Novel Biointegrative Cross-linked Degradable Polyurethane Scaffold for Cartilage Repair

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Introduction: Lesions in articular cartilage can cause considerable musculoskeletal morbidity. The primary arthroscopic treatment option for cartilage lesions is microfracture chondroplasty[1,2] [MFX] that involves the perforation of the subchondral plate 3 to 4 mm apart with an awl allowing blood perfusion and migration of resident marrow stromal cells into the cartilage defect to overcome inadequate repair caused by limited blood supply[3]. Limitations of MFX include uneven repair fill of defect site, a mixed quality of resultant tissue, and restriction in the clinical defect size < 2cm^2. It has been hypothesized that an appropriately designed degradable 3-D scaffold can overcome these issues; it needs to be press-fitted into the perforations, form a tight interface, allow for differentiation of marrow stem cells into articular chondrocytes by limiting the deposition of neocartilage, and provide substrate stiffness through the regeneration process that can be conducive in both early and terminal stem cell differentiation. Currently available synthetic resorbable thermoplastic polyesters and polyurethanes scaffolds suffer from non-optimized degradation rates, low interconnected porosity for tissue ingrowth at time of implantation, and slow elastic recovery and low resilience. Biological scaffolds such as collagen are costly and suffer from lack of 3-D structure, inadequate compressive stiffness, poor resilience, low permeability, fast degradation rates and risks of host immune system rejection. The long term efficacy for cartilage repair using both these types of scaffolds remains unsatisfactory. This purpose of this study was to evaluate whether a family of novel cross-linked, biointegrative, degradable elastomeric and resilient polyester urethane-urea scaffolds (PSPU-U) matrix scaffolds[4] consisting of fully interconnected and accessible open-cells with high void content (>95%) can be uses in conjunction with MFX for potential cartilage.

Methods: Both the short term low x-linked (~4 months) and long term moderate x-linked (~12 months) degrading PSPU-U scaffolds consisted of biostable diphenylmethane diisocyanate (MDI) derived hard segment (HS) and degradable 70:30 polycaprolactone (PCL):polyglycolic acid (PGA) copolymer polyol soft segment (SS). The 3-D scaffolds were made by a polymerization reaction between MDI and polyol in presence of cross-linkers and chain extenders, and a simultaneous blowing reaction between MDI and water that produces CO2 leading to an in situ cross-linked porous foam; it is followed by a controlled high temperature combustion reticulation process that converts the porous foam to an open cell matrix by removing the cell windows formed during the foaming process. The difference in degradation profiles, in spite of identical HS and SS, is attributed to the novel way of controlling the degradation through chain extension and cross-linking with additional advantage of using faster resorbing more resilient PGA in place of slower resorbing and bulkier PLLA (slows recovery) that would have normally been used for scaffolds > 4-6 months necessary for cartilage regeneration. Bilateral median parapatellar arthrotomies were made in 30 male Sprague-Dawley rats. A 1.5 mm osteochondral defect was treated with empty osteochondral defect (N = 30) as control, 2 mm OD 4-month degrading short term (N = 15) and 12-month degrading long term (N = 15) scaffold. They were sacrificed at 4, 8, and 16 weeks, cartilage defect and the histology (Safranin O/Fast green) were compared between implantation and control sites.

Results: At 4, 8, and 16 weeks the control knees exhibited only fibrous tissue ingrowth. For the short term scaffold group, at 4 weeks the resilient conformal scaffold interfaced tightly with the surrounding tissue, at 8 weeks, newly migrated chondrocytes were seen at the defect-subchondral bone interface and at 16 weeks, the defects show new subchondral bone formation with some scaffold degradation. Similar trends are observed for the long term scaffold except at 16 weeks, less cartilage repair and no evidence of degradation are observed compared to the short term scaffold although good bone repair is still observed. Defect measurements indicated that the sizes of cartilage defects were smaller in the implantation groups compared to the control groups. No evidence of any lymphocyte, giant cell, or macrophage foreign body response were detected in examined sample.

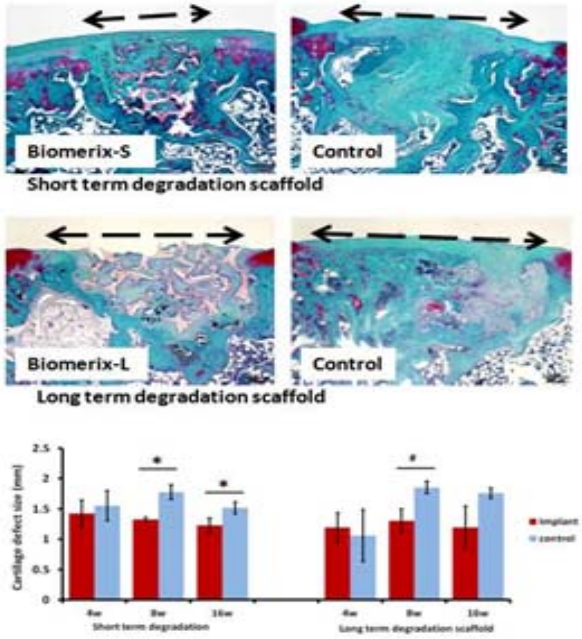

Fig 1: Histology and defect measurements at 16 weeks.

Conclusions: Both PSPU-U scaffolds support early migration of chondrocytes into articular cartilage defects. While both resulted in new subchondral bone formation, the short term scaffold exhibited better cartilage repair.

References:

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