In-vivo Evaluation of a New Bioactive Ligament Prosthesis for Anterior Cruciate Ligament (ACL) Reconstruction.

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Introduction

Tissue engineering strategies based on the elaboration of cell-seeded scaffolds are currently evaluated for ACL reconstruction. Members of our group have shown that surface grafting by a bioactive polymer (sodium sulfonate polystyren (pNaSS)) of a non-degradable, polyethylene terephthalate (PET) device which is used for ACL reconstruction in clinical situations, optimizes the adhesion and the distribution of human and sheep fibroblasts in culture conditions (Ciobanu et al, 2006, Migonney et al. 2007). However, the impact of grafting on the intra-articular inflammatory response and on the biomechanical properties of the device has not been studied in vivo. The purpose of the present study was to evaluate a pNaSS grafted PET device in a sheep model of ruptured ACL. We hypothesized that grafting would optimize in vivo tissue ingrowth within the device and subsequently improve its mechanical behaviour without generating an adverse inflammatory response.

Materials and Methods.

29 two year old sheep (60kg) were obtained from a licensed vendor and reared in keeping with the guidelines published by the European Committee for Care and Use of Laboratory Animals. The excision of the proximal third of the ACL and subsequent intra-articular joint stabilization with a 44 strands PET artificial ligament (ultimate tensile stress = 2500 N) was performed in the left stifle of each sheep which received either a PET ligament (Group 1, n=14) or a polyNaSS grafted PET ligament (Group 2, n=15). The type of device implanted was randomly assigned. Devices were implanted according to the procedure described in human. Briefly, the device was placed intra-articularly through femoral and tibial tunnels drilled from inside-out, at the site of the femoral insertion and immediately behind the tibial insertion of the native ACL. Device fixation was provided with 6 mm titanium alloy interference screws. Animals were left free to ambulate without restriction for the whole length of the experiment. Orthopaedic examinations and synovial fluid collection and analysis were performed at monthly intervals until sacrifice, three months post-operatively. Specimens were then explanted and processed for either: (i) histology to assess under standard and polarized light microscopy tissue ingrowth, cellularity and presence of wear debris in the intra-articular portion of the device; (ii) Collagen I and III gene expression by RT-PCR and; (iii) biomechanical tests including loading to failure in tension.

Statistical analysis: Quantitative data were analyzed by performing a Mann-Whitney-test. The confidence interval was set at 95%, and the significance level at p<0.05.

Results and Discussion.

Functional recovery was excellent in all animals in which normal weight bearing was observed at all strides within 15 days of surgery.

Intra-articular inflammatory response. In both groups, cellularity and protein contents of collected synovial fluid increased during the first two postoperative months and decreased until sacrifice, 3 months postoperatively. At that time point, these parameters remained slightly above the normal physiologic values and were similar between groups (Figures 1 and 2). At the time of explantation, three months postoperatively, similar capsular hypertrophies were observed in sheep implanted with ungrafted and grafted devices. Inflammatory reactions were similar and no wear debris were seen. Grafting thus did not generate adverse inflammatory response.

Conclusions

Ligament modification by grafting polymerization did not generate superior inflammatory response compared to ungrafted ligaments in a sheep model of ACL rupture. More uniform tissue ingrowth and higher Collagen III/I expression ratios were found in grafted devices compared to ungrafted devices.

References

