A Biologic Joint Replacement Strategy to Treat Patients with Severe Knee Trauma and Post-Traumatic Knee Osteoarthritis

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1. Background and Significance

Significant damage to the knee from athletic activities, military training, blunt trauma, or penetrating trauma inevitably leads to dysfunction, pain, and post-traumatic osteoarthritis (PTOA), and is the most common unfitting condition in medically retired military personnel [1-3]. As identified in the most recent Extremity War Injuries (EWI) symposium, PTOA accounts for more than $3 billion in aggregate financial costs [3]. Additionally, this symposium identified that "94.4% of the OA can be attributed to combat injury" [3], but fell short of identifying effective treatments other than joint replacement once OA develops. Cross et al. ranked degenerative arthritis with the third highest impact factor and the "most common unfitting condition" in their 2011 study of long-term disabilities in military personnel [1]. Damaged knees rarely demonstrate substantive functional healing. Current practices in orthopaedic surgery attempt to limit the incidence and severity of joint deterioration, but despite recent advances and state-of-the-art treatment protocols, trauma to the joints can be associated with as high as a 65% incidence of debilitating osteoarthritis (OA) [4].

The fundamental problem driving this high rate of OA is the relative inability of articular cartilage to functionally heal [5-8]. Risk factors that significantly influence the incidence and severity of OA after joint injury include the patient's age, extent of injury, and type and timing of treatments [7, 9]. Ideally, biologic "regenerative" treatments performed prior to the onset of debilitating OA would be used in these patients to prevent, or at least minimize, joint deterioration and dysfunction. However, regenerative strategies in orthopaedic trauma are not well-developed, and therefore, salvage procedures such as total joint replacements are often necessary. While joint replacement with metallic and plastic implants generally succeeds in decreasing joint pain and improving limb function, the limited lifespan of implants, associated morbidity and complications are significant concerns.

Perhaps more importantly, patients with total knee replacements cannot return to athletic activities, high-demand physical labor, or active military duty. Buckwalter and Lohmander have stated that "no currently available synthetic material or combination of materials duplicates the ability of articular cartilage to provide a painless, low-friction gliding surface and to distribute loads across a synovial joint [9]." Therefore, **our solution is to use novel articular tissue transplantation strategies to functionally rebuild damaged knees**, thus avoiding the limitations of plastic and metallic implants while restoring full use of the limb for patients. Specifically, we have developed three allografting techniques that allow us to replace damaged cartilage, meniscus and bone with viable tissues that can integrate and function at high levels. Our approach allows us to preserve

organ donor tissues at the highest level of quality for more than twice as long as current technology, replace entire joint surfaces with "young" cartilage, and replace the entire meniscus with a viable, healthy meniscus. Importantly, all of these techniques have been validated in our translational canine model and used to treat clinical canine patients at our veterinary medical teaching hospital. This biologic joint replacement strategy has proven successful in restoring native joint structure and function such that working and performance dogs have returned to full athletic function while further degradation of the joint has been avoided for up to 6 years after surgery.

This proposal stems from the critical clinical need for more optimal treatment options for the millions of young to middle-aged, active patients with damaged knees, including active duty and veteran populations who have demonstrated a risk of injury at a level 10 times that of the civilian population [10-12]. Our team, comprised of clinicians and basic scientists, has developed methods to address the current limitations in restoring these patients to high-level function. We subscribe to the "joint as an organ" philosophy and have used this philosophy to develop biologic solutions to articular disorders through a collaborative and comparative translational approach. The proposed research will allow us to move these solutions further forward in successfully treating traumatic joint injury in soldiers and civilians, while also benefitting their four-legged companions.

Preliminary Studies:

We recognize that successful completion of the specific aims for this proposal requires proven proficiency in cartilage harvest, preservation, and transplantation. These techniques have composed the core of our interdisciplinary research efforts for more than a decade. As such, we have produced a body of work covering the foundational basic science, translational, and veterinary and human clinical research that provides the inspiration and road map for achieving similar success in the proposed research. The following data from three of our previous studies summarize our capabilities and progress in the area of regenerative orthopaedics.

1. Improved Preservation of Osteochondral Allografts[13, 14]

Background: While osteochondral allografts (OCAs) provide a current method for regenerative treatment of focal cartilage defects in the knee, they presently have limited clinical use. Current storage protocols require that time from harvest of cadaveric tissue to implantation should be 28 days or less. Due to required disease testing and donor matching protocols, as many as 80% of potential OCAs go unused. In order to make biologic knee replacement a reality, it is necessary to improve preservation of OCAs such that they can be made more widely available. Therefore, we have developed The Missouri OCA Preservation System (MOPS), a novel patented preservation method, which has been shown *in vitro* to significantly prolong the period of time for which the grafts can be stored with sufficient viability prior to surgical implantation. In the following study, we optimized and validated this system *in vivo* with respect to functional outcomes of OCAs preserved using the MOPS compared to OCAs preserved using the current standard of care method for tissue banks.

Materials and Methods: All procedures were approved by the University of Missouri Animal Care and Use Committee (#7332). The stifles (knees) of skeletally mature adult male mongrel dogs were aseptically harvested after humane euthanasia was performed for reasons unrelated to this study. The knees were randomly assigned to one of four groups:

- Standard of care (SOC) 30 - 30-day storage at 4° C (4C) in standard tissue bank media (n=12)
- Missouri OCA Preservation System (MOPS) 30 - 30-day storage at 25° C (25C) in MOPS media (n=12)
- SOC 60 - 60-day storage at 4° C (4C) in standard tissue bank media (n=12)
- MOPS 60 - 60-day storage at 25° C (25C) in MOPS media (n=12)

All soft tissues were removed in the operating room and the knees were fully inspected to ensure no pathology was present. For samples assigned to the SOC groups, the distal femurs were placed in standard storage media and stored in a dedicated refrigerator at 4° C for 30 days or 60 days. For samples assigned to the MOPS group, the distal femurs were placed in defined media (proprietary) and stored in a dedicated clean room at 25° C for 30 or 60 days. Samples of media were collected weekly for both groups for microbial testing and metabolic assay for MOPS OCAs.

Sixteen adult mongrel female dogs (2-5 years old, 25-35 kg body weight judged free of OA in all joints based on complete examination and radiographs of the hips, elbows, and knees, were enrolled in the study. At 30 or 60 days after graft procurement, surgically created defects were filled with site-matched 8 mm OCAs obtained from the adult male cadaveric distal femurs preserved by either SOC or MOPS and implanted using the press-fit methodology of the OATS allograft system. At each time point (30 days or 60 days after graft procurement), each knee received one SOC graft and one MOPS OCA, which were alternated between medial and lateral femoral condyles. At the time of implantation, samples of the bone and cartilage from each distal femur and from the preservation media were obtained and processed for microbial testing.

Radiographic and arthroscopic evaluations were made at 12 weeks and 6 months post-surgery. The dogs were humanely sacrificed 6 months after surgery. Both knees of each dog were carefully disarticulated, and examined for gross appearance, cell viability, cell source determination, histologic assessment, biomechanical and biochemical characteristics.

Results: *Viability during storage*: Day 30 viability ranged from 22.9-99% with a mean of 60.2% for SOC grafts and a mean of 82.9% for MOPS grafts. Day 60 viability ranged from 24.7-99% with a mean of 52.7% for SOC grafts and a mean of 89.8% for MOPS grafts. Day 60 viability was significantly ($p=0.002$) higher for MOPS grafts than for SOC grafts.
Clinical assessments: All dogs were successfully implanted with OCAs and recovered well without complications for the intended study duration.
Radiographically: Immediate postoperative radiographs showed appropriate implantation of all grafts with no evidence for malpositioning or technical errors. Radiographic assessments performed at 3 and 6 months after implantation showed evidence for progressive osseous integration of both SOC and MOPS grafts with variable degrees of associated sclerosis.

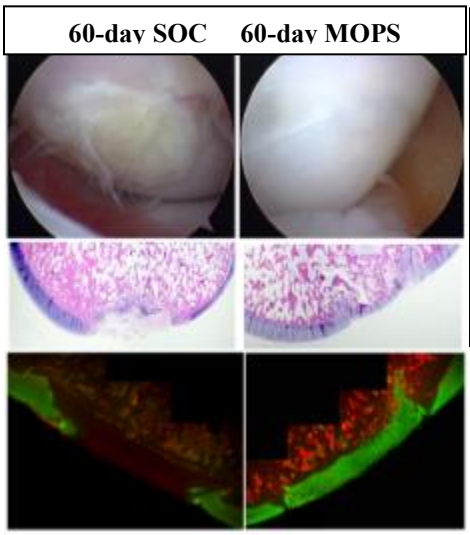


Fig 1. Arthroscopic (top) and histologic (middle) appearance of OCAs implanted into the femoral condyles of dogs in this study with corresponding cell viability images (bottom) demonstrating the consistently superior appearance of MOPS osteochondral allografts.

For 30-day preservation, MOPS and SOC grafts were similar in appearance based on arthroscopic, gross and histologic appearance performed 6 months after implantation, For 60-day preservation, MOPS grafts were subjectively superior to SOC grafts with respect to arthroscopic, gross and histologic appearance when assessed 6 months after implantation. For both preservation periods, chondrocyte viability at the time of implantation appeared to correspond well to subjective arthroscopic, gross and histologic assessments.

Biochemical Assessments: GAG content was significantly ($p<0.009$) higher in native articular cartilage compared to cartilage from SOC and MOPS 30-day grafts and SOC 60-day grafts when assessed 6 months after implantation. GAG content was not significantly different in native articular cartilage compared to cartilage from MOPS 60-day grafts when assessed 6 months after implantation. There were no statistically significant differences in collagen (HP) content in native cartilage compared to cartilage from SOC and MOPS 30-day or 60-day grafts when assessed 6 months after implantation.

Biomechanics: Young's modulus was significantly ($p<0.041$) higher in native articular cartilage and cartilage from MOPS 60-day grafts compared to SOC 60-day grafts when assessed 6 months after implantation. Young's modulus was not significantly different in native articular cartilage compared to cartilage from MOPS 60-day grafts when assessed 6 months after implantation.

Discussion and Conclusion: The Missouri OCA Preservation System allows for preservation of chondrocyte viability for up to 60 days at sufficient levels to result in functional outcomes in a canine model of articular defects in the knee. Functional outcomes associated with MOPS-stored OCAs were superior to those using the current standard of care system used by tissue banks suggesting that the MOPS system could be employed clinically at this time.

2. Mitigating Mechanical Damage to Osteochondral Allografts During Implantation[15]

Background: In order to treat large post-traumatic cartilage defects, more effective implantation techniques are needed in order to preserve a maximum amount of available viable tissue. Current techniques for osteochondral allograft (OCA) transplantation require insertion of the graft into a cylindrical cavity with a press-fit interface. Mechanical impaction to overcome frictional resistance has a negative effect on chondrocyte viability and long term clinical outcomes. Our goal was to develop and test a novel tapered OCA system that could maintain graft stability while mitigating detrimental insertion forces, thereby preserving chondrocyte viability in comparison to standard cylindrical systems.

Materials and Methods: Fresh femoral condyles were obtained from dogs euthanatized for reasons unrelated to this study. Cylindrical plugs (8mm diameter, 6mm depth) were harvested

and implanted in the same specimen using a commercially available system. In a similar manner, tapered plugs (8mm diameter top surface, 6mm depth) were harvested and implanted using our novel tapered system. Superficial cell death and total cell viability were assessed on Day 0 and Day 3, and compared statistically. Insertion force and extraction strength for cylindrical and tapered OCAs were tested using an Instron 8821S servo-hydraulic machine, and compared statistically.

Results: The total cell viability did not differ significantly between tapered and cylindrical OCA at Day 0 or Day 3 (p=0.535, p=0.147), however, tapered OCAs had significantly less superficial cell death compared to cylindrical grafts (p=0.003) (Figs 2 and 3).

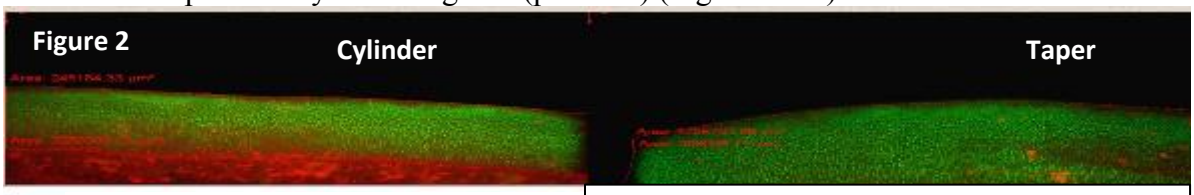
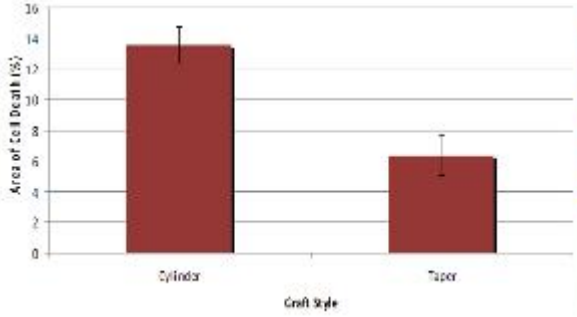


Figure 3. Area of Superficial Cell



Superficial Cell Death: The superficial area of cell death was found by taking the area of superficial death over the total area of the cartilage as seen in Figure 2. The area of superficial cell death was significantly lower (*p*=0.003) in tapered OCA plugs compared to cylindrical plugs (Figure 3). This signifies that there is less trauma received by the tapered plugs during impaction then compared to what cylindrical plugs experience.

Tapered OCAs required significantly less insertion force and energy for proper implantation compared to cylindrical OCAs (p=0.012, p=0.008). Importantly, there was no significant difference in extraction strength between tapered and cylindrical systems (p=0.881) (Figs 4-6).

Discussion and Conclusion: In this *ex vivo* model, our novel tapered OCA system required lower insertion force to properly seat the grafts without compromising extraction strength when compared to cylindrical OCAs. Importantly, plugs inserted using the tapered system had significantly higher chondrocyte viability in the superficial zone, which suggests that clinical outcomes associated with the tapered system would be improved based on current best evidence.

3. Unicompartmental Tibial Allografting with Native Meniscus

Background: Frozen meniscal allograft transplantation (MAT) can be an effective strategy for treatment of meniscal-deficient knees. However, graft extrusion and shrinkage, degeneration of the horns, and failure of fixation are frequent complications. These issues may be associated with the use of non-viable tissue and/or lack of anatomical placement and fixation of the graft to the tibia. Another factor affecting the clinical success of MAT is the state of the underlying tibial cartilage of the patient. Replacing the meniscus does not address cartilage pathology of the tibial plateau, which is a common and limiting component in most patients being evaluated as candidates for MAT. Therefore, use of a viable MAT that allows for anatomical placement of the graft on the tibial plateau could significantly reduce complications and improve long-term success of the procedure and increase the number of patients that MAT can be considered for clinically. After determining that the viability and structural properties of meniscal-tibial plateau

allografts (MTPAs) could be maintained for a clinically relevant period of time when stored at 25°C, we designed the present study to determine the feasibility of performing medial tibial plateau and meniscus replacement in research dogs using viable, stored MTPAs. We hypothesized that viable meniscal-tibial plateau allografts implanted into the medial compartment of the knee of dogs would effectively integrate with recipient tissues and maintain viability and function for at least 3 months after implantation.

Materials and Methods: Graft creation and assessment of viability were first determined by aseptically harvesting the entire tibial plateau (TP) from the hind limbs of 58 dogs euthanatized for reasons unrelated to this study. This initial research provided evidence for our ability to maintain cell viability, tissue composition and material properties at appropriate levels through 56 days of storage at room temperature using our preservation system. Based on the success of the *in vitro* study, *in vivo* implantation of MTPAs was undertaken with IACUC approval. MTPAs from the right knee of two purpose-bred research dogs were aseptically harvested and stored for 30 days using our tissue preservation system. After disease testing and assessment for viability during storage, the grafts were implanted into the knees of two size-matched purpose-bred research dogs. Using a medial mini-arthrotomy, the medial meniscus and medial tibial condyle were resected *en bloc* from each dog with preservation of the medial collateral ligament, cranial and caudal cruciate ligaments. The MTPA was then inserted and stabilized to the proximal tibia using divergent Kirschner wires. The dogs were recovered and allowed to use the limbs in their runs immediately after surgery. The dogs were assessed at weeks 5, 8, and 12 after surgery using measures of knee function, second look arthroscopy and radiographs. Three months after implantation, the dogs were humanely euthanatized and assessed grossly and histologically for evidence of graft location and stability, graft incorporation, tissue architecture, and articular cartilage health.

Surgical implantation of the MTPAs was accomplished in dogs without intraoperative or postoperative complications. Dogs ambulated on the operated limbs immediately after surgery and were using the limbs with no apparent lameness and normal knee range of motion (105º and 107º) 3 months after surgery. Five and twelve weeks after implantation, arthroscopic assessment revealed maintenance of meniscal positioning with evidence for synovial attachment to the periphery of the transplanted meniscus in both dogs. Femoral and tibial articular cartilage in the medial compartment showed no evidence of softening, fibrillation, or erosions. All other intra-articular tissues were normal in appearance with no evidence for untoward immune or inflammatory responses. Radiographic assessments at 8 and 12 weeks after surgery showed mild joint effusion and evidence for progressive healing of donor to recipient bone with maintenance of graft and implant positioning. Gross and histologic assessments at the time of sacrifice were consistent with all clinical findings. Meniscal positioning was maintained such that subluxation or extrusion was not noted. All articular surfaces were normal in appearance with no evidence of pathology. Evidence for bone union between donor bone and recipient bone was noted.

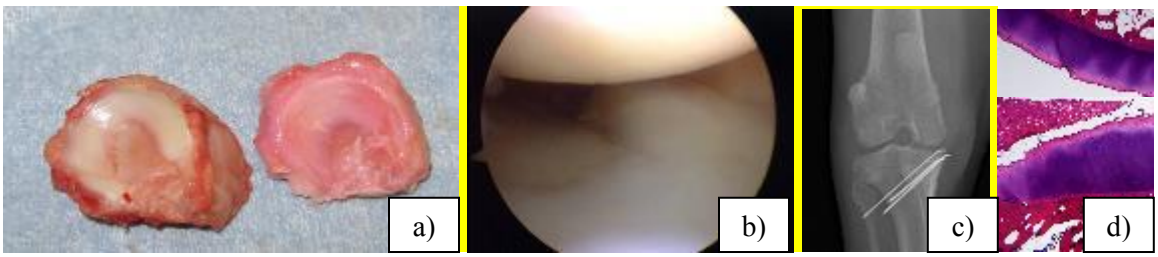


Figure 4. Representative images from clinical canine case of MTPA including a) resected meniscus and graft, b) scope at 3 mo post op, c) radiograph at 3 mo post op, and d) histologic section at 3 mo post op.

Discussion and Conclusions: These data provide initial evidence for the feasibility of performing complete replacement of the medial tibial plateau and meniscus using viable meniscal-osteochondral grafts stored using our preservation system for at least 30 days. Clinical, arthroscopic, radiographic, gross and histologic assessments all provided evidence for graft integration and healing, maintenance of function, and lack of associated morbidity.

Military Benefit: Combat and combat-related joint injuries account for more than $3 billion in aggregate financial costs. Outcomes for surgical interventions to repair articular fractures and ligament ruptures are quite good in short term follow-up studies. However, there is currently little that can be done to prevent/mitigate the development of PTOA following articular fracture and/or ligament injury long term. Thus, often the only option is joint replacement in a relatively young patient population. Our proposed interventions provide a vital surgical option for injured joints of military personnel, which addresses the risk of PTOA while still maintaining future surgical options if necessary.

2. Trial Objectives and Purpose

Evaluate safety and efficacy of unicompartmental biologic arthroplasty of the knee in a limited clinical trial.

With IRB approval, a limited pilot study will be performed to assess safety and efficacy of biologic unicompartmental arthroplasty. Ten patients who require tibial plateau and meniscus arthroplasty plus a femoral condyle arthroplasty, based on physical examination, radiographs, and knee arthroscopy, will be enrolled. Range of motion, VAS pain score, SF-12, Tegner score, International Knee Documentation Committee (IKDC) subjective and objective scores, PROMIS Bank v1.2 – Physical Function-Mobility, PROMIS v1.1 – Global Health, PROMIS Bank v1.1- Pain Interference, PROMIS Bank v1.2 – Physical Function, and Marx score as well as complete radiographs of the affected knee will be obtained prior to surgery and at 6 weeks, 3 months, 6 months, and 12 months after surgery to evaluate healing, function and evidence for arthrosis. We will document all complications, including joint or incision infection, graft failure, hardware failure, and arthrofibrosis. Patients with a VAS pain score >5 beyond 3 months postoperatively or clinical or radiographic evidence for nonunion or graft collapse will undergo MRI of the knee to determine the appropriate clinical course of action.

This proposal stems from the critical clinical need for more optimal treatment options for the millions of young to middle-aged, active patients with damaged knees. Our team, comprised of clinicians and basic scientists, has developed methods to address the current limitations in restoring these patients to high level function. We subscribe to the "joint as an organ" philosophy and have used this philosophy to develop biologic solutions to articular disorders through a collaborative and comparative translational approach. The proposed research will allow us to move these solutions further forward in successfully treating traumatic joint injury in soldiers, civilians, and their four-legged companions.

Rationale: Prior to widespread clinical use, the safety and efficacy of our unicompartmental biologic arthroplasty must be confirmed in a controlled clinical trial. Clinical patients (n=10) with unicompartmental post-traumatic knee OA will be treated with unicompartmental biologic knee arthroplasty and evaluated for functional outcomes.

Based on our preliminary studies and long-term outcomes in clinical veterinary patients, we are optimistic that the final technique for unicompartmental biologic knee arthroplasty that is optimized in specific aim 1 will prove to be vastly superior to non-surgical management of knee OA in the translational model described in specific aim 2. We are confident that clinical use of this technique in specific aim 3 will be safe based on our previous work in conjunction with current evidence regarding clinical use of allografts. If efficacy is as high as expected in the first 10 patients, we will initiate a multi-center clinical trial to include military bases while we continue to follow all patients long term.

3. Selection of Subjects

With IRB approval and informed consent, patients (n=10) (18-50 years old) with post-traumatic knee OA and requiring a tibial plateau and meniscus arthroplasty plus a femoral condyle arthroplasty will be enrolled in the study. Primary criteria for inclusion will be Grade IV changes in the articular cartilage of the femoral condyle and tibial plateau and meniscal pathology in the medial or lateral femorotibial joint as determined by physical examination, diagnostic imaging and knee arthroscopy by the PI. Exclusion criteria include Grade III or IV changes in any other compartment of the knee, acute injury to any other part of the affected lower extremity, or inability to comply with the protocol.

Inclusion Criteria:

1. Patient requiring repair via tibial plateau and meniscus arthroplasty plus a femoral condyle arthroplasty
2. The subject is able and willing to consent to participate in the study

Exclusion Criteria:

1. Acute injury to any other part of the affected lower extremity
2. The subject is unwilling, or unable to consent due to psychiatric condition or legal incompetence
3. BMI > 40
4. Age > 50 at the time of enrollment
5. The subject is either pregnant, or a prisoner
6. Currently involved in a workers' compensation case at the time of enrollment

4. Study Procedure

After enrollment, patients will undergo standardized knee radiography, and complete assessments (described below). Size-matched (standard clinical methodology) proximal tibia with meniscus and distal femur allografts from the same donor will be obtained from a tissue bank (Musculoskeletal Transplant Foundation, Edison, NJ) who has licensed the MOPS technology. The medial or lateral femoral condyle will be replaced using our novel instrumentation and technique described above. Tibial plateau-meniscus grafts will be trimmed and used to replace the entire medial or lateral tibial condyle while sparing the attachments of ACL, PCL and respective collateral ligament. The tibial plateau graft will be fixated using commercial available implants used for bone fixation. In the event that the meniscus has been detached from the tibial plateau during graft harvest, the periphery of the meniscus will be sutured to the capsule following standard meniscus transplant procedure.

Patients will undergo controlled post-operative rehabilitation according to standard protocols for osteochondral with concurrent meniscus allografts. .

Range of motion, VAS pain score, SF-12, Tegner score, International Knee Documentation Committee (IKDC) subjective and objective scores, PROMIS Bank v1.2 – Physical Function-Mobility, PROMIS v1.1 – Global Health, PROMIS Bank v1.1- Pain Interference, PROMIS Bank v1.2 – Physical Function and Marx score as well as complete radiographs of the affected knee will be obtained prior to surgery and at 6 weeks, 3 months, 6 months, and 12 months after surgery to evaluate healing, function and evidence for arthrosis[21].

We will document all complications, including joint or incision infection, graft failure, hardware failure, and arthrofibrosis.

Patients with a VAS pain score >5 beyond 3 months postoperatively or clinical or radiographic evidence for nonunion or graft collapse will undergo MRI of the knee to determine the appropriate clinical course of action.

For all specific aims, data will be compiled and analyzed using descriptive statistics as well as appropriate tests (*t*-Test, ANOVA, rank sum, repeated measures) for significant ($p<0.05$) differences using SigmaStat. The investigators on the research team have extensive experience in

data analysis and biostatistics and have the full resources of the university's medical informatics and department of statistics available if questions arise.

5. Safety Assessment

Patients will be monitored post-operatively for signs and symptoms indicating that an adverse event has occurred. The investigator will assess the patient for adverse events at scheduled SOC follow-up visits. Any signs and symptoms indicating that an adverse event may have occurred will be treated by the investigator, and the details will be collected for study purposes. The PI will determine whether an adverse has occurred, and if so, will determine if the event meets the submission requirements of the University of Missouri Health Sciences IRB.

Adverse events and serious adverse events are defined below.
Adverse events:

I. Bleeding
II. Infection
III. Pain that is uncontrolled with standard post-operative analgesia protocol

Serious adverse events:

I. Bleeding that is significant enough to require extended hospitalization or unplanned critical care interventions
II. Infection that is significant enough to require extended hospitalization or unplanned critical care interventions
III. Pain that is significant enough to require extended hospitalization or unplanned critical care interventions

6. Confidentiality of Data

Patient confidentiality during the course of this study will be protected in compliance with HIPAA requirements as well as the requirements of the University of Missouri Health-Sciences IRB.

After consent is obtained, all subjects will be assigned a study identification number that requires the use of a key in order to decipher a subject's personal identification information. The study identification number will be used to label all paper data collection instruments.

All subject information in electronic format will be kept in password-protected storage. All subject information in paper format will be kept in locked cabinets in a secured suite at either the Missouri Orthopedic Institute, and otherwise will be archived in a secure storage facility, or destroyed.

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List of Abbreviations

ACL – Anterior Cruciate Ligament
EWI – Extremity War Injuries
GAG – Glycosaminoglycans

HP – Hydroxyproline
IACUC – International Animal Care and Use Committee
IKDC – International Knee Documentation Committee
IRB – Institutional Review Board
MAT – Meniscal Allograft Transplantation
MOPS – Missouri Osteochondral Allograft Preservation System
MTPAs – Meniscal-Tibial Plateau Allografts
MR – Meniscal Release
OA – Osteoarthritis
OCAs – Osteochondral Allografts
PCL – Posterior Cruciate Ligament
PTOA – Post-traumatic Osteoarthritis
SOC – Standard of Care
TP – Tibial Plateau
VAS – Visual Acuity Scale

A Biologic Joint Replacement Strategy to Treat Patients with Severe Knee Trauma and Post-Traumatic Knee Osteoarthritis							
STUDY ACTIVITY	Pre-Op/Baseline	Surgery	6 weeks (+/- 2 weeks)	3 Months (+/- 2 weeks)	6 Months (+/- 2 weeks)	12 Months (+/- 1 month)	If Applicable Per Protocol
Consent/HIPAA	X						
Inclusion/Exclusion Evaluation	X						
Demographics	X						
ROM	X		X	X	X	X	X
VAS pain score	X		X	X	X	X	X
SF-12	X		X	X	X	X	X
Tegner Score	X		X	X	X	X	X
IKDC Subjective	X		X	X	X	X	X
IKDC Objective	X	X					
PROMIS - Mobility	X		X	X	X	X	X
PROMIS - Global Health	X		X	X	X	X	X
PROMIS Pain Interference	X		X	X	X	X	X
PROMIS Physical Function	X		X	X	X	X	X
Radiology	X		X	X	X	X	X
MRI (knee)							X