Technical Note

Anterior Cruciate Ligament Reconstruction With Amnion Biological Augmentation

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Abstract: Anterior cruciate ligament (ACL) ruptures are common and unfortunate injuries for many athletes. The standard therapy for ACL rupture is ACL reconstruction with either autograft, harvested from hamstring or patellar tendon, or allograft tendon from a tissue donor. Advances in tissue engineering have produced interventions to augment the healing process and may have applications when it comes to ACL reconstruction. In this Technical Note and accompanying video, we describe a simple technique to implant an amnion matrix graft with a tendon graft during ACL reconstruction. This procedure uses the proposed anti-inflammatory, scaffolding, and stem cell–producing effects of the amniotic membrane to biologically augment the healing process of an ACL reconstruction.

Anterior cruciate ligament (ACL) tears are the most common ligamentous knee injuries requiring surgery.[1-5] These injuries occur most often in athletes who participate in multidirectional sports, with female athletes having a 2 to 6 times higher risk of injury than male athletes.[1-5] ACL tears most often occur during noncontact activity while landing from a jump or lateral cutting maneuvers.[1-5] There is an estimated incidence of 200,000 ACL injuries per year in the United States, with approximately 60,000 to 150,000 requiring surgical reconstruction.[3-5] Without reconstruction, patients with a ruptured ACL will be at increased risk of continued instability and meniscal and chondral injuries.[1,2,4]

ACL reconstruction has remained the standard of care for treatment of ACL rupture in patients wishing to maintain stability and function.[1-4] Current surgical therapies aim to restore stability by preventing anterior translation of the tibia relative to the femur; however, even with proper allograft reconstruction, the risk of biological incorporation failure, post-traumatic osteoarthritis, and recurrent injury remains.[1-3] Advances in tissue engineering have produced biologically augmented ACL reconstruction techniques with the goal of improved biological incorporation and healing, as well as possible reduction in the long-term sequelae associated with ACL reconstruction.[6,7] The purpose of this Technical Note is to describe a straightforward application of amnion biological augmentation in ACL reconstruction.

Surgical Technique

Preoperative Evaluation

An ACL tear is diagnosed using a combination of patient history, clinical examination findings, and medical imaging. Patients presenting with an ACL tear are typically athletes who sustain a noncontact pivoting injury during rapid acceleration or deceleration with a change in direction. These patients will present with complaints of a swollen and painful knee and difficulty bearing weight on the affected extremity. Physical examination will often identify positive Lachman and anterior drawer tests, demonstrating an ACL-deficient knee. Radiographs of the knee typically show normal findings but may show an associated bony avulsion fracture of the tibial plateau. The diagnosis of an ACL

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tear is typically confirmed using magnetic resonance imaging, which will show ligament disruption with other possible associated meniscus or osteochondral injuries.

Patient Setup

The patient is placed supine on a standard operative table and anesthetized using general anesthesia. An arthroscopic lateral stress post is placed on the operative side of the table to provide leverage for the operative leg. A tourniquet is placed around the proximal thigh for safety in the case of excessive blood loss and to maximize visualization. The operative leg is prepared with preoperative skin preparation solution from the mid thigh to the foot and is then draped in the usual sterile fashion.

Arthroscopic Portal Placement

A 30° 4.0-mm arthroscope is used to perform a standard knee arthroscopy. The anterolateral portal is created with a No. 11 blade to make a vertical incision adjacent to the lateral border of the patellar tendon at the level of the joint line. The knee is then entered using a blunt trocar and arthroscopic sheath. The trocar is replaced with the arthroscope, and a complete diagnostic arthroscopy is performed, inspecting for associated chondral damage, loose bodies, or meniscus tears. A spinal needle is used to localize the anteromedial portal under arthroscopic visualization, and an incision is made in the same vertical fashion.

ACL Graft Preparation and Amnion Application

For allograft reconstruction, an appropriately sized SpeedGraft presutured tendon allograft (JRF Ortho, Centennial, CO) and ACL TightRope RT (Arthrex, Naples, FL) are prepared on the operating room back table. The graft is folded in half over a No. 2 FiberWire suture strand (Arthrex) and trialed through a graft sizing block to measure the graft diameter and ensure proper fit. The graft diameter is usually between 9.0 and 9.5 mm. The graft is then looped in half through the TightRope RT. A 3 × 6−cm Amnion Matrix Thick graft (Arthrex) (Fig 1) is placed around the graft with the epithelial layer facing the graft (Fig 2) and is slightly rehydrated with sterile saline solution as necessary (Fig 3). The Amnion Matrix Thick graft is sutured into place using multiple interrupted No. 2-0 Vicryl sutures (Ethicon, Somerville, NJ) to secure the matrix to the graft (Fig 4). The Amnion Matrix spans the graft from the proximal to distal end to allow surface contact with the femoral notch and tibial tunnel (Fig 5). These key steps are demonstrated in Video 1.

Tunnel Placement and Femoral Fixation

A 3-mm 90° radiofrequency ablation wand and No. 4-0 shaver are used to debride the femoral and tibial ACL footprints. An anteromedial-portal ACL guide is used to aim a spade-tip drill pin at the appropriate location over the femoral ACL footprint. The knee is hyperflexed, and the drill pin is fired through the femoral condyle; the width is then measured, and the pin is advanced through the skin. A low-profile reamer is used to drill an appropriate-depth tunnel, leaving a minimum of 7 mm of bone between the graft and button. A free suture is passed through the eyelet of the drill pin and then shuttled through the femoral socket, as the pin is removed laterally. The knee is brought to 90° of flexion, and a 1.5-cm incision is made approximately 2 cm medial and 3 cm distal to the tibial tubercle. The tibial drill guide, set to 55°, is placed through the tibial incision with the targeting guide placed in the anteromedial portal at the tibial ACL footprint. A drill pin is fired at the tibial ACL footprint in line with the posterior aspect of the anterior horn of the lateral meniscus. The tibial socket is then drilled, equal to the diameter of the graft, using the pin as a guide.

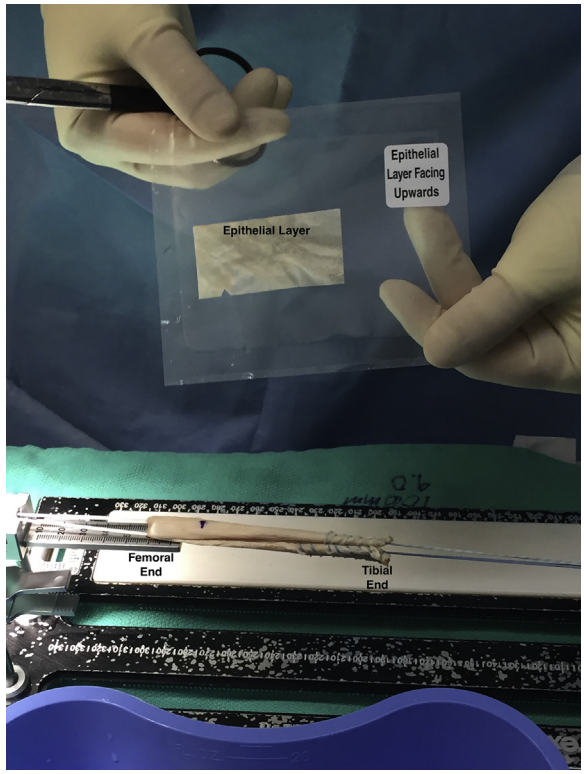

Fig 1. Sterilely packaged Arthrex Amnion Matrix Thick graft. The epithelial layer of the Arthrex Amnion Matrix is facing upward when the triangle notch is on the upper left-hand corner of the graft. The epithelial layer is facing the camera and will be wrapped around the anterior cruciate ligament allograft with this layer touching the graft.

ACL Graft Advancement and Tibial Fixation

The passing suture is pulled through the tibial tunnel and then used to advance the TightRope and graft with amnion through the tibial and femoral tunnels. The blue passing suture is used to advance the TightRope

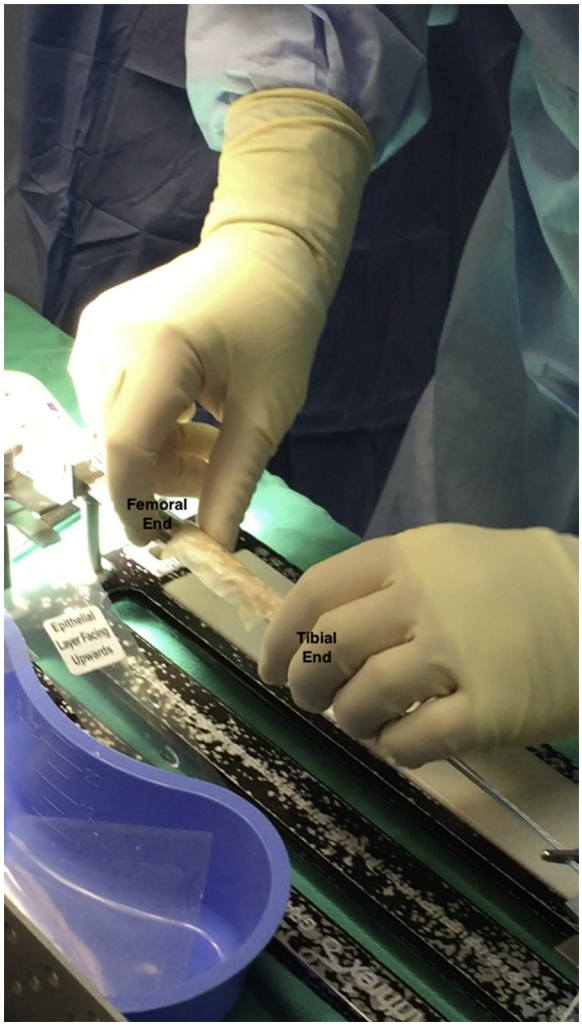

Fig 2. The Arthrex Amnion Matrix Thick graft is placed on the anterior cruciate ligament tendon allograft with the epithelial layer facedown, toward the graft. The amnion matrix is placed approximately 1 cm from the femoral end of the allograft.

button through the femoral tunnel, while tension is maintained on the ends of the white tensioning suture. During advancement of the graft, tension should be maintained on the tibial tails of the graft until the button has been pulled through the femur and has exited onto the lateral femoral cortex. To advance the graft, each of the white tensioning sutures is pulled 1 cm at a time, alternating both sides. This is done until approximately 5 mm of the proximal femoral socket remains, which is used for final tensioning of the graft. The knee is then cycled approximately 20 times to remove graft creep and seat the Amnion Matrix Thick graft. With the knee in 20° of flexion and a constant posterior drawer force applied to the knee, the tibial tunnel is increasingly dilated, using a GraftBolt dilator (Arthrex), until a tight fit is achieved. A GraftBolt sheath and screw (Arthrex) are selected, typically of equal diameter to the final dilator. While constant tension is maintained on the tibial tails of the graft and with an applied posterior drawer, the sheath is impacted into the tibial tunnel at the level of the anterior tibial cortex, using the aid of a guidewire. The screw is then inserted into the sheath and tightened with a driver until fully seated.

Final Examination and Postoperative Care

Lachman and pivot-shift tests are performed to examine knee stability. A final intraoperative fluoroscopic image of the distal femur and proximal tibia is taken to ensure the ACL button sits flush on the lateral femoral cortex and there is a desired tibial tunnel trajectory. The excess ACL graft is then excised so that it is flush with the tibial tunnel cortex. The wounds are irrigated and closed in the standard fashion. The knee is placed in a functional brace locked in extension immediately after surgery, until regional anesthesia has worn off. The brace is worn for a total of 6 weeks postoperatively. The brace is unlocked to a maximum

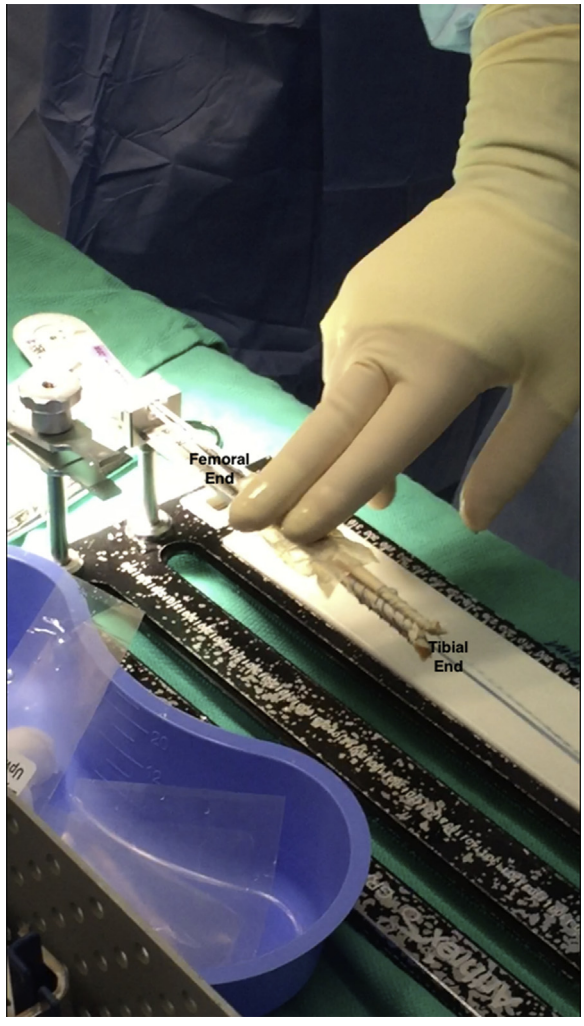

Fig 3. The Arthrex Amnion Matrix Thick graft is rehydrated as necessary to make the graft pliable and able to wrap around the anterior cruciate ligament tendon allograft.

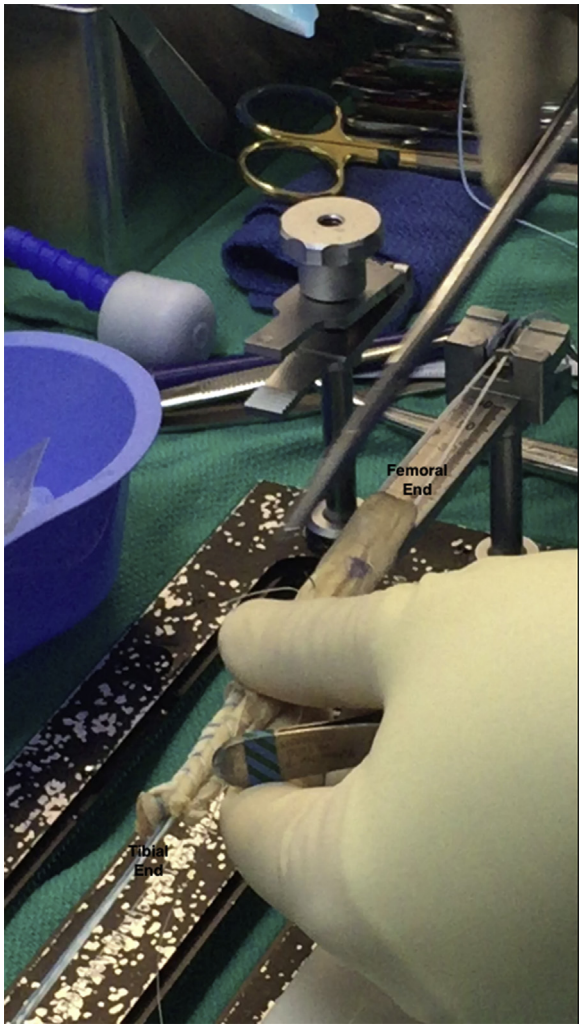

Fig 4. The Arthrex Amnion Matrix Thick graft is secured with simple interrupted Vicryl sutures from the femoral end to the tibial end of the allograft.

90° of knee flexion with gradual increased range of motion over the next 48 to 72 hours postoperatively.

Discussion

Tendon-to-bone healing of a reconstructed ACL is of tremendous importance after ACL surgery to decrease a patient's risk of ACL reconstruction failure.[7] Although there are multiple causes of ACL reconstruction failure, there are 3 early clinical signs and symptoms of failure: instability, continued effusion, and chronic pain.[7] Amnion biological augmentation may be able to reduce these signs and symptoms by improving biological incorporation and reducing the inflammatory response postoperatively.[6] Amniotic membrane–derived products have been studied and shown successful use in ophthalmology, plastic surgery, and wound care; however, amnion-derived products have had little application in ligament reconstruction.[6,8]

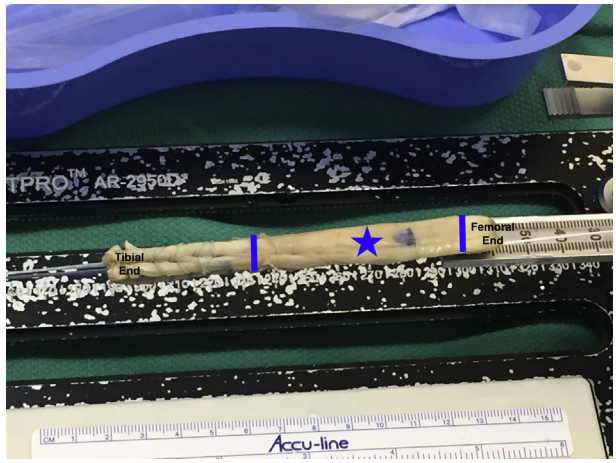

Fig 5. Pre-sutured allograft tendon (star) with Arthrex Amnion Matrix Thick graft sutured into place. The blue lines indicate the edges of the amnion graft.

The Arthrex Amnion Matrix is a semitransparent, collagenous membrane allograft derived from the amnion layer of the fetal membrane. The amniotic membrane contains and secretes extracellular matrix macromolecules including collagen (types I, III, IV, and V), growth factors, cytokines, and matrix proteins (Table 1).[10] Together, these aspects of the amniotic membrane have been proposed to have a multifactorial effect on wound healing.[6,8-11] The amniotic membrane has been shown to act as a scaffold for complex tissue regeneration and has been used as a biological scaffold for the treatment of skin defects since 1910.[6,8,11] The amniotic membrane's ability to act as a biological scaffold is attributed to its biocompatibility, permeability, stability, and ability to resorb.[11] The basement membrane of the amniotic membrane is the thickest in the human body, providing remarkable structural integrity.[10,11] The extracellular matrix of the amniotic membrane acts as a natural scaffold, providing adhesion, growth, and differentiation of the overlying stem cells.[11]

The amniotic membrane has been shown to be an important and ethical source of pluripotent stem cells.[11]

Table 1. Biomolecules Contained in Amnion

Type of Biomolecule	Biomolecule
Growth factors	HGF, IGF-1, IGF-2, TGF-β1, PDGF-BB, GRO-α, EGF, TGF-β2, bFGF, TGF-α, TNF-α
Cytokines	IL-1RA, IL-6
Chemokines	MCP-1
Protease inhibitors	TIMP-2, TIMP-3, TIMP-4

bFGF, basic fibroblast growth factor; EGF, epidermal growth factor; HGF, hepatocyte growth factor; IGF, insulin-like growth factor; IL, interleukin; MCP, monocyte chemoattractant protein; PDGF, platelet-derived growth factor; TGF, transforming growth factor; TIMP, tissue inhibitor of metalloproteinase; TNF, tumor necrosis factor.

Because the amniotic membrane undergoes continuous remodeling as the embryo develops, it has the innate ability to retain a reservoir of stem cells throughout the pregnancy.[10,11] The stem cells derived from the amniotic membrane have a distinct advantage over stem cells derived from embryonic tissue, in that the amniotic-derived cells do not show teratogenic transformation or pose harm to the fetus.[6,11] There are 2 types of stem cells produced within the amniotic membrane: amniotic epithelial cells (AECs) and amniotic mesenchymal stromal cells (AMSCs).[11] AECs have the ability to differentiate into all 3 germ layers (mesoderm, endoderm, and ectoderm), whereas AMSCs are derived from mesoderm and have the ability to differentiate into mature lineages.[11] Both AECs and AMSCs have the ability to differentiate into mature cell lineages for orthopaedic tissue engineering.[11]

The amniotic membrane has been shown to have anti-inflammatory properties.[6,8-11] The amniotic membrane contains intrinsic immunomodulatory properties that are related to the lack of major histocompatibility antigens and the production of anti-inflammatory cytokines.[10,11] The stem cells of the amniotic membrane have effects on both the innate and adaptive immune systems.[8,10,11] These effects lead to a decrease in antigen presentation, resistance to lysis of stem cells by natural killer cells, decreased proliferation of T cells, and variable effects on the concentration of circulating cytokines.[11] Furthermore, the anti-inflammatory properties of the amniotic membrane have been implicated in the amniotic membrane's ability to actively decrease adhesion formation and promote scarless healing.[6,8-11] The amniotic membrane inhibits transforming growth factor β, which is known to induce fibrotic responses through the activation of fibroblasts.[11]

Amniotic membrane has been reported to have antimicrobial effects; however, the mechanism is poorly understood.[11] Amniotic membrane has been documented to have efficacy against both gram-negative and gram-positive microbes.[11] These antimicrobial effects may be the result of secretion of antimicrobial molecules such as β-defensins and lactoferrin, or it may be that the amniotic membrane acts as a physical barrier against microbial inoculation.[11]

The addition of amniotic membrane to an ACL reconstruction has advantages and risks (Table 2). An additional benefit of amniotic tissue is that it is safely obtained and harvested after childbirth. Amniotic tissue is typically discarded after childbirth, and tissue harvesting does not pose any added risk to the mother or fetus. It is obtained with consent from healthy mothers during cesarean section delivery, processed using aseptic techniques, and then dehydrated. A risk of adding amnion allograft material to the procedure is the increased possibility of disease transfer from donor to recipient. However, acceptable tissue donors are screened and found to have negative results for human immunodeficiency virus, hepatitis B virus, hepatitis C virus, human T-cell lymphotrophic virus I or II, and syphilis; therefore, the increased risk of disease transfer is low.

Table 2. Advantages and Risks of Amnion Application

Advantages
Amniotic tissue is readily available, does not pose any additional threat to the fetus or mother, and is often discarded after childbirth.
Tendon wrapping with amnion is superior to collagen because amnion actively contributes to healing through growth factor production.
Amniotic biological augmentation has the potential to improve tendon-to-bone healing.
Risks
Increased cost of procedure
Increased time to prepare ACL graft during procedure
Increased risk of disease transmission with additional allograft material

ACL, anterior cruciate ligament.

Numerous in vitro studies and in vivo animal studies have shown promising outcomes of the application of amnion in orthopaedic cases.[6,7] Furthermore, tendon-wrapping applications of amnion have been reported, with studies showing decreased complication rates, reduced pain, and greater functional outcomes.[6,7] The potential of amnion biological augmentation to improve healing in ACL reconstruction through anti-inflammatory, scaffolding, and stem cell–producing effects should be further studied to determine whether this technique can improve patient outcomes.

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