INTRODUCTION:
Meniscectomy is one of the most common procedures performed in orthopaedic surgery. The meniscus plays a critical role in knee joint biomechanics. With loss of meniscus function there is an increased risk of arthritic changes in the knee. 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 an improved allograft scaffold for use as an alternative to fresh frozen allograft transplantation. Our approach to overcoming the limitations of current allograft transplantation is to utilize a natural bioscaffold to mimic natural tissue architecture and 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 provide an autologous cell source for meniscus tissue 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:
All studies were performed on skeletally mature sheep under an approved protocol from the Institutional Animal Care and Use Committee. Medial menisci from sheep were extirpated, decellularized, and oxidized to remove cellular and nuclear components. Thirty five sheep were divided into four groups and each animal underwent a medial meniscus transplant in the stifile joint. Autologous Bone marrow samples were taken from animals in groups 3 and 4. Bone marrow mesenchymal stem cells (EMMSC) were isolated and characterized using flow cytometry. Stem cell phenotype was characterized using positive markers vimentin and CD44 and negative markers von Willebrand Factor and CD45. Only cells that scored above 90% positive staining and below 10% negative staining were used. The third group (3-day construct, n=7) consisted of scaffolds from group two seeded with autologous BMSCs.

The first group (allograft, n=12) consisted of fresh frozen ovine allografts. The second group (scaffold, n=8) consisted of ovine menisci that were decellularized and chemically oxidized in 2.5% peracetic acid and 2% Triton-X100. The fourth group (3-week construct, n=8) consisted of scaffolds seeded for 3 weeks with autologous BMSCs.

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RESULTS:
All four groups maintained gross structure but showed incomplete healing in the posterior rim (Figure 1). Allograft transplants demonstrated a 10.58±1.14 average OA score (Figure 2), and 7.25±2.09 implant score (Figure 3). Scaffold and constructs demonstrated better healing to the native meniscal rim. Scaffolds had an average OA score of 10.63±1.45 (Figure 2) and an average implant score of 7.0±2.47 (Figure 3). 3-Day seeded constructs had an average OA score of 6.86±1.03 (Figure 2) and an average implant score of 7.71±2.92 (Figure 3). 3-Week seeded constructs had an average OA score of 8.00±0.57 (Figure 2) and an average implant score of 5.5±1.94 (Figure 3). No significant difference in the OA (p=0.07) or implant scores (p=0.81) was observed between the groups.

DISCUSSION:
Initial in vivo studies support biocompatibility and improved biointegration potential of decellularized allograft scaffolds for meniscus transplantation. Our findings support that scaffolds and constructs appear to integrate better than allografts. While no significant difference was observed between the groups with respect to implant score or OA score, this demonstrates that while the scaffolds do not perform better than allografts, they also do not perform worse than currently used allografts. These studies demonstrate the feasibility of using this approach to improve upon allograft meniscus transplantation.