INTRODUCTION:
Injuries to the meniscus remain a difficult challenge to the orthopaedic surgeon, particularly those located in the innermost avascular region. There are a number of different surgical procedures available that achieve stabilization of the defect, such as staples and arrows, but oftentimes, these do not result in the integrative and functional repair of the injury. The purpose of this study was to explore cell sources that could be harvested and used in the operating room in a reasonably rapid time frame. Synovial- and adipose-derived cells were deemed highly useful for the proposed application, and compared to meniscus cells as a benchmark standard. Several methods to deliver the cells that could be adapted for use by arthroscopic methods, including fibrillar scaffolds and hydrogels, were also evaluated. Furthermore, the effect of cell doubling in vitro was studied to determine whether these cell types would be stable in vivo for a longer period of time; thus, making them viable as expanded populations capable of multiple patient use. We hypothesized that the adjunct use of a scaffold would better retain the transplanted cells within the defect and serve as a network to more quickly immobilize recently-synthesized collagen.

METHODS:
Cell Isolation and Culture: Meniscus fibrochondrocyte cell lines derived from adult bovine knee joints were isolated and cultured for use in the experiment. The adipose- and synovial-derived cells were harvested from bovine knee joints, and the cells were enzymatically digested in vitro.

Scaffolds Utilized: In addition to cells alone, collagen gel, collagen scaffold, and hyaluronic acid were employed as cell delivery vehicles for this study. The collagen gel, after being prepared, was mixed with cells and pipetted directly into the meniscus defect and allowed to polymerize for ten minutes at 37°C. The collagen scaffold was seeded with cells just prior to its surgical implantation and inserted into the defect site.

Preparation of Meniscus Xenografts: In order to prepare the meniscus xenografts, additional menisci were harvested from bovine knee joints and cut into 1.5 cm segments. A bucket handle tear was made and either left empty (control), filled with one of the cell grafts described above, or filled with a cell biomaterial construct. The menisci defects were then xenografted subcutaneously onto the dorsum of athymic rats, and incubated in vivo for 3, 6, and 9 weeks, at which time the harvested tissue was prepared for histology.

RESULTS:
Control: At the time of necropsy, samples were harvested and examined macroscopically for evidence of healing. Following tissue retrieval, the control meniscus implants were bisected through the central region of the created tear, and characterized as containing a conspicuous gap in the central region of the defect with no healing observed. Histological evaluation confirmed no cells or integrative repair had taken place in any of the control specimens, and showed a lack of outward host cell migration from the meniscus in an attempt to heal the defect. Collagen scaffold material was observed in the gap in those specimens treated with this scaffold (Fig. 1A).

Experimental: The macroscopic examination of harvested menisci that received cell implants regardless of scaffold type all demonstrated closure of the lesion with varying degrees of new filling. The thickest tissue fill was observed in menisci that had received collagen implants. The thinnest fill were in menisci that were treated with cells alone (Fig. 1B, 1C). All menisci were prepared for histological examination and scored for the ability to bridge the defect gap with new tissue and synthesize collagen into the extracellular space. There was a general trend of better healing with time.

The localization of cells by fluorescence microscopy was observed in all experimental groups that received cell transplants. The number of cells did not decline with time, as the nine week group demonstrated highly positively-tagged cells still within the defect site. The cells in all groups remained localized within their respective defect or carrier material and did not migrate into the meniscus tissue.

The cells alone group (1), regardless of the cell of origin, resulted in generally superior repair compared to the addition of scaffolds. The group with the next highest rate of repair was collagen gel (2), followed by the use of collagen scaffold (3). The hyaluronic acid group (4) was the least effective of the scaffolds tested.

Comparing the cells with respect to the tissue of origin (Fig. 2), cells derived from the meniscus were able to repair defects faster and with more collagen than adipose- or synovium-derived cells. Adipose cells were the least effective in comparison. Synovial-derived cells demonstrated a mixed capacity for cell based repair.

DISCUSSION:
The meniscus is considered a vital tissue that imparts load-bearing properties and provides crucial joint stability to preserve joint biomechanics. Any loss or disruption of the meniscus may lead to irreversible degeneration of the articular cartilage. Injuries to the meniscus often do not heal well; most currently available treatments are less than ideal. Therefore, there is a need for novel methods to repair the meniscus and prevent the onset of degenerative changes.

This study evaluated several cell-based strategies for the repair of meniscus lesions. Our results demonstrate that the delivery of cells alone outperforms the additional use of biomaterials. This was surprising, since we hypothesized that the adjunct use of a scaffold would better retain the transplanted cells within the defect and serve as a network to more quickly immobilize recently-synthesized collagen. The opposite finding was observed; scaffold materials, depending upon the type of material, impaired the ability to biologically “weld” the defect sides.

Passage number also demonstrated a significant effect that became more apparent as a determining factor with later passages, suggesting that early passage cells more readily repair and integrate a meniscus defect than do late passage cells.

Based on successful findings in the literature with both autologous as well as allogeneic sources of cells, \(^1\) it is possible to envision a strategy that would be able to bank both meniscus and synovial cells for arthroscopic meniscal repair.

SIGNIFICANCE:
To our knowledge, this is the first study to evaluate and compare different combinations of cell types, tissue culture passage number, and biomaterial carriers for their effect on meniscus repair. Meniscus repair, especially in the avascular inner third, remains a significant challenge to the orthopaedic surgeon. Cell-based strategies that can be adopted for arthroscopic delivery are one potentially viable option.

REFERENCES: