Hydrogel Meniscal Replacement in the Sheep Knee

Preliminary Evaluation of Chondroprotective Effects

Bryan T. Kelly,*† MD, William Robertson,† Hollis G. Potter,† MD, Xiang-Hua Deng,† MD, A. Simon Turner,‡ MS, Stephen Lyman,† PhD, Russell F. Warren,† MD, and Scott A. Rodeo,† MD
From the †Hospital for Special Surgery, New York, New York, and ‡Colorado State University, Fort Collins, Colorado

Background: Meniscal allograft transplantation has become a viable surgical alternative for a select group of patients with deficient or irreparable menisci. Subjective results are encouraging; long-term success, durability, and safety of allograft meniscal transplantation are uncertain.

Purposes: To evaluate a novel hydrogel meniscal replacement implant in an ovine model and assess chondroprotective effects of this hydrogel meniscal replacement using several validated outcome measures.

Study Design: Controlled laboratory study.

Methods: Fourteen skeletally mature sheep underwent hydrogel meniscal replacement; 45 additional animals had previously undergone 1 of 3 operations: lateral meniscectomy (24), meniscal allograft transplant (17), and sham (4). Animals were sacrificed at 2, 4, or 12 months. Cartilage was assessed by magnetic resonance imaging, gross inspection, biomechanical testing, and semiquantitative histological analysis.

Results: There were no differences between the sham operation and nonoperated control limbs. Compared with meniscectomy, hydrogel meniscal replacement resulted in significantly decreased cartilage degeneration with all outcome parameters (P < .05). Compared with nonoperated control limbs, hydrogel meniscal replacements demonstrated no significant differences at 2 months in any category. By 4 months, hydrogel limbs demonstrated significantly greater cartilage degeneration than did nonoperated control limbs in all categories. Compared with meniscal allograft transplantation animals, hydrogel meniscal replacements demonstrated no differences at 2 months but had significantly increased cartilage degeneration in the peripheral zone of the tibial plateau at 4 months (P < .05). At 1 year, all hydrogel implants had developed complete radial splits in the posterior third of the implant.

Conclusion: Although promising preliminary results for hydrogel meniscal replacement were seen at early time points, significant cartilage degeneration and implant failure were seen at 1 year, and overall performance was worse than was allograft transplantation. Improvements in hydrogel material properties and surface characteristics and more accurate size matching may improve outcomes.

Clinical Relevance: Improvements in the hydrogel material properties and surface characteristics and more accurate size matching may lead to the use of hydrogel implants in humans.

Keywords: hydrogel; meniscus; replacement; cartilage

It is well established that the menisci play an important role in load transmission, lubrication, cartilage nutrition, and motion and stability of the knee joint.5,18,20,24 Partial or total meniscectomy can have many deleterious effects on articular cartilage, ultimately resulting in degenerative changes within the knee joint.24,31 Although meniscal repair has become an accepted and commonly practiced treatment for select meniscal injuries, conditions arise in which partial or even total meniscectomy is still necessary.26 In patients who have undergone meniscectomy or patients with irreparable meniscal damage, meniscal transplantation may alleviate the otherwise inevitable process of knee joint degeneration.

Meniscal transplantation has been performed in the United States for more than a decade with good to excellent
results with regard to pain and functional ability.9,26,31 Although encouraging, much of the outcome data following this procedure have been subjective and of limited follow-up. Uncertainty still exists with regard to the structural integrity of the articular cartilage and long-term functional outcome. Nevertheless, meniscal allograft transplantation is considered a viable surgical option for patients with symptomatic meniscal deficiency.

Despite moderately favorable short-term results with allograft meniscal transplantation, concerns surrounding the use of allograft tissue still remain. Potential problems associated with meniscal allograft implants include cost, availability, size matching, and the risk of disease transmission.26,29,30,35 These concerns have provided the impetus to develop synthetic meniscal implants.

Meniscal tissue is a biphasic material composed of a solid phase (about 26% of the total weight) and a fluid phase (about 74% of the total weight). The solid phase is a porous permeable structure with low permeability and consists mainly of collagen, proteoglycans, and other noncollagenous proteins. The fluid phase consists of water and interstitial electrolytes. When the tissue is compressed, fluid is forced through the solid matrix, but frictional drag is exerted on the fluid by the low permeability of the solid phase. The fluid becomes pressurized within the solid matrix and helps to resist the deformation being applied to the meniscus; that is, fluid pressurization helps to carry compressive load. Collagen is the major constituent of the solid phase and provides the tissue with its tensile properties. The distribution of collagen is inhomogeneous and anisotropic. At the articulating surface, there exists a fine meshwork of woven collagen fibrils.3 Approximately 100 µm from the surface layers are large, rope-like collagen fiber bundles that are arranged circumferentially.29 The core of the meniscus contains more randomly arranged smaller collagen fibers.30 The challenge in developing a synthetic meniscus, therefore, is to create an implant that can provide similar biomechanical function to that of the native meniscus yet reside safely within the knee joint. As inert structures with similar biomechanical properties, hydrogel meniscal implants may offer a solution to this problem.

Hydrogels are biocompatible materials that can be synthesized with a wide variety of mechanical and structural properties, providing them with characteristics similar to that of soft tissues. To date, their use has been largely limited to contact lenses and drug delivery, but they have been suggested as a possible solution toward designing more physiological load-bearing implants.17,21 Hydrogel menisci have proven to be very durable in small-animal models.14,15 By closely matching the regional variations of the native meniscus, hydrogels may provide a safe, long-lasting chondroprotective alternative to the meniscal allograft.

In phase 1 of this study, we developed a reproducible surgical technique for meniscal allograft transplantation in an ovine model.12 The chondroprotective effects of this technique were then assessed using several validated measures (india ink staining of the articular surface, MRI, biomechanical testing, and semiquantitative histological analysis). The purposes of this phase (phase 2) were to (1) develop a custom hydrogel-based meniscal replacement in an ovine model and (2) to assess the chondroprotective effects of this hydrogel meniscal replacement using several of these same validated outcome measures.

MATERIALS AND METHODS

After institutional animal care and use committee approval was obtained, 59 skeletally mature Columbian X Rambouillet ewes weighing approximately 70 to 80 kg were allocated for use. On arrival at the Colorado State University Veterinary Teaching Hospital, the sheep were placed in the large-animal research barn. They were dewormed and ear tagged for identification. Physical examination was performed, and only appropriate animals were selected for the study.

Study Groups

The animals were randomly assigned to 1 of 4 groups. Three groups (sham, lateral meniscectomy, and meniscal allograft transplantation) were previously reported in phase 112 of this study and provide comparison data for a fourth group, the hydrogel artificial meniscal replacement group. In phase 1, 4 animals underwent a sham operation involving exposure of the lateral joint with a release and repair of the lateral collateral ligament and popliteus tendon insertion. Twenty-four animals underwent a lateral meniscectomy after exposure of the lateral compartment. Seventeen animals underwent lateral meniscal allograft transplantation immediately after meniscectomy with size-matched donor menisci.

In phase 2 of this study, immediately after lateral meniscectomy, 14 additional animals underwent lateral meniscal transplantation with an artificial hydrogel meniscal implant (Salumedica, Inc, Atlanta, Ga). For the sham and the meniscectomy groups, half of the animals were sacrificed at 2 months, and the other half were sacrificed at 4 months. For the meniscal allograft transplantation group, 8 were sacrificed at 2 months, 8 were sacrificed at 4 months, and the final animal was sacrificed at 1 year. In the hydrogel replacement group, 7 animals were sacrificed at 2 months, 4 animals were sacrificed at 4 months, and the remaining 3 animals were sacrificed at 1 year.

Surgical Procedures

Based on ovine menisci previously obtained from comparably sized animals, synthetic hydrogel meniscal replacements were engineered. Two sizes of hydrogel implants were created to aid in size matching. Sutures were fashioned into the construct of the implants to re-create the anterior meniscotibial and posterior meniscofemoral attachments (Figure 1). Accurately fixing these sutures to the anatomical locations, as previously described,12 allows for re-creation of the normal posterior excursion of the meniscus that occurs with knee flexion in these animals. A lateral incision was made over the lateral collateral liga-
applied to the knee joint to fully expose the meniscus. The peripheral rim of the meniscus was dissected sharply from the capsule, dividing the coronary ligament. The anterior and posterior horn attachments of the meniscus were then detached, and the meniscus was removed from the knee. Special care was taken to avoid any articular cartilage damage during the lateral meniscectomy. The meniscotibial attachment site was exposed, and a drill tunnel was made entering at the anatomical insertion site and exiting the tibia on the medial side of the knee. The meniscofemoral attachment site was then palpated, and a second drill tunnel was made entering the anatomical insertion site on the posterior aspect of the medial femoral condyle and exiting the femur on the medial side of the knee. The prefashioned anterior and posterior sutures were then passed through the corresponding drill tunnels and fixed over buttons on the medial aspect of the knee, thus recreating the proper anatomical meniscal attachments for the hydrogel implant. To avoid overconstraint of the meniscus and to allow for its normal posterior excursion with knee flexion, the posterior horn was fixed first with the knee flexed. The anterior horn was then fixed with the knee in extension. Tracking and appropriate sizing of the meniscus were confirmed after fixation. The lateral collateral ligament was reattached to the femur using a 4.0-mm cancellous bone screw. The joint capsule, overlying fascia of the tensor fascia lata, subcutaneous tissues, and skin were closed in layers.

Postoperative Care

After surgery, postoperative activity was restricted for the first 2 weeks by housing the animals in closed confinement. The limbs were not immobilized.

POSTSACRIFICE ANALYSIS

Analysis of the sham, meniscectomy, and lateral meniscal allograft groups was previously reported.12 After sacrifice, the operative knees were detached at the level of the midfemur and midtibia. All of the limbs were immediately frozen and stored for analysis. The time between euthanasia and analysis of the frozen limbs was between 5 and 7 days. The frozen knees were thawed before analysis and then assessed sequentially by gross inspection with india ink staining, biomechanical testing of cartilage stiffness, and semiquantitative histologic analysis. Complete analysis of each limb was performed within a 24-hour period to avoid any potential degradative effects from exposure to air. The specimens were kept refrigerated between tests during that 24-hour period, and all tests were performed in a temperature-controlled laboratory set at 65°F. None of the tests resulted in heating of the tissue. The tissues were kept moist with normal saline during the testing. All limbs were treated with the same protocol, eliminating the potential for any significant differences due to prolonged exposure. The 3 limbs harvested at 1 year underwent MRI before the gross dissections to allow for additional analysis of the hydrogel implants before explantation.

Gross Inspection

All limbs were dissected, and the tibial plateaus were cleared of all surrounding soft tissues. The cartilage surfaces were stained with a dilute (1%) india ink solution (Higgins waterproof india ink), and all specimens were photographed for determination of gross evidence of cartilage degeneration as demonstrated by uptake of india ink stain. Mean stain areas overlying the tibial plateaus (milimeters squared) were measured using the Metamorph image analysis software program (Universal Imaging Corporation, Downington, Pa).

Biomechanical Testing

Cartilage stiffness was measured over the central weight-bearing zone of the lateral tibial plateau. The area tested represented the area of greatest wear in the postmeniscectomy knees.12 Three measurements were collected from 3 different locations along the central contact area of the tibia: anterior, central, and posterior. The location of these data points was the same in all specimens and was verified by dividing the central weightbearing zone into thirds and finding the center point of each section. The data points from each location were averaged. Stiffness was measured using a cartilage indentation probe specifically designed for thin cartilage (Artscan, Inc, Helsinki, Finland). The probe consisted of a measurement rod with a 100-µm-diameter indenter located in the center of a reference plate at the end of the probe. The value of the indenter force (newtons) reflects the force that the cartilage exerts against the indenter and can reliably be used as an index of cartilage stiffness. Several studies have demonstrated the association between cartilage degeneration and decreased cartilage stiffness.4,8,25,32

Histological Analysis

Histological sections were subsequently prepared and scored by an attending pathologist blinded to the procedure performed. The specimens were sectioned in the coronal plane at
the midpoint of the weightbearing zone of the tibial plateau. The osteochondral specimens were then fixed in 10% neutral buffered formalin (Sigma Diagnostics, St Louis, Mo) and then decalcified in 5% nitric acid. As soon as the decalcification was complete, the tissues were removed so as to avoid prolonged exposure to the nitric acid. Tissue processing and paraffin embedding were then performed using the Tissue Tek VIP1000 tissue processor. Five-micrometer-thick sections were cut and then stained with hematoxylin and eosin and safranin O. Histological slices were taken from the central third of the tibial plateau extending from the peripheral lateral margin to the central medial region of the intercondylar notch. This area was identified within a rectangular zone overlying the central region of the lateral plateau (Figure 2). The central zone corresponded to the area of greatest wear that was evaluated with the biomechanical testing.

The histological sections were graded using the modified Mankin grading scale for hyaline cartilage degeneration.22,33 This semiquantitative analysis assessed cartilage structure (0-6), cellular abnormalities (0-3), matrix staining (0-4), and tidemark integrity (0-1). A minimum score of 0 denotes no cartilage degeneration, and a maximum score of 14 indicates severe cartilage destruction. Regional differences between the central and peripheral zones were evaluated.

Polarized light microscopy was performed to further assess collagen organization within 4 layers of the matrix: superficial layer, transitional zone, radial zone, and calcified zone. The collagen was scored as organized (0) or disorganized (1) in each of these 4 zones, resulting in a score ranging between 0 and 4. Regional differences between the central and peripheral zones were also evaluated with polarized light analysis.

Magnetic Resonance Imaging

The 3 limbs harvested at 1 year underwent MRI before dissection and explantation of the hydrogel implants. These limbs were imaged in a clinical 1.5-T superconducting magnet (Signa Horizon LX, General Electric Medical Systems, Milwaukee, Wis) with a 5-in curved, receive-only linear shoulder coil (linear shoulder coil, IGC-Medical Advances, Milwaukee, Wis). The imaging used a fast spin echo sequence in the coronal and sagittal planes with a repetition time of 4200 to 5000 milliseconds, effective echo time of 17 milliseconds, 31.2-kHz receiver bandwidth, and field of view of 8 x 6 cm with a matrix of 512 x 384, yielding an in-plane resolution of 156 µm x 156 µm x 1-mm slice resolution. Images were obtained with 3 excitations. Tailored radiofrequency (GE Health Care, Milwaukee, Wis) was used to reduce interecho spacing, with echo train lengths ranging between 8 and 12.

The fast spin echo images were analyzed to assess morphologic changes in cartilage, bone, and bone marrow edema, as well as the presence or absence of osteophytes. The integrity of the hydrogel was also assessed with regard to signal characteristics, presence of tear, and healing to the tibial attachments.

Statistical Methods

Means and SDs were calculated for all measurements. The results obtained for the hydrogel meniscal implant group were compared with the control, meniscal allograft, and meniscectomy groups previously reported.12 Because of the small sample size and possibility of a nonnormal distribution, a Kruskal-Wallis analysis of variance rank test was used to identify differences between control, allograft, meniscectomy, and hydrogel groups. For the Kruskal-Wallis analysis of variance tests, a critical P value of .01 was used because of the multiple comparisons. Where a significant overall test result was obtained, a post hoc analysis was conducted using a Mann-Whitney test between each of the groups. A critical P value of .05 was used to identify statistical significance for these post hoc tests. All analyses were conducted using SPSS for Windows version 13.0 (SPSS Science Inc, Chicago, Ill).

RESULTS

General Findings

There were statistically significant differences (P < .01) between the hydrogel meniscal transplant limbs and the meniscectomy limbs in all outcome measures at both 2 months and 4 months after transplantation (gross inspection with india ink, biomechanical testing, and histological analysis) (Table 1). Although no significant differences were seen between the hydrogel and intact control groups at 2 months, the hydrogel group exhibited significantly worse results (P < .001) with regard to gross inspection, cartilage stiffness, and histological grading compared with controls at 4-month follow-up (Table 1). In comparing the hydrogel replacements to the meniscal allograft transplants, there were no significant differences at 2 months after surgery (Table 1). At 4 months, however, the hydrogels demonstrated significantly more peripheral wear with both the modified Mankin scores as well as the polarized light scores (Figure 3).
Gross Inspection

The nonoperated control limbs demonstrated minimal staining over the lateral plateau at 4 months. At 2 months after transplantation, the hydrogel group demonstrated minimal staining over the lateral plateau (averaging 3.76 ± 9.96 mm²), appearing grossly similar to the control limbs (Figure 4). At 4 months after hydrogel implantation, there was significantly increased stain consistent with mild cartilage degeneration (averaging 20.7 ± 9.22 mm²). This increased india ink staining was most pronounced at the peripheral edge of the lateral tibial plateau, representing the area underlying the hydrogel meniscus (Figure 5). Despite this finding, on gross inspection the articular cartilage in the hydrogel-implanted limbs was objectively better (P < .001) than that of the postmeniscectomy limbs at both 2 months and 4 months.

Three of the hydrogel specimens demonstrated incomplete, small radial tears in the posterior one third of the implant at 2 months. This was thought to be related to intraoperative trimming of the implant before implantation. None of the remaining nonmanipulated 2-month hydrogel implants or any of the 4-month implants showed evidence of deformation or breakage. There was no evidence of infection or graft dislocation at 2 months, 4 months, or 1 year. The meniscal implants remained well fixed in all specimens at 1 year; however, a complete radial tear was seen in the posterior aspect of all 3 implants at 1 year (Figure 6).

Biomechanical Testing

At 2-month follow-up, the stiffness of the articular cartilage in the hydrogel limbs was not significantly different from that of the control limbs, but they were both significantly stiffer (P < .001) than was the cartilage seen after meniscectomy. At 4 months after transplantation, the cartilage stiffness had

TABLE 1

Summary of Outcome Measures for Control, Allograft, Meniscectomy, and Hydrogel Animals

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Allograft</th>
<th>Meniscectomy</th>
<th>Hydrogel</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects</td>
<td>12</td>
<td>9</td>
<td>12</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mankin central^b,c</td>
<td>0.25 ± 0.45</td>
<td>0.33 ± 1.00</td>
<td>7.25 ± 1.55</td>
<td>0.57 ± 0.79</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mankin peripheral</td>
<td>3.78 ± 1.09</td>
<td>4.43 ± 1.99</td>
<td></td>
<td></td>
<td>.298</td>
</tr>
<tr>
<td>Polar central^b</td>
<td>0.00 ± 0.00</td>
<td>0.00 ± 0.00</td>
<td>2.17 ± 0.84</td>
<td>0.29 ± 0.49</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Polar peripheral</td>
<td>1.33 ± 0.50</td>
<td>1.00 ± 0.82</td>
<td></td>
<td></td>
<td>.144</td>
</tr>
<tr>
<td>Biomechanics^b</td>
<td>0.63 ± 0.08</td>
<td>0.64 ± 0.11</td>
<td>0.37 ± 0.13</td>
<td>0.63 ± 0.15</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>India ink^b</td>
<td>2.98 ± 6.24</td>
<td>6.01 ± 7.36</td>
<td>36.06 ± 9.94</td>
<td>3.76 ± 9.96</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects</td>
<td>12</td>
<td>7</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Mankin central^b,c,e</td>
<td>0.67 ± 0.89</td>
<td>0.71 ± 0.95</td>
<td>11.33 ± 1.61</td>
<td>3.00 ± 2.71</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mankin peripheral</td>
<td>3.86 ± 1.68</td>
<td>8.50 ± 2.52</td>
<td></td>
<td></td>
<td>.010</td>
</tr>
<tr>
<td>Polar central^e</td>
<td>0.00 ± 0.00</td>
<td>0.86 ± 0.69</td>
<td>3.50 ± 0.80</td>
<td>0.75 ± 0.96</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Polar peripheral</td>
<td>1.29 ± 0.49</td>
<td>2.75 ± 0.96</td>
<td></td>
<td></td>
<td>.015</td>
</tr>
<tr>
<td>Biomechanics^b,c,e</td>
<td>0.64 ± 0.09</td>
<td>0.43 ± 0.06</td>
<td>0.25 ± 0.08</td>
<td>0.44 ± 0.02</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>India ink^b,c,e</td>
<td>2.75 ± 7.04</td>
<td>17.64 ± 5.51</td>
<td>46.68 ± 12.98</td>
<td>20.73 ± 9.22</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

^aMeans and standard deviations of control animals, allograft transplantation animals, postmeniscectomy animals, and hydrogel-replacement animals of outcome measures evaluating the tibial plateaus at 2 months and 4 months after surgery. Modified Mankin scores are between 0 and 14; polarized light scores are between 0 and 4; biomechanical data are reported in newtons (N); india ink values are reported in millimeters squared. Significant differences were set at P < .05.

^bMeniscectomy group significantly different from control, allograft, and hydrogel groups (P < .01).

^cHydrogel group significantly different from control group (P < .01).

^dAllograft group significantly different from hydrogel group (P < .01).

^eAllograft group significantly different from control group (P < .01).

Figure 3. Comparison of histology scores in the peripheral zone between the allograft and hydrogel animals at both 2 and 4 months.
significantly decreased compared with controls. The cartilage of the hydrogel group was significantly stiffer (0.44 ± 0.02 N) than that of postmeniscectomy limbs (0.25 ± 0.08 N) and nearly identical to the allograft transplant group (0.43 ± 0.06 N) at 4 months (Table 1).

Histological Analysis: Hematoxylin and Eosin

Histology specimens were cut in the coronal plane and extended from the periphery of the tibial plateau to the central (intercondylar notch) region at the midpoint of the tibial plateau. Normal articular cartilage was seen in all nonoperated controls. The peripheral zone underlying the native meniscus showed no appreciable histological changes in the control group. There was no significant histological difference between the hydrogel group and controls at 2 months, but by 4 months, there were significant changes in the central and peripheral areas (Table 1).

Histological analysis of the hydrogel-implanted limbs showed increased peripheral cartilage wear at 4 months. Interestingly, the control and postmeniscectomy groups demonstrated a central wear pattern, with relative sparing of the periphery. At 2 months, the peripheral zones of the hydrogel meniscal group and the allograft meniscal group were histologically similar. At 4 months after transplantation, however, the histological grade (Mankin score) of the peripheral cartilage in the hydrogel group was significantly worse than the peripheral cartilage underlying the allograft menisci (P = .01) (Figure 7). Characteristic histological findings included disorganization of cartilage structure, hypocellularity, reduced matrix staining, and loss of tidemark integrity.
Histological Analysis: Polarized Light

Polarized light microscopy was used to further evaluate the collagen organization. The control animals demonstrated normal cartilage with polarized light analysis, which was reflected by maintenance of collagen organization within the 4 layers of the matrix (superficial layer, transitional zone, radial zone, and calcified zone; polarized light score of 0). The collagen organization in the central tibial plateau in the hydrogel limbs did not differ significantly from the control limbs at 2 months or 4 months ($P < .001$). The peripheral cartilage was not significantly different between the hydrogel and allograft meniscal groups at 2 months;

Figure 6. A, complete radial tear of the hydrogel implant in the posterior one third of the meniscus was seen in all 3 implants taken out to 1 year. B, an explanted implant clearly demonstrates the location of the radial split.

Figure 7. Hematoxylin and eosin histological sections from the peripheral zones of the 4-month allograft meniscus (A) compared with the 4-month hydrogel meniscus (B). Significantly worse histological grades were seen in the peripheral zone of the hydrogels compared to the allograft and control animals.
however, at 4 months the collagen organization underlying these implants was significantly worse after hydrogel meniscal implantation ($P = .015$). These histological differences in the peripheral zone (by both Mankin score and polarization) seen at 4 months suggest that the hydrogel meniscus caused more abrasive wear than did an allograft meniscus with repeated cycling of the knee.

**Magnetic Resonance Imaging**

Magnetic resonance imaging demonstrated that the hydrogels were of intermediate signal intensity, indicating more mobility of water, in contrast to the marked signal hypointensity of the native menisci. Distracted radial splits were discernable in the posterior horn body junctions (Figure 8). There was consistent subchondral bony remodeling over the hydrogels because of the prominent thickness (compared with the native menisci), seen to best advantage over the body segment in the coronal plane (Figure 9). Relative preservation of cartilage was noted in the central margin of the joint, approaching the intercondylar notch, compared with the marked wear of cartilage over the peripheral margin of the knee. Osteophyte formation was most conspicuous at the peripheral margin and absent from the central margin at the intercondylar notch.

**DISCUSSION**

The meniscus is a biphasic material composed of a solid phase (approximately 25% of its total weight) and a fluid phase (approximately 75% of the total weight). The solid phase is a porous permeable structure that acts in concert with the fluid phase to both resist deformation and help transmit joint loads. The material properties of a meniscal allograft may be adversely affected by graft processing, surgical manipulation, cellular repopulation and revascularization, and graft remodeling.

Hydrogels are biocompatible materials that are also biphasic in nature with load-rate–dependent mechanical properties that make them ideal candidate materials for synthetic meniscal replacement. Kobayashi et al reported on the use of hydrogel menisci in a small-animal model. Using both gross and histological parameters, they compared lateral meniscal transplantation using a hydrogel implant versus lateral meniscectomy in 19 rabbits with a 2-year follow-up. They found slight macroscopic and microscopic changes in the articular cartilage in the early stages (4 and 6 months). However, the hydrogel meniscal group showed little progression of cartilage degeneration, by both gross and histological examination, at 1- and 2-year follow-up. Conversely, the meniscectomy group exhibited severe cartilage wear and osteophyte formation at 1 year. The hydrogel implants demonstrated good wear characteristics (no breakage, shrinkage, dislocation, or deformation) and no evidence of infection or immune-mediated response.

In this study, we were successful in developing a synthetic hydrogel meniscal implant for use in a large-animal ovine model. Excluding the 3 hydrogel menisci that were trimmed intraoperatively, the implants showed no evidence of deformation or fatigue-related failure at 2 or 4 months. There was no evidence of infection or graft dislocation at 2 months, 4 months, or 1 year. The implant design allowed for anatomical reconstruction of the native meniscal anterior and posterior attachment sites. The meniscal implants remained well fixed in all specimens at 1 year. Although short-term durability of the hydrogel implant was excellent at 4 months, a radial tear was seen posteriorly in all 3 implants at 1-year follow-up. We hypothesize that the source of the graft failure may be owing to size mismatch, inadequate peripheral fixation of the hydrogel implant, or the structural composition of these particular implants.

Although it has been estimated that meniscal graft size should be within 5% of the native meniscus, the knee's tolerance for meniscal size mismatch has not yet been determined. Because of the preliminary nature of this study,
the hydrogel meniscal implants used were available in only 2 sizes, limiting our ability to provide a precise size match. One possible cause of graft failure may have been the use of a slightly undersized hydrogel meniscus. The use of a meniscal implant that is smaller than its native counterpart but anatomically attached at both its anterior and posterior horns may result in abnormal meniscal kinematics during repetitive cycling of the knee. The implant may have become entrapped beneath the lateral femoral condyle, subjecting it to excessive shear forces, and over time resulted in radial tearing of the posterior margin. Further studies are required to determine the tolerance of the knee to meniscal size mismatch and to understand how sizing affects the kinematics and function of a meniscal replacement device.

Another possible source of graft failure at 1 year may have been inadequate peripheral fixation of the hydrogel meniscus. Kobayashi et al.13,15 peripherally secured their rabbit menisci with sutures. Although they found no peripheral ingrowth, the menisci remained attached to the capsule rabbit menisci with sutures. Although they found no peripheral capsular attachment is needed to augment the short to intermediate term, the long-term results are still compared with normal knees. A further concern that was evident on both gross and histological inspection of the hydrogel-implanted knees was increased wear in the peripheral zone of the tibial plateau underlying the meniscus. Sham, control, and postmeniscectomy knees showed a rather consistent pattern of central cartilage wear, with sparing of the periphery. Although the allograft meniscal-transplanted limbs exhibited earlier peripheral wear, the changes seen in this area after hydrogel meniscal transplantation were significantly worse. This may have been caused by abrasive wear of the articular cartilage by the undersurface of the hydrogel meniscus. Excessive meniscal motion and texture of the hydrogel undersurface may have further contributed to this problem. In developing future implants, this issue will need to be addressed. Future studies will consider the use of an inhomogeneous and anisotropic hydrogel design, whose regional variation in tensile and compressive properties matches that of the native sheep meniscus. This variation in meniscal design may provide (1) a more durable meniscal implant, (2) a less abrasive meniscal undersurface, and (3) improved ability for peripheral tissue ingrowth. These modifications could lead to a longer lasting hydrogel meniscal implant with improved chondroprotective characteristics.

ACKNOWLEDGMENT

Research assistance from Peter Torzilli, Manjula Bansal, and Li Foong Foo. This research was supported by grants from the American Orthopaedic Society for Sports Medicine Young Investigator’s Award, National Football League Charities, and Aircast Foundation.

REFERENCES


