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Original Research

Rabbit Trochlear Model of Osteochondral Allograft Transplantation

Nhat To,[1] Shane Curtiss,[1] Corey P Neu,[3] Christopher J Salgado,[4] and Amir A Jamali[2,*]

Allografting and autografting of osteochondral tissues is a promising strategy to treat articular cartilage lesions in damaged joints. We developed a new model of fresh osteochondral allografting using the entire rabbit trochlea. The objective of the current study was to demonstrate that this model would achieve reproducible graft–host healing and maintain normal articular cartilage histologic, immunolocalization, and biochemical characteristics after transplantation under diverse storage and transplantation conditions. New Zealand white (n = 8) and Dutch belted (n = 8) rabbits underwent a 2-stage transplantation operation using osteochondral grafts that had been stored for 2 or 4 wk. Trochlear grafts harvested from the left knee were transplanted to the right knee as either autografts or allografts. Grafts were fixed with 22-gauge steel wire or 3-0 nylon suture. Rabbits were euthanized for evaluation at 1, 2, 4, 6, and 12 wk after transplantation. All grafts that remained in vivo for at least 4 wk demonstrated 100% interface healing by microCT. Trabecular bridging was present at the host–graft interface starting at 2 wk after transplantation, with no significant difference in cartilage histology between the various groups. The combined histology scores indicated minimal evidence of osteoarthritis. Immunostaining revealed that superficial zone protein was localized at the surface of all transplants. The rabbit trochlear model met our criteria for a successful model in regard to the ease of the procedure, low rate of surgical complications, relatively large articular cartilage surface area, and amount of host–graft bone interface available for analysis.

Abbreviations: DB, Dutch belted; NZW, New Zealand white; SZP, superficial zone protein.

The limited healing potential of mature articular cartilage in response to mechanical injury is widely recognized.[31] Due to its avascular nature, superficial lesions of articular cartilage fail to undergo the entire sequential 3 phases of healing response—necrosis, inflammation, and repair—that normally occur in injured vascularized tissue.[31] The inflammatory phase, mainly mediated through the vasculature, is almost entirely absent in superficial articular cartilage lesions, limiting the inflow of healing factors needed to mount an effective repair response.[4,8,12,31] Deep articular cartilage lesions with subchondral bone involvement can elicit a complete healing response when exposed to mesenchymal progenitors from the bone marrow.[11] However, the repair tissue generated from this type of injury is a mixture of fibrocartilage and hyaline cartilage that may undergo degeneration over time.[13,31,33] The healing potential of articular cartilage is complicated further depending on the amount of marrow involvement, age, the stability of the joint, the size of the injury, and the use of continuous passive motion.[5,17,34,43,49,53]

A number of intervention strategies have been proposed to treat articular cartilage injuries.[48] With a clinical history of over a century, fresh osteochondral allografting remains the only technique that restores mature hyaline cartilage and mimics normal joint biology.[15,29] Since the 1990s, the clinical use of allografts for biologic joint resurfacing has increased in the United States as these products have become more widely available through tissue bank distribution to meet increases in patient and physician demand for alternatives to prosthetic joint replacement and restoration.[15]

The use of allografts has presented a variety of unanswered questions regarding graft storage conditions, the immunoprivileged status of these tissues, and graft incorporation. The most pressing of these issues is optimizing storage conditions to maximize the cell viability of grafts. Much of this work has involved human grafts in vitro.[6,7,37,40,44] Further questions regarding fresh osteochondral allografts remain, including the presumed immunoprivileged status of these transplants and the mechanisms by which these grafts avoid immune surveillance by the host. The site at which allografts fail can involve either the host–graft bone interface or the articular cartilage surface secondary to chondrocyte death and surface degeneration.

Current animal models used in the study of osteochondral allograft transplantation have several limitations. Osteochondral transplantation rabbit models using osteochondral plugs and the press–fit method are known for incomplete host–graft incorporation and provide a small surface area for analysis.[10] Large animal models such as horses, sheep, and dogs offer a thicker articular cartilage layer; however, these animals require special facilities and are costly to maintain.[14,21,23,45,46]

An in vivo model for fresh osteochondral allografting is thus required that mirrors the clinical challenges associated with the

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[1]Department of Orthopaedic Surgery, University of California, Davis, Medical Center and [2]Joint Preservation Institute, Sacramento, California; [3]Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana; [4]Department of Plastic Surgery, University of Miami Miller School of Medicine, Miami, Florida.
[*]Corresponding author. Email: contactus@jointpreservationinstitute.com

Table 1. Summary of experimental parameters

				Storage				Histology			
Rabbit no.	Recipient	Donor	Category	Time (wk)	Solution	Fixation method	Time in vivo (wk)	Grade	Stage	Score[a]	CT score
1	DB	NZ	Allograft	2	DMEM + 10% FBS	Wire	2	2.50	3.17	7.92	100% healed
2	DB	NZ	Allograft	2	DMEM + 10% FBS	Wire	4	1.83	2.67	4.89	100% healed
3	DB	NZ	Allograft	2	DMEM + 10% FBS	Wire	6	0.17	0.67	0.11	100% healed
4	DB	DB	Same strain allograft	2	DMEM + 10% FBS	Wire	6	1.33	2.33	3.11	100% healed
5	DB	NZ	Allograft	4	DMEM	Nylon suture	12	0.00	0.00	0.00	100% healed
6	DB	NZ	Allograft	4	DMEM	Nylon suture	2	0.00	0.00	0.00	Visible interface
7	DB	NZ	Allograft	4	LR	Nylon suture	1	0.50	1.67	0.83	Visible interface
8	DB	DB	Same strain allograft	4	LR	Nylon suture	6	0.17	0.67	0.11	100% healed
9	NZ	NZ	Autograft	2	DMEM + 10% FBS	Wire	6	1.33	2.33	3.11	100% healed
10	NZ	DB	Allograft	2	DMEM + 10% FBS	Wire	6	2.17	2.17	4.69	100% healed
11	NZ	DB	Allograft	2	DMEM + 10% FBS	Wire	4	0.17	0.67	0.11	100% healed
12	NZ	DB	Allograft	2	DMEM + 10% FBS	Wire	2	4.17	3.83	15.97	Visible interface
13	NZ	NZ	Autograft	4	DMEM	Nylon suture	6	0.33	0.50	0.17	100% healed
14	NZ	DB	Allograft	4	DMEM	Nylon suture	12	4.00	3.67	14.67	100% healed
15	NZ	DB	Allograft	4	LR	Nylon suture	6	3.33	2.33	7.78	100% healed
16	NZ	DB	Allograft	4	LR	Nylon suture	12	2.17	2.67	5.78	100% healed

DMEM, Dulbecco Modified Eagle Medium, LR, lactated Ringers solution
Complications occurred in rabbits 7 (fell out of cage) and 12 (fractured spine).
[a]Grade × scale

procedure and is more biologically relevant than in vitro experiments performed on osteochondral plugs. Preferably, the ideal in vivo model would be in a small, inexpensive animal yet provide a large surface area for sampling. Because restricting weight-bearing in animals is problematic, such a model would maintain success despite unrestricted weight bearing. Further, the new model would require the minimal amount of metallic hardware to facilitate imaging. Finally, this model would address both modes of failure that occur in fresh allografts: the host–graft bone interface and the articular cartilage layer. The models described in the current literature fulfill these requirements to various degrees.

Here, we developed a model involving transplantation of the entire rabbit trochlea. The model allows for histologic analysis of the articular cartilage and host–graft incorporation. The objective of the study was to demonstrate the feasibility of the rabbit trochlear transplantation model, specifically that this model would demonstrate reproducible graft–host healing and maintain normal articular cartilage histologic, immunolocalization, and biochemical assays after transplantation under diverse storage and transplant conditions.

Materials and Methods

Surgical procedure. Animal care and use were in strict compliance with federal regulations as stated in the Animal Welfare Act.[1] The IACUC granted approval for this investigation prior to its initiation. Surgical, perioperative, housing, sanitation, husbandry, and veterinary care followed the recommendations of the *Guide for the Care and Use of Laboratory Animals*.[2] Animal care personnel were qualified based on previous animal research experience as well as certification.

Female New Zealand white (NZW) rabbits (n = 8; age, 2 to 5 mo; weight, 1.8 to 2.3 kg) and male Dutch Belted (DB) male rabbits (n = 8; age, 4 to 7 mo; weight, 3.0 to 5.0 kg) underwent a 2-stage operation with an intervening storage period. During the first stage, rabbits were anesthetized through intramuscular injection of ketamine (35 mg/kg), butorphanol (0.02 mg/kg), and xylazine (5 mg/kg) and received infection prophylaxis (5 mg/kg IM; Baytril, Bayer Animal Health, Shawnee, KS). The left leg was clipped, prepped with povidone–iodine, and draped. A 4-cm, medial parapatellar arthrotomy was performed. The patella was

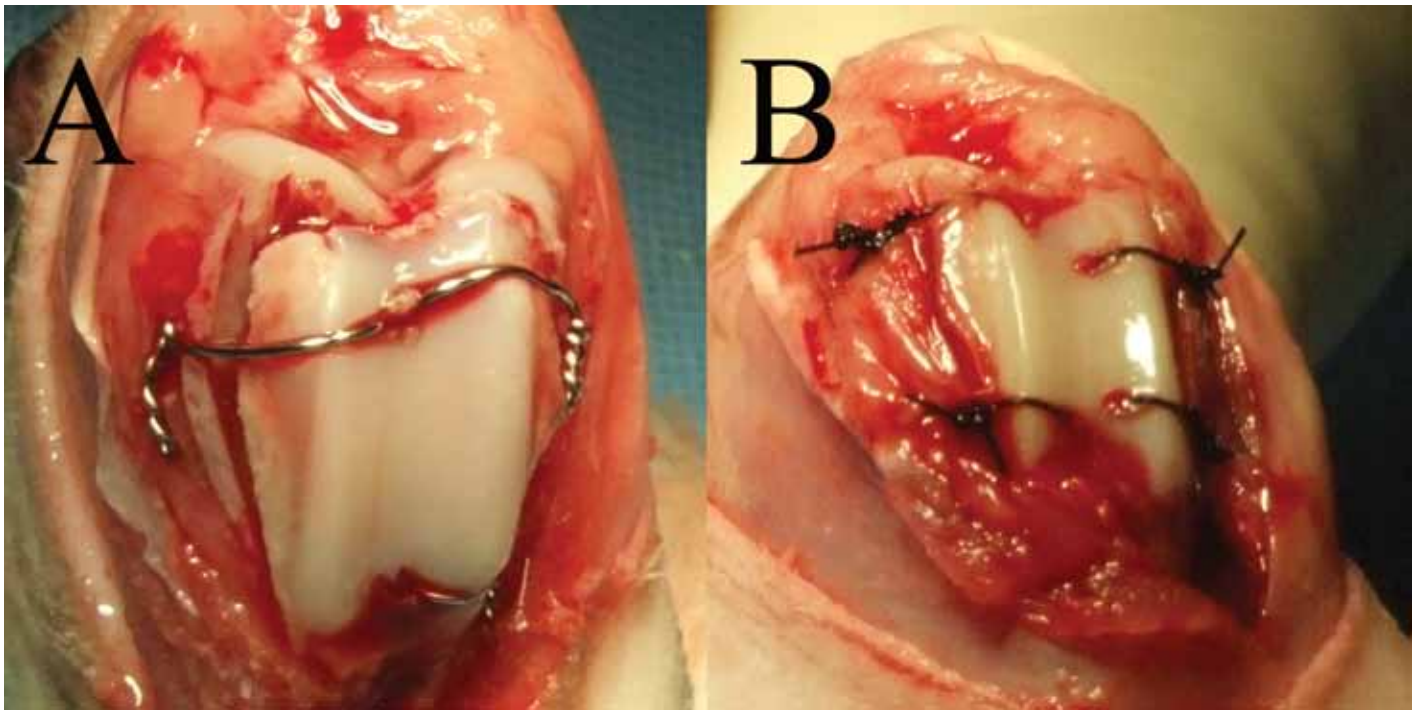

Figure 1. Femoral trochlear grafts were fixed to the host by using (A) 22-gauge wire passed through 3 or 4 drill holes at the corners of the graft and (B) 3-0 nylon suture at the 4 corners of the graft.

retracted laterally, exposing the anterior surface of the trochlea. An oscillating saw with a 1-cm blade (Stryker, Kalamazoo, MI) was used to resect the entire trochlea with a variable thickness of 1.5 to 4 mm.

Transplantation of osteochondral tissue was demonstrated over a range of source tissue (autograft compared with allograft), storage culture media, and culture time (Table 1). After surgery, the trochlea was placed immediately in tissue culture media (DMEM, Invitrogen, Carlsbad, CA) or sterile lactated Ringers solution. In some samples 10% fetal bovine serum was added. All sample storage solutions included antibiotics (1% penicillin–streptomycin). A trochlear groove was reconstituted with a small rongeur and the patella reduced. Lack of lateral subluxation was confirmed, and the medial parapatellar arthrotomy was closed with 3-0 Vicryl (Ethicon, Cincinnati, OH) in an interrupted pattern. The skin was closed with 3-0 Vicryl in a running subcuticular pattern. The tracking of the patella was checked after arthrotomy and skin closure to confirm the absence of mechanical obstruction and maltracking. Rabbits received postoperative pain management (0.025 to 0.05 mg/kg every 12 h for 2 d; Buprenex, Reckitt and Colman, Slough, United Kingdom). No rabbit showed evidence of limping or knee discomfort after 24 h.

The grafts were stored in 12 mL of tissue culture media for either 2 or 4 wk. The media was changed under aseptic conditions under a laminar flow hood every 3 d. After graft storage, rabbits underwent an identical procedure on the contralateral (right) knee. The stored grafts were implanted into the recipient site of the trochlea of either the same animal (autograft) or a different rabbit (allograft) of the same or different strain according to a randomized matching assignment (Table 1). Two methods of fixation were used: 22-gauge wire passed through 3 or 4 drill holes at the corners of the graft for the first 8 animals and 3-0 nylon suture (Ethicon) passed through drill holes at the corners of the graft for the remaining 8 rabbits (Figure 1).

The method of graft fixation was changed from wire to suture due to the finding that wire could generate greater synovitis. In addition, graft fixation with wire led to prominent wire ends despite our efforts to bend the ends away from the soft tissues. Furthermore, suture was preferable due to elimination of radiographic artifact on microCT. Both groups recovered equivalently, and there was no evidence of increased postoperative pain in either the wire fixation or the suture fixation group. Rabbits were euthanized at various time points after transplantation according to randomized assignment. The distal femora were harvested and processed for histologic analysis.

MicroCT analysis. The distal femora were scanned by using microCT (microCAT II, ImTek, Bridgeport, NJ). The axial microCT sections were randomized and identifying data were removed. The images were analyzed by 2 independent observers for completeness of healing at the graft–host interface (either 100% bridging or less than 100% healing; Figure 2). The κ statistic was used to determine the interobserver reliability of this analysis.[50]

Histologic analysis and scoring. Tissue sections were fixed in Bouin solution for 1 h, followed by paraffin embedding and sectioning (5-µm sections). Briefly, the distal femora were decalcified in 15% EDTA pH 7.4 for 4 wk. The decalcification solution was changed every 48 h. After decalcification was complete, the samples were dehydrated in an ethanol series, cleared with xylene, and embedded in paraffin for sectioning (Accu-cut SRM 200, Torrance, CA) into 5-µm thick tissue samples for further processing.

Three sections each at the proximal, middle, and distal aspects of the graft were obtained from each transplant. The articular cartilage was divided into 3 zones, from medial, midregion, and lateral portions of the surface. Each of these zones was photo-

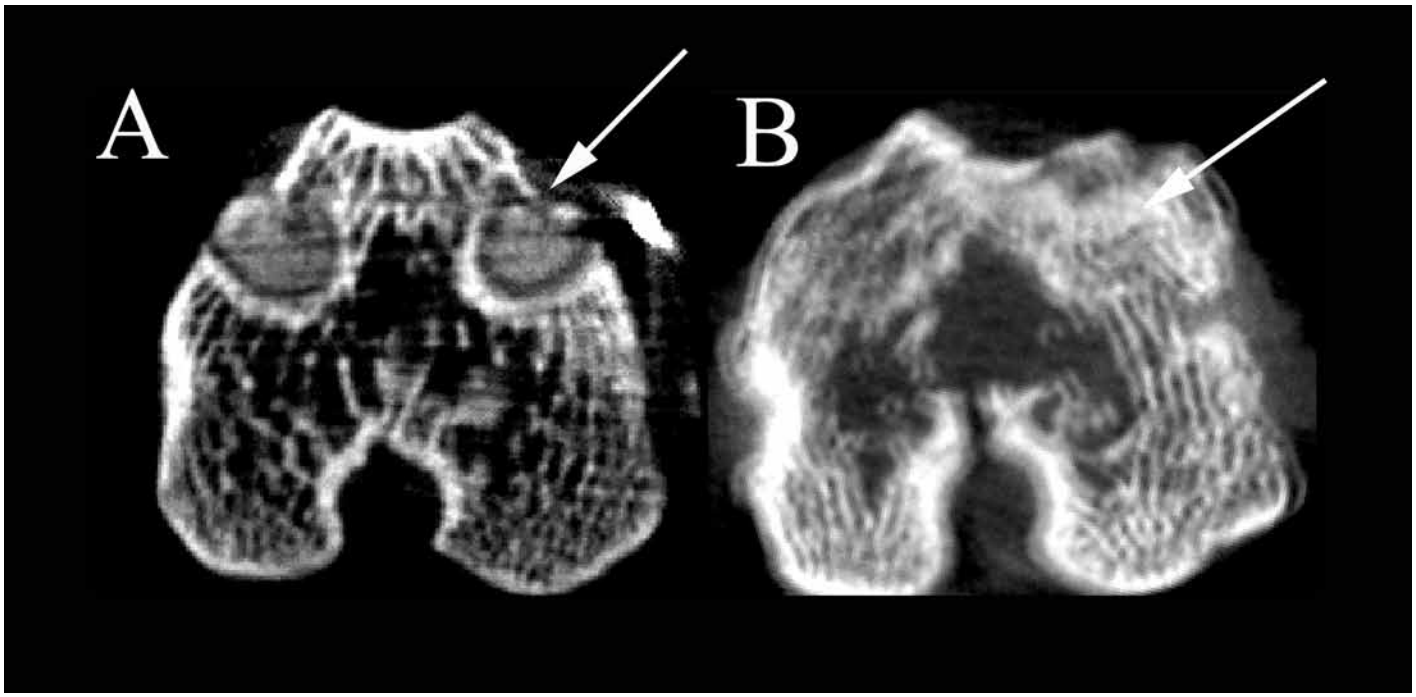

Figure 2. MicroCT axial images demonstrating (A) an unhealed bone interface (white arrow) in an allograft transplant at 2 wk (rabbit 12 in Table 1) and (B) a healed interface (white arrow) in an allograft transplant at 12 wk (rabbit 14 in Table 1).

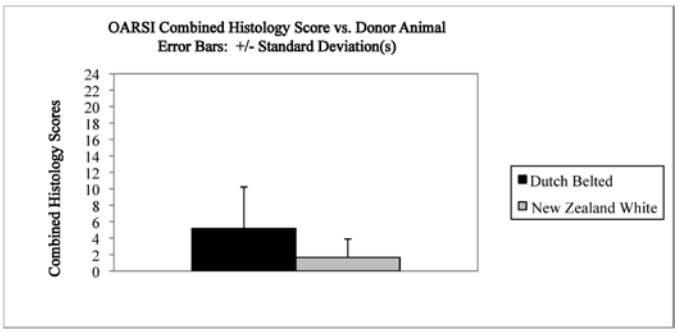

Figure 3. OARSI scores (mean ± 1 SD) for grafts originating from New Zealand white (NZW) and Dutch belted (DB) rabbits.

graphed at a magnification of ×40 on an upright light microscope with a camera head (Axiocam, Zeiss, Thornwood, NY). Random safranin-O-stained images were analyzed by using the OARSI cartilage OA histopathology grading system[38] by 2 independent observers with experience in histologic analysis of cartilage. In this system, scores range from 0 (normal cartilage) to a maximum of 24 (severe, global osteoarthritis). Reliability of the scoring analysis was performed by determining the intraclass correlation coefficients for the combined score (grade × stage). The combined histologic scores then were analyzed relative to the donor animal origin. In addition to the transplants analyzed, 2 control rabbit trochleae were analyzed and had a combined histologic score of 0.

Localization of superficial zone protein. The localization of expression of superficial zone protein (SZP) in osteochondral allografts was investigated by using immunohistochemistry. Immunostaining by standard methods was performed by using S6.79 (1:5000; donation by Dr Thomas Schmid, Rush University) as the primary antibody[52] and an ABC kit (Vector Laboratories, Burlingame, CA), with mouse IgG secondary antibody for signal detection. Qualitative assessment of SZP localization was performed by using light microscopy.

Statistical analysis. The κ statistic and intraclass correlation coefficients used in determining the reliability of histologic analyses and microCT analyses were obtained by using SPSS (version 9; IBM, Chicago, IL). Nonparametric analysis of the combined histology scores relative to the donor animal was performed with the Mann–Whitney test by using Statview (SAS Institute, Cary, NC). Statistic significance was set at $P < 0.05$. Data are presented as mean ± 1 SD.

Results

Surgical procedure. As assessed by independent observers, the surgical procedure was well controlled with standard pain medications. Two rabbits experienced complications in the postoperative period. One rabbit fell out of its cage at 1 wk after graft implantation and died prior to its predetermined endpoint. The second rabbit awakened violently from anesthesia during microCT of the graft and sustained a lumbar dislocation with paraplegia. This rabbit was euthanized immediately (at 2 wk after implantation).

MicroCT analysis. All of the remaining 14 transplanted specimens that remained in vivo for at least 4 wk showed 100% healing at the graft–host interface (Figure 2) according to both observers, indicating a reliable healing response regardless of the graft treatment. The interrater reliability of the CT scoring system was determined across all specimens by 2 independent observers in a blinded fashion. The κ statistic for the analysis was 0.82, indicating excellent correlation.[27]

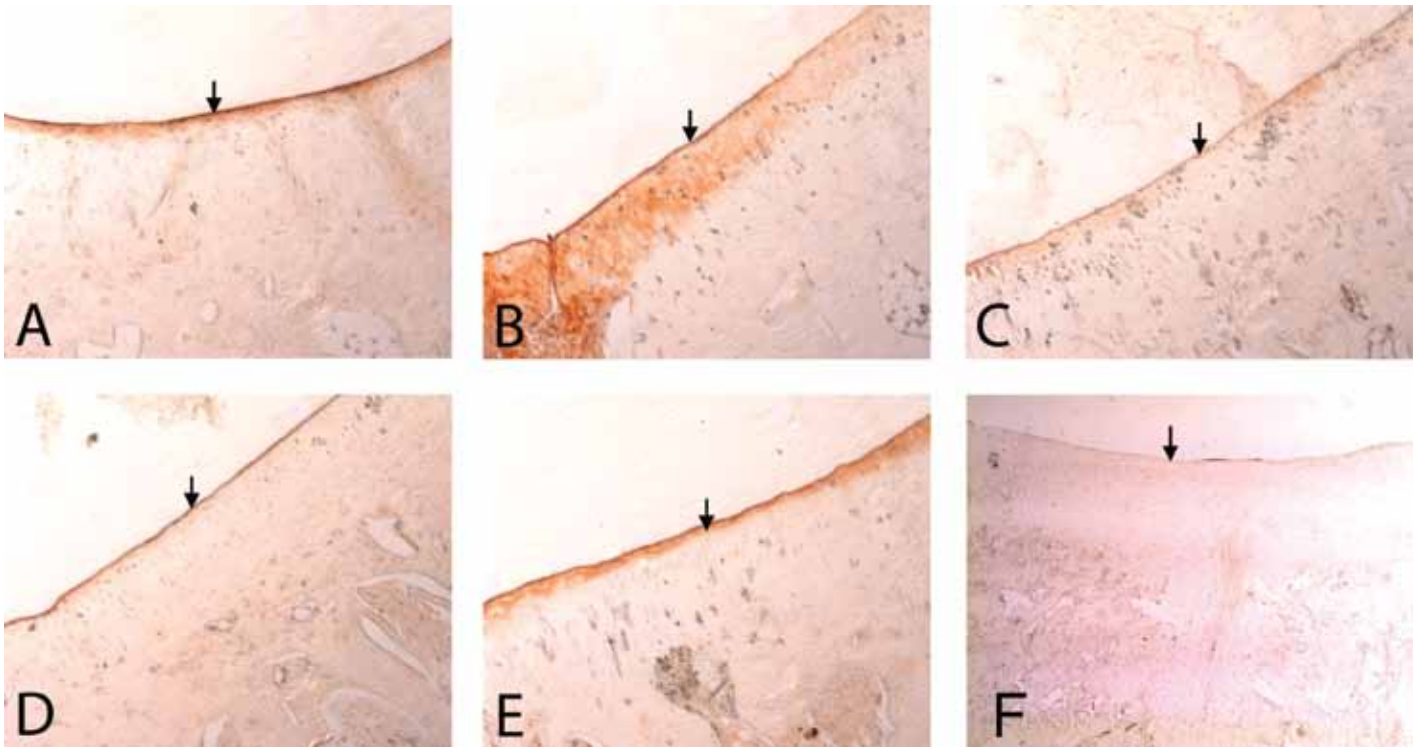

Figure 4. The boundary-lubricating molecule superficial zone protein (SZP) was observed in all transplanted allografts. SZP staining was localized near the articular surface in representative images from (A) NZW rabbit controls and (B through E, respectively) samples from 2, 4, 6, and 12 wk after transplantation. Variation in the depth of staining has been observed elsewhere.[35] Axial images of 5-µm sections of the distal femora were captured at ×10. (F) An osteochondral section from a control rabbit knee that was stained by using the same protocol demonstrates no edge-effect staining.

Histologic analysis and scoring. Among decalcified transplanted distal femora sections that had remained in vivo for at least 4 wk, the combined histologic score for transplants originating from DB rabbits ($n = 7$) was 5.179 ± 5.050 compared with 1.656 ± 2.231 for transplants from NZ animals ($n = 5$; Figure 3). However, this difference was not statistically significant ($P = 0.19$) at the sample size available. The overall combined histology score for all transplants with a minimal in vivo duration of 4 wk was 3.71 ± 4.36. The interobserver reliability for histologic grade was 0.89, for histologic stage was 0.66, and for histologic score was 0.91.

Localization of SZP. SZP was observed in all 14 remaining osteochondral allografts investigated (Figure 4). SZP was localized near the articular surface with a variable depth of staining (to a maximum of several cell layers within the tissue).

Discussion

Treatment of articular cartilage injuries continues to be a challenging area in musculoskeletal medicine, largely because of the limited regenerative capabilities of the tissue and limited understanding of the natural history of cartilage injuries and their progression to osteoarthritis.[18,31] The transplantation of fresh osteochondral allografts has been used widely for more than a century to repair articular lesions.[3,16,32] The potential drawbacks to this procedure include the lack of tissue availability, short storage period prior to onset of chondrocyte death, immune rejection, and risk of disease transmission. None of the small animal models currently available address all of these potential sources of failure for this procedure (Table 2). The current study demonstrates a rabbit model of fresh osteochondral allografting in which the entire surface of the trochlea is transplanted. The model allows for early weight-bearing, minimal pain, a low complication rate, a high degree of bone-to-bone healing, and a large articular surface for analysis. This model permits assessment of chondrocyte death, bone-to-bone healing, and cartilage histology and potentially could be used to study disease transmission, surface lubrication, and immunologic factors involved in the success of fresh osteochondral allografts.

The procedure was performed as both a same-strain transplantation and as a strain-to-strain transplant between NZW and DB rabbits. The rabbits tolerated the 2-stage procedure well and were able to bear weight, as demonstrated by uninhibited movement and normal feeding behavior, within 24 h after both the harvest and transplantation procedures. We found 100% healing at bone-to-bone interfaces in all transplants that were in place for at least 4 wk. One of the challenges of this experimental model was the size mismatch between the 2 strains of rabbit, as NZW rabbits are substantially larger than DB rabbits. We therefore used skeletally immature NZW rabbits and mature DB rabbits. As a result, analysis of the healing interface between the 2 strains was challenging. We elected to assess the linear percentage of healing between the graft and host by using a randomized, blinded technique with 2 independent observers. This technique demonstrated high interobserver reliability. On the basis of this analysis, we feel that the most important finding of our study is the demonstration that these grafts achieve a high degree of graft–host healing despite strain, age, and size mismatch between the rabbits.

Articular histology has been assessed with a variety of rating systems. We used the OARSI scoring system because of its

Table 2. Literature review of osteochondral allograft animal models

Graft type	Graft storage duration and condition	Survival after transplantation	Procedure site	Animal model	Graft fixation	Weight-bearing after surgery	Analytic methods	Comments	Reference
Osteochondral plug	Fresh grafts stored 21 d in 8% DMEM at 4° C; grafts stored at −70 °C; freeze-dried at room temperature	6 or 12 wk	Femoral trochlea	NZW rabbit	Press–fit	Unrestricted	Hematoxylin and eosin; safranin O; histologic scoring	Incomplete host–graft incorporation	10
Osteochondral plug	Not reported	3 or 6 mo	Medial femoral condyle	Mixed-breed dog	Press–fit	Unrestricted	Gross morphology; plain radiography; biomechanical testing; MRI; hematoxylin and eosin; safranin O	Bony trabecular graft incorporation at 6 mo; persistent cleft between graft and host articular surface	14
Osteochondral dowel graft	4 wk at −80 °C	4 wk	Medial femoral condyle	Suffolk–Romanoff crossbred sheep	Press–fit	Unrestricted after the first 3 to 5 d in small enclosure	Gross morphology; biomechanics; cartilage thickness; safranin O; Mankin Scoring	Inexact graft contour fit in host	21
Cartilage graft	30 to 120 min in PBS at room temperature	3, 17, 26, or 52 wk	Medial tibial plateau	Spanish goat	Screws	Unrestricted	DNA analysis; toluidine blue, safranin O, alcian blue, magnesium chloride staining	Progressive degenerative changes of allograft articular cartilage over time	23
Distal femur osteoarticular graft	6,12,24, or 48 h at 4 °C; 5 d at −80 °C	2, 6, or 12 wk	Distal femur	Sprague Dawley rat	Pins	Unrestricted	Cytotoxicity assay	Impractical to repair ligaments adequately due to small size, leading to possible joint instability; low cost	42
Osteochondral dowel graft	Not reported	3, 6, or 12 mo	Medial femoral condyle	Suffolk–Romanoff crossbred sheep	Press–fit	Unrestricted after the first 3 to 5 d in small enclosure	Gross morphology; biomechanical testing; fluorescein diacetate; safranin O; Mankin scoring; hexuronic acid	Inexact graft contour fit in host	46
Proximal part of the radius	3 h in RPMI 1640 at 37 °C; 12 h at −80 °C	11 mo	Proximal radius	Beagles	Plate and screws	Unrestricted	Immunologic assays	No loosening of implants reported	51

Graft type	Graft storage duration and condition	Survival after transplantation	Procedure site	Animal model	Graft fixation	Weight-bearing after surgery	Analytic methods	Comments	Reference
Whole knee joint; osteochondral trochlear graft	36 h in Ringers lactate, Betadine, Triton X at 4 °C; 80 h with or without Triton X irrigation at 4 °C	4 wk; 6 mo	Knee joint; trochlear	Lewis rat; sheep	Sutures and staples	Unrestricted after the first 1 to 2 wk in small enclosure	Clinical assessment; plain radiographs; hematoxylin and eosin, safranin O; radioactive sulfate; biomechanics; cytotoxicity assay	Rat model: immune response study only. Joints too small for graft function evaluation Sheep model: large joint available for functional and immunologic evaluation	41
Osteochondral graft	14 d in tissue culture medium at 4 °C	12 wk	Medial femoral condyle	Dog	Pins	Unrestricted	Biomechanical testing; hematoxylin and eosin, safranin O; gross morphology	No difference between fresh and stored allografts	36
Proximal part of the humerus	Cryopreserved	3, 6, 19, 12 mo	Proximal humerus	NZW rabbit	Plate and screws	Unrestricted	Collagen synthesis, proteoglycan synthesis, and water, hydroxyproline, hexosamine, and hexuronic acid contents	Minor joint instability reported; Proximal humerus doesn't represent classic weight bearing joint	45
Osteochondral plug	RPMI-1640 media, 10% fetal bovine serum at 4-6 °C	7, 14-15, 18, 21, 28, 85 d	Distal femoral condyle	*Papio hamadryas* baboon	Press–fit	Unrestricted	Gross and histologic scoring, hematoxylin and eosin, Giemsa stain, periodic acid–Schiff stain, trichrome stain, safranin O, toluidine blue	Anatomically similar to human joints	30

simplicity, consistency, and high interobserver reliability in our analysis. Unfortunately, it is impossible to draw strong statistical conclusions about the cartilage histology in our study due to the variations in storage time, storage solution, and fixation method. However, despite these factors, the average histologic combined score for grafts with a minimum of 4 wk in vivo was 3.71 ± 4.36 (maximal possible score, 24), demonstrating overall minimal osteoarthritic changes in these grafts. Again, a major limitation of this analysis was the small sample size in each group. However, the objective of the current study was not to compare the individual animals or storage protocols but rather to demonstrate effective maintenance of cartilage histology and adequate graft–host bone healing.

The Krogh principle emphasizes the existence of a suitable animal model for the study of each specific physiologic question.[26] However, this principle is not entirely applicable for the field of cartilage repair. Several animal models have been used to study of articular cartilage injury; each has certain advantages and disadvantages (Table 2).[11] Because of the unique biologic characteristics of the human joint, the selection and justification of each animal model in assessing cartilage injury and repair must be performed cautiously.[19] Large animals such as horses, dogs, and baboons have been proposed to better represent the clinical scenario seen in humans,[19,30,36,51] and the use of small animals for the assessment of cartilage injury and repair has been criticized.[24] Small animal models, however, possess merits that validate their worth, as evidenced by our study and in light of the higher purchase costs, maintenance costs, and space required for larger animals.

Limitations of osteochondral allografts in the rabbit model include incomplete graft–host incorporation, which can contribute to poor graft outcome,[10] and application of the pressure-fit technique for graft fixation, which may compromise quality and survival of surface cartilage.[10,20] Transplantation of the entire knee (or entire distal femur as in the rat model) may be suitable for immunologic studies but may be too small for the study of joint mechanics.[40,42] In addition, our suture method of graft fixation nullifies concerns regarding the press-fit technique and avoids screw fixation. Our model uses the knee joint of the rabbit hindleg, which represents

a classic weight-bearing joint that is large enough for the study of joint mechanics but does not require extended postoperative recovery or expensive animal maintenance costs.

SZP is a glycoprotein secreted by chondrocytes in the superficial layer of articular cartilage[22,47] and is thought to be a key surface molecule involved in boundary lubrication. The protein is also known as lubricin,[25] MSF precursor,[9] and proteoglycan 4 (PRG4).[22] In addition to its function as a boundary lubricant, SZP also functions to inhibit synovial cell overgrowth.[9] Downregulation of the protein has been associated with the pathogenesis of osteoarthritis.[54] SZP was present in the articular surface of all osteochondral allograft specimens in the current study. This finding is important in supporting the use of fresh osteochondral allografts and the mechanisms by which they help in restoration of joint mechanics after implantation. Therefore, the presence of SZP at the articular surface is expected to impart normal function during locomotion of the animal by minimizing friction and potentially minimizing wear.[28,39]

Despite the success of the allografting procedure in the rabbit trochlea model, the current study presents several limitations. The small size and thin articular cartilage layer of rabbits are not comparable to those of humans. Vital staining of the rabbit articular cartilage is not possible due to its minimal thickness. The hindlimb weight-bearing function and normal joint angle of a quadrupedal animal such as rabbits are substantially different than those of bipedal humans. The accelerated subchondral graft–host healing and high rate of graft incorporation in our rabbit model, although attractive from an animal care point of view, deviate from the human clinical condition in which healing is much slower and graft failure at the bone–bone interface is more common. Although we demonstrated no significant difference between the articular cartilage histology of the 2 rabbit strains and survival groups, a larger sample size is needed to support this conclusion with confidence.

In conclusion, our rabbit femoral trochlea osteochondral transplantation model is an effective and economical model that offers several strengths and weaknesses. We anticipate that this model will facilitate further investigations into optimization of fresh osteochondral allograft storage and transplant conditions and graft incorporation and potentially can be applied to the analysis of tissue-engineered osteochondral constructs, without the limitations of current animal models. We especially hope that this model will identify transplantation conditions that favor maximal cell viability to ensure the best possible transplantation success. Future investigations are required to better define storage intervals, storage solutions, and conditions to optimize graft viability to help overcome current issues of limited clinical graft availability.

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