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DOI: 10.1177/0363546515595065

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OnlineFirst Version of Record - Aug 21, 2015

What is This?
Successful Total Meniscus Reconstruction Using a Novel Fiber-Reinforced Scaffold

A 16- and 32-Week Study in an Ovine Model

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Background: Meniscus injuries in the United States result in an estimated 850,000 surgical procedures each year. Although meniscectomies are the most commonly performed orthopaedic surgery, little advancement has been made in meniscus replacement and regeneration, and there is currently no total meniscus replacement device approved by the Food and Drug Administration.

Hypothesis: A novel fiber-reinforced meniscus scaffold can be used as a functional total meniscus replacement.

Study Design: Controlled laboratory study.

Methods: A tyrosine-derived, polymer fiber–reinforced collagen sponge meniscus scaffold was evaluated mechanically (tensile and compressive testing) and histologically after 16 and 32 weeks of implantation in an ovine total meniscectomy model (N = 20; 16 implants plus 4 meniscectomies, divided equally over the 2 time periods). The extent of cartilage damage was also measured on tibial plateaus by use of toluidine blue surface staining and on femoral condyles by use of Mankin scores on histological slides.

Results: Scaffolds induced formation of neo meniscus tissue that remained intact and functional, with breaking loads approximating 250 N at both 16 and 32 weeks compared with 552 N for native menisci. Tensile stiffness values (99 and 74 N/mm at 16 and 32 weeks, respectively) were also comparable with those of the native meniscus (147 N/mm). The compressive modulus of the neo meniscus tissue (0.33 MPa at both 16 and 32 weeks) was significantly increased compared with unimplanted (time 0) scaffolds (0.15 MPa). There was histological evidence of extensive tissue ingrowth and extracellular matrix deposition, with immunohistochemical evidence of types I and II collagen. Based on significantly decreased surface damage scores as well as Mankin scores, the scaffold implants provided greater protection of articular cartilage compared with the untreated total meniscectomy.

Conclusion: This novel fiber-reinforced meniscus scaffold can act as a functional meniscus replacement, with mechanical properties similar to those of the native meniscus, while protecting the articular cartilage of the knee from the extensive damage after a total meniscectomy.

Clinical Relevance: This meniscus replacement scaffold has the potential to improve surgical treatment and provide better long-term outcomes for those suffering from severe meniscus damage.

Keywords: meniscus; implant; scaffold; regeneration

Meniscus injuries result in an estimated 850,000 surgical procedures each year in the United States.18 While meniscectomies do provide symptomatic relief, they often lead to negative long-term outcomes, including osteoarthritis,4 and there is currently no total meniscus replacement device approved by the Food and Drug Administration. This tissue is critical to healthy joint function, and its removal (both partial and total) has been repeatedly correlated with detrimental effects to the surrounding cartilage.11,15,31 The C-shaped fibrocartilaginous menisci of the knee provide protection to the articular surfaces by transmitting loads through the joint, distributing high peak stresses on the underlying surfaces, providing shock absorption, and aiding in joint lubrication.2,26 The wedge-shaped cross-sectional profile and the primarily circumferentially oriented collagen fibers allow the tissue to convert axial compressive loads into circumferential tensile loads, reducing potentially damaging stresses on the articular cartilage.

Unfortunately, treatment options for patients suffering from significant meniscus damage are limited and thus far
have not shown long-term protection of the underlying cartilage. One option currently being explored is the use of tissue-engineered scaffolds for the replacement of damaged menisci. While several implants composed of various synthetic and natural biomaterials have been tested, they have had very limited success.\(^{13,23,29,45,46}\) These implants were primarily amorphous structures that lacked the structural properties to take over the load-bearing role that is required of the meniscus. Another option, allograft replacement, provides good short-term symptomatic relief, but its long-term results are not fully understood and may be inadequate.\(^{36}\) Aside from the debate over patient eligibility criteria, there remain the issues of disease transmission, size matching, healthy donor availability, postimplantation graft shrinkage, and poor graft remodeling.\(^{12}\)

Our laboratory is developing a novel biomechanically functional scaffold based on the microstructure of the normal meniscus. The scaffolds are composed of a type I collagen and hyaluronic acid sponge reinforced with a unique pattern of continuous tyrosine-derived, biodegradable polymer fiber. The scaffolds have previously been shown to possess structural properties appropriate for meniscus replacement, and they convert a portion of an applied axial compressive load to circumferential tensile loads measured at their anterior and posterior horn attachments.\(^{9}\) This fiber-reinforced structure provides a theoretical advantage over other meniscus scaffolds that are amorphous structures unable to effectively transfer compressive loads to tensile loads. The novel implant design is patented (US Patent No. US8623085 B2)\(^{19}\) and has been licensed for product development (Meniscofix, Novopedics Inc).

In this study, the first in vivo evaluation of the fiber-reinforced meniscus scaffold design was performed in an ovine model. We hypothesized that the meniscus scaffolds (1) would remain intact and functional and would preserve their size and shape, (2) would become more resistive to compressive loads after implantation, (3) would maintain sufficient tensile loads over time after implantation, (4) would promote cellular ingrowth and new tissue deposition, (5) would allow infiltrating cells to produce collagens type I and II in native locations/organization, and (6) would have a protective effect on the articular surface of knee compared with the untreated meniscectomies.

### METHODS

Scaffolds were implanted at the site of a total medial meniscectomy in an ovine model and were biomechanically and histologically evaluated after 16 and 32 weeks.

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One or more of the authors has declared the following potential conflict of interest or source of funding: Research was funded by the Armed Forces Institute for Regenerative Medicine (AFIRM I, Grant W81XWH-08-2-0034) and the New Jersey Center for Biomaterials–Center for Military Biomaterials Research (CeMBR, Grant W81XWH042003). Neither funding agency played a role in the investigation. C.J.G. is on the board of directors of, is interim president of, and owns stock in NovoPedics Inc, a startup company developing the meniscus implant for potential future commercialization. M.G.D. is interim secretary of and owns stock in NovoPedics Inc. Neither receive any salary from the company. C.J.G. and M.G.D. are inventors on 2 United States patents, and A.R.M. is an inventor on 1 United States patent for the meniscus implant described in the manuscript.

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Articular cartilage was also evaluated grossly and histologically. The ovine model was selected based on shape, size, and structural similarities between the ovine and human meniscus.\(^{12}\)

**Scaffold Fabrication**

As previously described, scaffolds were composed of 2% (wt/vol) acid-insoluble bovine tendon collagen (Worthington Biochemical Corp) with 1.25% (wt/wt) hyaluronic acid (HA) (H5388; Sigma-Aldrich) and a quasi-wound single filament polymer fiber (-100 \(\mu\)m diameter) composed of poly(desamino-tryosyl-tyrosine dodecyl ester dodecanoate)(12,10) (pDTD DD); New Jersey Center for Biomaterials).\(^{9}\) These scaffolds included extended tails for surgical fixation and radial tie fibers and were fabricated, crosslinked by 1-ethyl-3-(3-dimethyl aminopropyl)carbodiimide (EDC), and gamma sterilized as previously reported\(^{9}\) (Figure 1).

**Implantation**

Total medial meniscectomies were performed on the right limb of 20 sheep for evaluation at 2 time points, 16 and 32 weeks. Sixteen of these sheep had their meniscus replaced with the fiber-reinforced scaffold (n = 8 per time point; 4 samples for histological evaluation, 4 for mechanical testing), leaving 2 untreated total meniscectomies per time point. All surgeries were performed at the Rutgers–Robert Wood Johnson Medical School Vivarium using a protocol approved by the Institutional Animal Care and Use Committee (IACUC)

An endotracheally anesthetized sheep was placed in a supine position; the surgical extremity was prepared and draped by use of sterile technique. A vertical incision was created on the medial side of the joint, and a medial...
parapatellar arthrotomy was used to expose the knee joint. The anterior and posterior horns of the medial meniscus were transected, leaving a small stump for tunnel placement. An aiming guide was used to place a guide wire from the anteromedial tibial cortex to the anatomical location of the medial meniscus posterior horn attachment. A 6-mm-diameter bone tunnel was created with a cannulated reamer. The anterior tunnel was made with a similar approach but in an antegrade fashion from the anatomical anterior attachment exiting on the anterolateral tibia.

After a 20-minute soak in sterile saline, the posterior and anterior horn and tail of the scaffold were passed through the corresponding tunnels with a suture passer. The graft was pulled to appropriate tension, ensuring the scaffold was confluent with the rim of the tibial plateau. The extended horns were passed completely through the bone tunnels, where they were fixed in the tibia by use of cannulated titanium interference screws (7 × 25 mm, 8-mm heads; Smith & Nephew). The superior and inferior surfaces of the implant were sutured to the joint capsule with 2.0 Vicryl (Ethicon) interrupted vertical mattress sutures. The joint was irrigated, hemostasis was ensured, and the incision was closed in layers.

The sheep were then returned to their cages and allowed unlimited movement. Once the animals had achieved normal gait movement and had no signs of infection (typically 2-3 weeks postoperatively), they were transferred to an IACUC-approved sheep farm for unrestricted movement and exercise. All animals were euthanized at their appropriate time points, 16 or 32 weeks, and explants and articular surfaces were recovered and photographed. At each time period, explants were divided into 2 groups: 4 samples for mechanical testing and 4 for histological evaluation.

Confined Compression Testing

The explanted scaffolds were soaked in saline before testing. A 4-mm tissue punch was used to collect plugs from the anterior, body, and posterior portions of the explants, and the proximal side was trimmed to reach a height of 4 mm. The plugs were then loaded into a custom-made jig, with an approach similar to that used by Armstrong and Mow.6

A total of 24 experimental samples (4 explants × 3 locations × 2 time points) and 12 native meniscus samples (4 menisci × 3 locations) were tested in compressive creep (Instron material testing system model 5542 with a 100-N load cell and BlueHill software). A smooth and rapid load of 1 N was applied to the sample and held for at least 3600 seconds, and the aggregate modulus and permeability were calculated using the Mow biphasic theory.34,39

Uniaxial Tensile Testing

Four explanted scaffolds per time point and 4 native ovine medial menisci were soaked in saline before testing. Samples were loaded into cryogenic freeze clamps (Bose ElectroForce Systems), where the clamps held the posterior and anterior regions of the sample, leaving a 10-mm gauge length for testing in the approximate circumferential direction, as demonstrated by Newman et al.35 The samples were then pulled at a rate of 10 mm/min by use of an Instron materials testing system (model 5569) with a 10-kN load cell until failure.

Histological Testing (Explant)

Immediately after excision, explants for histological examination were divided into anterior, body, and posterior cross sections, exposing their wedge-shaped profile, and then fixed in 10% Carson buffered formalin. After paraffin embedding, 8-μm-thick cross sections were cut and stained with either hematoxylin and eosin (H&E) or Masson trichrome (AML Laboratory). Slides were evaluated blindly for the extent and type of tissue ingrowth.

Immunohistochemical Testing (Explant)

Immunofluorescence staining was used to identify collagen type I and II content in the explants. After sacrifice, anterior, body, and posterior cross sections (in the same manner as those prepared for histological evaluation) of the meniscus scaffold and contralateral medial meniscus were harvested, embedded in OCT compound (Tissue-Tek; Sakura), and frozen in liquid nitrogen. Subsequently, 8-μm-thick sections were fixed and incubated in their respective primary and then secondary antibodies (type I collagen primary antibody diluted 1:300 [AB745; Millipore], type II collagen primary antibody diluted 1:200 [Ab34712; Abcam Inc]; secondary antibody AlexaFluor 594 diluted 1:1000 [Invitrogen]). Sections were then treated with ProLong Gold Antifade Reagent with DAPI (Invitrogen), and images were then taken with a Zeiss Observer.D1 microscope with an X-Cite series 120Q light source (Lumen Dynamics Group Inc) and a ProgRes MF scan camera (Jenoptik; software: ProgRes CapturePro 2.8).

Femoral Articular Surface: Histological Evaluation

To determine the extent of articular cartilage damage on the medial femoral condyle, histological analysis was performed on all 20 ovine joint surfaces. The medial aspect of the ovine knee was sectioned according to the International Cartilage Repair Society (ICRS) mapping scheme.48 The sections were sent to AML Laboratory for decalcification and slide preparation. Slides were stained with safranin O and fast green dye and graded blindly according to the Mankin scoring system.37,38

Tibial Articular Surface: Image Analysis

Knee joints were excised, cleaned of soft tissue, and photographed perpendicular to the tibial surface. The plateau was then stained with 0.4% (wt/vol) toluidine blue so that degenerative wear that had disturbed the normally smooth and impermeable surface became macroscopically visible (adapted from Aagaard et al11). A photograph was taken of each stained articular surface. The images were then converted to black and white and analyzed using a custom-designed MatLab program (MathWorks Inc) to...
determine the percentage area of degenerative changes, based on area of the black (toluidine blue–stained) region above the background threshold. A quantitative analysis of the surface area damage was then performed on all samples.

Statistical Analysis

Data were analyzed statistically with a 1-way analysis of variance (ANOVA) and multiple pairwise comparisons determined using the Student-Newman-Keuls method. P values <.05 were considered statistically significant. Calculations were performed using Sigma-Stat software (Systat Software Inc).

RESULTS

Gross Observations

All explanted scaffolds were successfully recovered and were found fully intact, with no ruptures or fixation failures. At the 16-week time point, 2 of the 8 explants had a thinning of the body inner margin while the remainder had excellent appearances. After 32 weeks, 3 of the 8 explants had this same thinning, which was exacerbated by mild extrusion of the explant from the joint. Even so, all explants at all time points had tissue infiltration and fiber preservation at the anterior and posterior sections. Figure 2 shows the tissue infiltration of the explants and
their resemblance to the size and shape of the native meniscus.

There was little visible damage to the cartilage surfaces of the implanted knees at either time point (Figure 2). In sharp contrast, the cartilage of the meniscectomized knees was consistently and badly damaged.

Confined Compression Testing

Confined compressive creep showed that the explants were 25% to 40% as stiff in compression as the native meniscus (Figure 3A). The 32-week explants were significantly stiffer than the time zero (nonimplanted) scaffolds ($P = 3.0 \times 10^{-5}$). No significant differences were discovered between regions of the scaffolds (anterior, body, or posterior). The permeability of the scaffolds became greatly reduced after implantation, with values approaching those of the native structure (Figure 3B).

Uniaxial Tensile Testing

The ultimate tensile load of the explants at both 16 and 32 weeks was found to be approximately half that of the native medial menisci (Figure 4A). By 32 weeks, the tensile stiffness of the explants was significantly different from that of the native menisci and time zero scaffolds ($P = .008$) (Figure 4B).

Histological Testing (Explant)

Excellent tissue adherence and incorporation was observed, both grossly (Figure 2) and histologically (Figures 5 and 6) within all explants, forming neomeniscus tissue. Staining with Masson trichrome showed no remaining bovine collagen within the explant at 16 and 32 weeks. Lymphocytes were mostly found within the areas formerly occupied by the collagen scaffold, while multinucleated giant (MNG) cells were sometimes found around the polymer fibers. Cell density data were determined by ranking cellularity of slides from 1 (low) to 4 (high); the results were not significantly different for anterior, body, and posterior sections at both 16 and 32 weeks. There was a general trend of a reduction of polymer fiber and MNG cells from 16 to 32 weeks.

Vascularization was found throughout the explants at both time points, unlike the native meniscus, which is primarily vascularized in the outer one-third. There was significantly more tissue organization from 16 to 32 weeks, with the most organized tissue being found in the posterior section of the explant with fewer fibers, fewer inflammatory cells, and less vasculature.

Immunohistochemical Testing (Explant)

All explants and native meniscus expressed fluorescence when exposed to wavelengths of 594 nm for collagen types I and II (Figures 7 and 8), while negative controls showed
little to no expression. Strong expression of type I collagen was found throughout the explants at both time points and within the native meniscus. In the explants near the inner margin, type II collagen was expressed in similar amounts and locations as the native meniscus (Figure 8). Type II collagen was also found in the body of the explant, with a slight increase in amount and organization from 16 to 32 weeks. Some areas of the 32-week explants expressed similar structures as seen in the native meniscus (Figure 7, bottom row/center). Collagen organization tended to be more pronounced in areas of the explants that had fewer fibers.

Cartilage Damage Based on Histological Testing and Surface Staining

Representative photographs of histological sections of femoral condyles and surface-stained tibial plateaus from each group are shown in Figure 9. Differences in the appearances of the groups are clearly evident. The data confirming these differences (Mankin scores for the femoral condyle and the percentage surface area damaged on the tibia) are shown in Figure 10. For both variables, and at both time points, the values were significantly lower (less cartilage damage) for the scaffold-implanted knees compared with untreated meniscectomies.

For the femoral condyle, damage to the articular surface was exclusively found in the central/central and central/posterior sections as defined by the ICRS mapping scheme. Thus, the following results focus on these sections.

Figure 9 shows micrographs of safranin O– and fast green–stained cartilage sections from the medial femoral condyles of implanted knees and meniscectomies. In the native knee, the surface of the cartilage was relatively smooth and continuous, with an even arrangement of cells throughout the cartilage. The native knees also retained all of the red safranin stain and had an undisrupted tidemark. In the meniscectomized knees, there was moderate

Figure 5. Entire cross-section of a 32-week explant stained with hematoxylin and eosin. The white void spaces represent polymer fibers; pink represents new collagen deposition. This is from the center of the device; the distance from the inner to outer margin is approximately 10 mm, and the height approximately 5 mm, similar to the dimensions of the native ovine meniscus.

Figure 6. (A) Sixteen-week explant; (B) 32-week explant. White void spaces represent polymer fibers (F), pink depicts new collagen deposition, white arrows depict cells, black arrows depict blood vessels. (C) Native meniscus with sparser cellularity. Hematoxylin and eosin stain; magnification 40×; bars = 100 μm.

Figure 7. Immunofluorescence staining of type I collagen, inner margin (top row) and center (bottom row). Shown are a 16-week explant (left), a 32-week explant (center), and a native meniscus (right). Magnification 100×; bar = 100 μm.

Figure 8. Immunofluorescence staining of type II collagen, inner margin (top row) and center (bottom row). Shown are a 16-week explant (left), a 32-week explant (center), and a native meniscus (right). Magnification 100×; bar = 100 μm.
to severe surface damage, hypocellularity, substantial loss of safranin stain, and disruption of the tidemark in both the posterior and central portions at both time points. One meniscectomized joint had severe damage down to the subchondral bone.

The scaffold-implanted knees at both time points received significantly better Mankin scores than their respective meniscectomized groups in the posterior and central locations (Figure 10). As there was little to no damage in the anterior locations, these same differences were not noted at that location. At both time points for the implanted joints, there was slight surface cartilage disruption confined to the outer one-third or less of the cartilage surface, starting at the central section and tapering off to the posterior section. This damage occasionally led to a slight loss of cellularity near the surface and a slight reduction of safranin stain, but it did not affect the tidemark. There were no statistically significant differences between the Mankin scores at the 2 time points of the implanted joints, suggesting that any slight damage did not get worse over time. The central/central section, as defined by the ICRS, of the implanted femurs had significantly more structural irregularities than any other location.

Based on quantitative analysis of toluidine blue surface staining, the percentage area damaged on the tibia was about 5% for the implanted knees compared with about 20% for the meniscectomized knees (Figure 10). Collectively, the gross observations, the histological Mankin scores, and the percentage area damaged of tibial plateaus consistently showed that meniscectomized knees had more severe articular cartilage damage than those treated with the meniscus scaffold implant.

**DISCUSSION**

The purpose of this study was to investigate the mechanical and histological properties of a novel fiber-reinforced scaffold after implantation as a full meniscus replacement in an in vivo model. To our knowledge, this is the first study to examine the performance of a total meniscus replacement scaffold with substantial continuous fiber reinforcement with rigid anchoring in bone tunnels. Through 32 weeks after implantation, the scaffolds remained intact and functional and their size and shape were preserved, supporting our first hypothesis.

Our second hypothesis, that the scaffolds would become more resistive to compressive loads after implantation, was supported by the data. Confined compressive creep showed that the explants were about 2 times stiffer at 16 and 32 weeks than the unimplanted (time zero) scaffold. This
suggestions tissue ingrowth and perhaps remodeling in response to mechanical stimulation, creating neomeniscus tissue that can resist the loads that it experiences.

Comparison of in vivo compressive properties to other meniscus replacements was difficult, as most investigators did not report these values.5-6 Heijkants et al39 did report an unconfined compressive modulus of 0.012 MPa, at 20% compression, after 24 weeks of implantation. However, it is difficult to compare our modulus to this because we used a different testing method—confined compression.

To our knowledge, no one has reported permeability values of implanted meniscus replacements. Thus, our comparison is limited to reports of native structures. Martin Seitz et al32 used confined compressive creep and determined that human meniscus had a permeability of 8.0039 mm²/N·s, and Joshi et al32 found that the ovine meniscus value was 0.0019 mm²/N·s. We observed an average permeability higher than these values for all samples tested: 0.041 mm²/N·s at 16 weeks, 0.035 mm²/N·s at 32 weeks, and 0.015 mm²/N·s for the native ovine meniscus. Differences in values may have occurred from the testing procedure or the mathematical model used to calculate the permeability. In either case, our implanted scaffold had an 87.7% decrease in permeability from time zero to 8 months after implantation, a positive result, perhaps due to the tissue infiltration into the device. Compression of the implant from weightbearing is another potential cause of decreased permeability.

As anticipated, there was a reduction in ultimate tensile load as well as stiffness of the fiber-reinforced scaffold after implantation, due to polymer fiber degradation. The fact that we saw little change in tensile properties from 16 to 32 weeks suggests either that the fiber degradation had stopped or, more likely, that the neomeniscus tissue was beginning to organize and take over the load that the fibers could no longer bear in their degrading state. Even so, at the currently evaluated time points, the meniscus scaffold bears loads above the normal functional tensile load of the native meniscus, supporting our third hypothesis that scaffolds would promote cellular ingrowth and new tissue deposition, as also proven true. We observed cellular ingrowth and tissue deposition that persisted through both time points. The cellular response to the scaffold followed the expected progression, with a primarily lymphocytic reaction between the fibers (where the collagen matrix had degraded) and MNG cell reaction to the polymer fiber that decreased as the fibers began to degrade.5 We also observed fibrochondrocyte-like cells within the explants at both time points.

Cellular reactions to implanted meniscus replacements varied widely between investigators. Unsurprisingly, those using synthetic sponges had a much stronger MNG cell response and encapsulation of the polymer, with fewer lymphocytes found in the implants.13,29,46,47 While we saw a slight decrease in the quantity of MNG cells from 16 to 32 weeks, Tienen et al17 observed a significant increase in the number of giant cells from 3 to 6 months. The larger amount of degrading polymer in their device may cause a cellular cascade, resulting in this strong encapsulation response. Those using collagen scaffolds showed a stronger lymphocytic response.4,44 Collagen degradation has been shown to have a strong chemotactic effect, eliciting more cells as it breaks down. As the original collagen matrix is resorbed, there is less reactive material and the cellular response decreases. We expect that as the polymer fibers continue to degrade, the neomeniscus tissue will be exposed to more mechanical stimulation and will develop and organize in response. Longer time points will help to clarify the extent to which the neomeniscus tissue will remodel.

Remodeling of meniscus replacements is a widely controversial topic. Some investigators report excellent production of fibrocartilaginous tissue,7,21,24 while others report abnormal tissue deposition.16,33 Even when there is excellent tissue incorporation, investigators still frequently report negative changes to the cellularity28,39 and biochemistry of the joint.17 This creates difficulty in making comparisons between devices. In addition, most devices, aside from allografts, were never designed to accommodate tensile loads, and thus tissue remodeling is usually limited to a compressive response. Reguzzoni et al41 evaluated the collagen meniscus implant (CMI) and found that the gluteraldehyde crosslinking of the collagen sponge greatly reduced its ability to degrade, to the extent that it persisted even after 6 months. This likely extended the inflammatory response, causing detrimental effects to the joint. Our device used EDC crosslinking, and we noted that all of the original implanted collagen was degraded by 16 weeks.

Our fifth hypothesis was that infiltrating cells would produce appropriate proteins in native locations and organization. To determine the types of collagens being synthesized and deposited, immunofluorescence staining was used to identify collagen I and II expression within the explanted scaffold. The meniscus is predominantly made of fibrillar protein: collagens I and II.2 As such, it was important that we observed large amounts of both of these proteins within the explants. Although the entire explant expressed type I collagen, we did not see many dense clusters or signs of organization. By 32 weeks, type II collagen was found in dense amounts in the inner margin and surface of the explant, similar to the native meniscus. At this time point we also observed sections of organized collagen II within the interior of the explant that were comparable in appearance to the native meniscus. The data support the hypothesis that infiltrating cells would produce meniscus appropriate proteins.

Other investigators also reported the presence of type I and type II collagen in implanted meniscus scaffolds.23,27 Using a synthetic sponge in a rabbit model, Kang et al23 saw both collagen I and II in amounts similar to those in the native rabbit meniscus. Klompmaker et al27 investigated a polyurethane sponge replacement in a dog model and detected more collagen II than collagen I.

The final hypothesis was that the scaffold would have a protective effect on the articular surface of the knee compared with the untreated meniscectomies. Gross observations and data from surface staining of tibial plateaus
were consistent with this hypothesis. Furthermore, staining with safranin O and fast green allowed us to use the scoring system developed by Mankin, which comprehensively analyzes the structural, cellular, proteoglycan, and tidemark changes associated with cartilage damage.37,38 Compared with the untreated meniscectomies, both 16- and 32-week implanted femoral condyles had significantly better structural, cellular, proteoglycan, and tidemark scores. Kelly et al35 performed total meniscectomies at similar time points as our study (8 and 16 weeks); Mankin scores increased from 7.25 to 11.33 (out of 14), indicating progressive cartilage damage. Kon et al30 evaluated the effect of total meniscectomies in 6 sheep after 12 months. Joint gross assessment was used in their study, and subchondral bone was exposed in 6 of 6 animals. In our study, untreated meniscectomies had scores of 12 (16 weeks) and 10 (32 weeks), while implanted joints had scores of 3.7 (16 weeks) and 3.1 (32 weeks). As hypothesized, the meniscus scaffolds had a protective effect on the articular surface of knee compared with the untreated meniscectomies.

In contrast, most investigators implanting allografts, collagen devices, or synthetic devices observed little to no protective effects of the implants on the articular surfaces.13,17,21,28,29,40,46,47 The CMI had inconclusive chondroprotective effects.10 The evaluation of a polymer sponge scaffold by Tienen et al47 showed highly variable cartilage health throughout their study and found no protective effect after 2 years.

Limitations

The nature of our fiber design does not allow for tensile testing of dumbbell sections. Thus, we used a method used by both Newman et al35 and Balint et al25 that allows for testing of full menisci, scaffolds, and explants in tension. Although this method uses an abnormal length to width ratio, it is the only feasible way of determining the structural tensile properties of these structures.

We used a small group of untreated meniscectomies (n = 2) because our previous unpublished studies (Balint8) as well as those of other investigators (Kelly et al25 and Kon et al30) demonstrated significant cartilage degeneration after total meniscectomy. While this lowers the power of our statistical comparisons, it would have been unethical to use more sheep to further demonstrate what has been established in the literature, especially considering this is a feasibility study. Furthermore, the efficacy of this implant will ultimately be compared with that of a clinical standard of care—for example, a partial meniscectomy or a meniscus allograft—and not just an untreated total meniscectomy.

CONCLUSION

Designing a mechanically functional meniscus device is not a trivial undertaking. As proven by so many investigators, it is extremely difficult to create a meniscus replacement that can properly protect the articular cartilage of the joint. Fabricating the correct dimensions, mechanical properties, and biological properties coupled with proper degradation rate and tissue remodeling is challenging. In addition, scaffold placement, fixation, movement, and deformation can further impede this development. In this study, we were able to demonstrate that a fiber-reinforced meniscus scaffold could act as a functional meniscus replacement and have a protective effect on the articular surfaces of the knee through 32 weeks of implantation. Based on these promising results, longer implantation time points will be evaluated in the ovine model, and a scaffold with the corresponding size and shape of the human meniscus will be developed and tested.

ACKNOWLEDGMENT

The authors thank the Rutgers-RWJMS Orthopaedic Research Laboratory, the vivarium staff, and especially Barbara Perry for their assistance with the surgeries and postoperative care. They also thank Rita Hahn and Marion Gordon, from the Ernest Mario School of Pharmacy, Rutgers–Robert Wood Johnson Medical School, for their support and assistance with immunohistochemistry.

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