Bioscaffolds for Meniscus Transplantation: An In Vivo Sheep Study

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Statement of Purpose: Meniscectomy is one of the most common procedures performed in orthopaedic surgery. Loss of meniscus function leads to increased joint degeneration. The gold standard treatment for symptomatic meniscus deficiency is allograft transplantation. Current meniscus transplants are associated with incomplete cellular incorporation, absence of cell proliferation, and microscopic immune response. The objective of this project is to develop a tissue engineering approach to recapitulate the native meniscus.

Our approach to overcoming the limitations of current allograft transplantation is to utilize a natural bioscaffold to mimic natural tissue architecture and mirror native biomechanical properties. In addition, we remove native cellular components to limit immunogenicity and increase porosity to facilitate cellular and vascular in-growth. Finally, we seed the scaffold with undifferentiated stem cells to allow for regionally specific differentiation. Our central hypothesis is that a cell seeded allograft based construct will recapitulate native meniscus structure and function better *in vivo* than allograft transplants.

Methods: Medial meniscus transplants were performed on skeletally mature ovine. Four types of transplants were used in this study. The first group (allograft) consisted of fresh frozen ovine allografts. The second group (scaffold) consisted of ovine menisci that were decellularized and chemically oxidized in peracetic acid and Triton-X100. The third group (3-day construct) consisted of scaffolds from group two seeded with bone marrow derived mesenchymal stem cells (BMMSC). The fourth group (3-week construct) consisted of scaffolds seeded for 3 weeks with BMMSC. Post surgery, animals were allowed normal activity for six months. The harvested joints were graded for meniscus transplant condition, tissue biointegration, and osteoarthritis.

Surgical Groups
• Group 1: Allograft (n=8)
• Group 2: Scaffold (n=8)
• Group 3: 3-Day Construct (n=6)
• Group 4: 3-Week Construct (n=7)

Results: Allograft transplants demonstrated incomplete healing, maintenance of gross allograft structure, 11.25±4.13 average osteoarthritis score, and 8.88±7.16 implant score. Scaffold and construct transplants demonstrated better healing to the native meniscal rim and better shape and position compared to allografts. Scaffolds had an average osteoarthritis score of 10.63±4.10 and an average implant score of 7.0±3.21. Three day constructs had an average osteoarthritis score of 6.67±2.94 and an average implant score of 8.0±5.69.

Three week constructs had an average osteoarthritis score of 8.00±1.73 and an average implant score of 5.86±1.21.
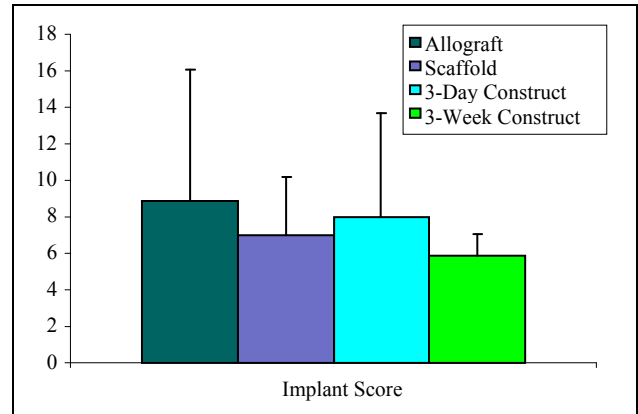

Figure 1: An implant score was assigned to each transplant based on rating 9 aspects of the tissue such as integration, position, presence of tears, etc. Each aspect was graded on a scale of 0-4 with 0 being the best score. No significant difference was found between the four groups; however there does appear to be a trend toward improved integration in both the scaffold and constructs compared to allograft.
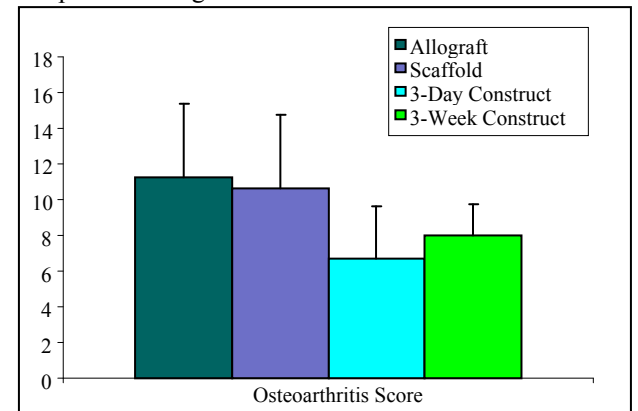

Figure 2: An osteoarthritis score was assigned to each implant based on rating 12 regions of the joint. Each region was graded on a scale of 0-4 with 0 being the best score. A significant difference was found between allografts and 3-day constructs (p=0.02) and between allografts and 3-week constructs (p=0.03).

Conclusions: Initial *in vivo* studies support biocompatibility and improved biointegration potential of decellularized allograft scaffolds for meniscus transplantation. Early findings support that scaffolds and constructs appear to integrate better, have better total implant scores, and better osteoarthritis scores than allografts at 6 months