectomy correlates significantly with symptoms, function, and activity after 2 years. We confirm importance of preserving the meniscus at meniscectomy to minimize symptoms of DJD.

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Induction of endostatin expression in mensical fibrochondrocyte by coculture with endothelial cells

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Purpose: The highest goal after meniscus damage is the preservation of the meniscus. Therefore, the goal of our investigations was the analysis of expression of different angiogenic factors, growth hormones and cytokines in human meniscus cells (fibrochondrocytes) to examine the molecular bases of the healing of meniscus tears in vascularized zones more exactly.

Methods and Materials: Cocultures of mensical fibrochondrocytes and HUVEC were analyzed for the expression of Angiopoietin-1, Angiopoietin-2, Endostatin, VEGF, SMAD-4, Thrombospondin-1, Aggrecan, Biglycan, Fibronectin, Vimentin, Connexin-43, IL-1 β , iNOS, MMP-1, MMP-3, MMP-13, collagen-I, -II, -III, -VI, X, and -XVIII by RT-PCR and immunohistochemistry. A proliferation assay was used to investigate the mitotic activity after 4 and 12 days.

Results: In presence of HUVEC, mensical fibrochondrocytes expressed the following factors at rates comparable to cells w/o HUVECS: Angiopoietin-1, Angiopoietin-2, VEGF, SMAD-4, Aggrecan, Biglycan, Fibronectin, Vimentin, Connexin-43, iNOS, MMP-1, MMP-3, MMP-13, Thrombospondin-1, collagen-I, -II, -III, -VI, X, and -XVIII. The expression of endostatin (5.1-fold \pm 1.2, $p<0.01$) and IL-1 β (10.3-fold \pm 2.3, $p<0.003$) were expressed significantly higher in the coculture and the proliferation rate of HUVEC was significantly decreased in coculture: 22 % after 7 days and 35 % after 14 days ($p<0.001$).

Conclusions: We could show that coculture of meniscus cells with endothelial cells revealed an increased expression of the anti-angiogenic factor endostatin and the pro-inflammatory IL-1 β . This suggests that meniscus cells are trying to inhibit proliferation of endothelial cells in their neighbourhood, which implicates huge problems in the research field of neoangiogenesis and tissue engineering in meniscus tissue.

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Collagen Meniscus Implant (CMI) - treated patients have increased activity levels after two years

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Purpose: We reported significant correlation between actual measured amounts of meniscus tissue removed at meniscectomy and symptoms, function and activity 2 years after surgery. Patients with >50% remaining meniscus were significantly better in all categories than patients with <50% remaining. We determined, prospectively, changes in Tegner scores from preoperative to 2 years postoperative in patients who received Collagen Meniscus Implants (CMI) and had >50% meniscus at 1-year relook.

Methods and Materials: In a Level of Evidence I clinical trial, 138 patients 18 to 60 years old underwent partial medial meniscectomy and placement of CMI. Sixty-four had no prior meniscus surgery and 74 had 1 to 3 prior partial meniscectomies. At index surgery, meniscus defect size was measured and percent meniscus loss calculated. Relook arthroscopy was performed at 1 year on 124 patients (90%), and percent meniscus (remnant + new tissue) was determined. Patients were followed >2 years after CMI placement. At follow-up, patients completed a Tegner activity score. We determined changes in Tegner from index surgery to 2 years F/U.

Results: 111 patients (90%) had >50% total meniscus tissue. Their average Tegner scores improved two levels from 3 to 5 over 2 years. This increased activity level significantly correlated with meniscus tissue >50% ($r=0.21$, $p=0.02$).

Conclusions: There is significant correlation between increase in Tegner scores over 2 years and percent meniscus tissue in CMI patients who have >50% meniscus. We confirmed importance of preserving as much meniscus as possible at time of repair or meniscectomy. Data support the potential positive benefits of regenerating meniscus tissue.