Biologic Orthopedic Journal

Review Article
DOI: 10.22374/boj.v3iSP2.31

# TISSUE WRAPPING AUGMENTATION FOR ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: A REVIEW OF CLINICAL LITERATURE

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**Submitted: 3 August 2021. Accepted: 27 November 2021. Published: 20 December 2021**

**Abstract**

Anterior cruciate ligament reconstruction (ACLR) has become a popular surgery in orthopedic practice today, and the technique has evolved significantly over time. Surgical procedure, graft choice, and fixation systems have varied over the years. Nonetheless, several challenges like insufficient graft ligamentization, tunnel enlargement, and insufficient reestablishment of proprioception remain in ACLR. A vision of better graft healing and integration for improved outcomes after ACLR introduced the idea of the biological ACLR. Various techniques with growth factors, cellular therapies, or tissue augment have been researched with ACLR surgery for better integration and ligamentization. This review highlights the tissue wrapping modalities currently being explored in biological ACLR.

**Keywords**: *biological ACL*, *amnion*, *periosteum*, *tissue wrapping*

## INTRODUCTION

Because of the high incidence of anterior cruciate ligament (ACL) injury this has had an effect of increasing utilization of anterior cruciate ligament reconstruction (ACLR) surgery in orthopedic practice today.[1,2] ACLR evolved as an invasive procedure before the arrival of arthroscopy because there was no need for an arthrotomy. The development of fixation devices and methods has shown ACLR to become quite a streamlined procedure with good outcomes. Current shortcomings of this surgery include inconsistent graft integration, tunnel enlargement, and insufficient restoration of proprioception.[3–6] One of the primary reasons could be the poor vascularity in the intra-articular compartment, therefore reducing the number of cells and growth factors available for healing. Current graft choices in ACLR include tendons from muscles such as hamstrings, peroneus longus, quadriceps, and the bone patella bone tendon-bone graft (BPTB).[7,8] Among this BPTB, is the most popular followed by hamstring grafts. However, these are tendons used

to reconstruct ligaments. Therefore, when compared with each other, they vary in their structure and composition. These tendons must undergo a process of ligamentization, and the tendon must undergo osteointegration within the bone tunnels to perform comparably to a native ACL ligament.[4] To address the deficiencies in ACLR, researchers have turned to biological options and augmentation with cellular therapies, growth factors, and tissue engineering.[9] Tissue wrapping the tendon graft has been one such approach to enhance ACLR when using soft tissue hamstring grafts.[10] BPTB have bone plugs on either side of the graft, which allows the bone to bone growth and better integration. Tissue wrapping is being used to emulate the native ACL, which has a synovial lining around that potentially promotes its blood supply and improves its tunnel integration.[11] Tissues studied in the past include amnion and periosteum.[10,12,13] Synovium has also been postulated but is not formally reported. The idea is for this tissue to act as a fertilizer to improve graft integration. Our review aims to enumerate the explored tissues used in ACLR graft wrapping.

## PERIOSTEUM

The periosteum is the outermost covering layer of every bone in the entire human body and consisting of an outer fibrous layer and cambium inner layer with a considerable concentration of mesenchymal progenitor cells.[14] This layer has high osteogenic potential and is imperative for regular bone growth. This potential has been noted to vary with age and location of the tissue.[15] Preclinical rabbit models using bone tunnels and an ACLR model have shown positive results. In the bone tunnel models, the periosteum demonstrated a fibrovascular layer which allowed the cancellous bone in the tunnel to interdigitate with itself at 4 weeks postsurgery. At 8 weeks, there was excellent tendon to bone integration with collagen fiber-bone anchoring.[10] In the ACLR model, radiographs confirmed enhanced new bone formation and matrix deposition around the tendon-bone interface within the tunnels. At 8 weeks, there was further maturation of the bone tunnel interfaces with direct new bone apposition to the tendon.[16] As early as 1930, Burman and Umansky demonstrated an experimental model wherein a transplanted free periosteal flap wrapped around a tendon could promote bony ingrowth even at 2 weeks after wrapping.[17] These studies form the basis that wrapping the tendon with periosteum can promote earlier graft integration, reduce tunnel enlargement, and improve the pull-out strength of the graft. The wrapping also theoretically allows for a tighter snugger seal in the tunnel, reducing the amount of synovial fluid reflux within the tunnel that usually disrupts healing.[18]

With such evidence, a clinical study was performed by Chen et al.[10] using the periosteum from the anterior cortex of the tibia to wrap the ends of the semitendinosus and gracillis graft during ACLR. The periosteum is wrapped with the inner cambium layer facing outwards owing to its greater osteogenic potential. About 62 patients underwent ACLR with hamstring tendons wrapped in the periosteum and were followed up for 2 years. The mean Lysholm score increased from 59 to 94, which was a significant increase, and 81% of the patients were able to return to moderate to strenuous activities. Bone tunnel enlargement of more than 1 mm, was found in 5% of femoral tunnels and 6% of tibial tunnels. Wang et al.[19] performed a comparative study using single bundled ACLR with periosteal wrapping in 68 participants including 31 patients with periosteal wrapping and 37 with a normal ACLR. Patients were followed up for a mean of 26 months and assessed for tunnel enlargement using computer tomography and outcome scores. The outcomes showed that tunnel enlargement was significantly less in the periosteum-wrapped group (16%) than the normal ACLR group (37.8%) and concluded that periosteal wrapping could improve tendon to bone healing within the bone tunnels. Robert et al.[20] performed a comparative study between the periosteum-wrapped hamstring tendons versus those without ACLR. Their main objective was to study tunnel widening in 41 patients of which 21 underwent ACLR with the periosteal flap and 20 without. At 2.5 months and 11 months, a significantly less tunnel widening at the tunnel outlet in the periosteal flap group was noted; however, widening did occur in both groups. In

2010 another group reported a similar comparative study in 110 subjects with a 19-month follow-up. Of these, 52 received a periosteal wrapped hamstring graft, and both groups underwent standard ACLR. They reported a significantly lower incidence of tunnel enlargement in the periosteum group (17.3% vs. 34.5%).[21]

Preclinical studies are still being conducted to improve graft integration. The periosteum is the focus because of its easy availability during graft harvest without much donor site morbidity and cost-effectiveness. Recently magnesium pretreated periosteal grafts have shown improved osteointegration with improved pull-out strength and reduced tunnel enlargement. Further studies are needed to identify the biological mechanisms to optimize tendon-bone healing. Figure 1 shows a schematic demonstration of periosteal tissue sutures to the ends of a hamstring graft before a graft passage.

## AMNIOTIC TISSUE

Amnion and chorion are layers found in the placenta of a developing embryo. The amnion is the innermost layer, and the chorion is its adjacent layer.[22] Amniotic tissue, a vital part of embryonic development, is a potent source of stem cells and growth factors along with functioning as a scaffold with anti-inflammatory and antimicrobial properties.[23] The scaffold nature of the amnion also provides a matrix for cellular migration and proliferation. Amnion also allows for an ethical source of pluripotent cells as there is no need to sacrifice a blastocyst.[24] Amniotic tissue has been used immensely in medicine, but only a few studies have utilized it in ACLR. Preclinical data have suggested that amnion-derived cells can differentiate into ACL fibroblasts, and several culture techniques and growth factors can be used to upregulate ligament-specific genes.[25] Clinical reports of using amnion in ACLR are few, with clinical trials underway. Woodall et al.[12] described the technique of wrapping and suturing the intra-articular part of the ACLR hamstring graft with an amniotic membrane. Another technique using an amniotic membrane included the use of bone marrow aspirate concentrate (BMC) and a suture tape. The authors dubbed the fertilized ACLR technique, wherein an internal bracing was performed in addition to the hamstring ACLR, the graft was enveloped in an amniotic membrane graft and further BMC was injected into the tunnel sites and the amniotic-membrane covered ACL graft. The study stated all possible available biological advantage was applied to the hamstring graft to promote ligamentization and graft integration and reduce tunnel enlargement.[26] Levengood et al.[27] published a case report using amniotic membrane in ACLR. Here a postoperative magnetic resonance imaging (MRI) scan was performed at 3 months and 6 months. They noted early vascularization and maturation of the graft at 3 months, where the MRI demonstrated a graft with a uniform dark signal in the T2 MRI images.

At present, several animal trials have reported outcomes after the amniotic membranes use in

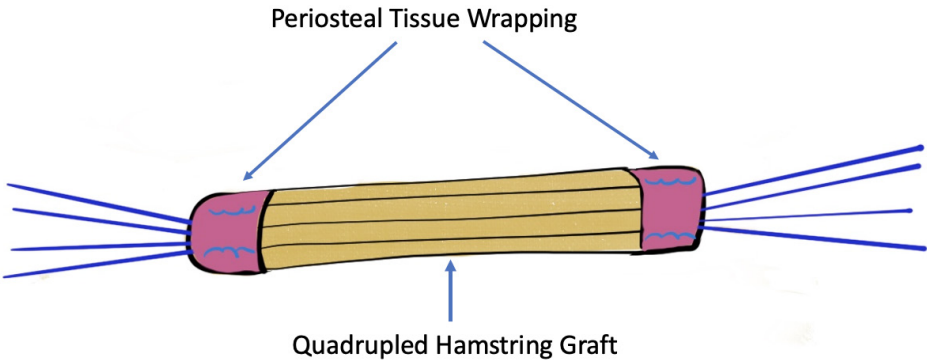


**Figure 1.** Schematic diagram showing periosteal tissue wrapping around the bone tunnel exposed parts of the hamstring tendon graft.

ligament reconstruction. Equine studies have shown reduced ligament reinjury rates when using amniotic cells.[28,29] *In vitro* studies remain the positive indicator for the use of amnion in ligament reconstruction, where amnion cells have shown the capability of differentiating into tenocytes with increased collagen production and cross-linking. Resulting in a graft with superior biomechanical characteristics and improving the subject's functional outcome and activity regain. In a clinical setting, we still do not have objective outcome data of the advantages of tissue wrapping with amnion. Figure 2 summarizes the harvest to implantation of amniotic tissue for graft wrapping.

## FUTURE DIRECTION

Tissue wrapping has been proposed for hamstring grafts mainly since they are purely soft tissue grafts and do not have bone plugs for tunnel integration. Research has shown that these grafts never become a bone within the femoral and tibial tunnels.[30] Wrapping the graft ends with periosteal tissues with high osteogenic potential may help stimulate the tissue to become a bone over time. On the other hand, amnion contains pluripotent mesenchymal stem cells, which can aid in osteogenic differentiation in the tunnels and ligamentization and graft maturation through the entire graft tissue. Growth factors such as platelet- rich plasma have been used in clinical studies with little objective outcome data; however, preclinical studies have shown benefit with the bone morphogenic proteins (BMPs) use in a rabbit model.[31,32] In these studies, BMP-2 was injected at the ends of the semitendinosus tendons of the hamstring graft before ACLR. Both studies showed new bone formation at the ends of the hamstring graft and superior pull-out strengths than the control group. This outcome could be an option in the future to address tunnel enlargement and improve graft fixation.

## CONCLUSION

Hypothetically, the concept of tissue wrapping to address the biological deficiencies in ACLR does seem to have a rationale. Fertilizing the hamstring graft with progenitor cells could improve its healing and biomechanical function addressing the present biological shortcomings of current ACLR. However, there is no compelling evidence for the use of amnion or periosteum in ACLR, and it remains to be determined with randomized trials that are underway. Delivery of growth factors may also play a role in the promotion of tunnel-bone healing. Future research is needed.

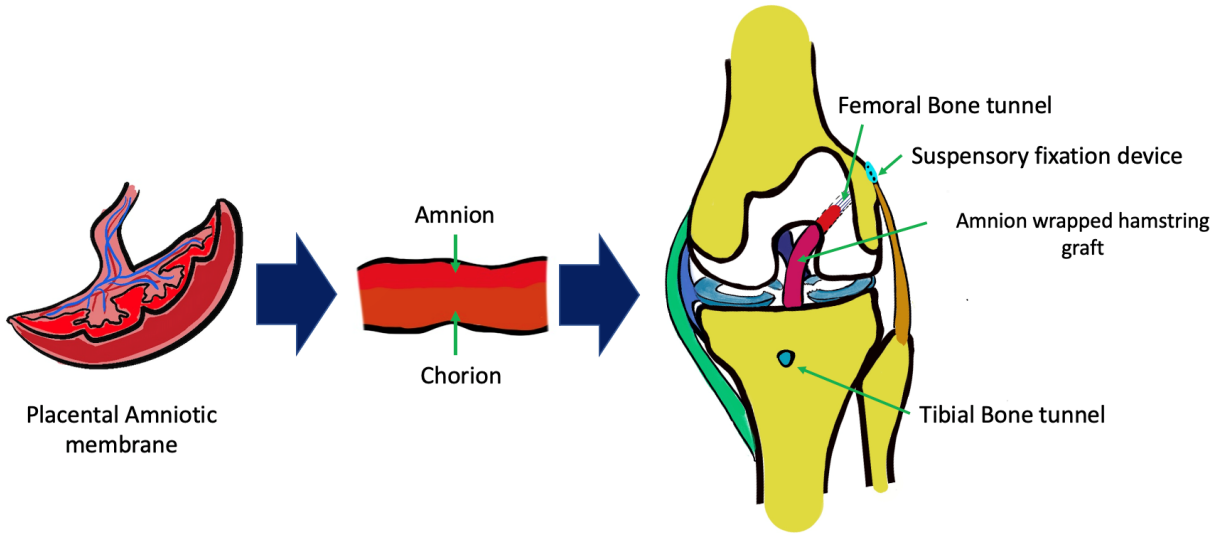


**Figure 2.** Amnion is harvested from placental membranes, and after processing the tissue is wrapped around the ACL graft with the amnion side facing inwards and the chorion side facing outwards.

## AUTHOR CONTRIBUTIONS

GJ and KS: Conception, design, acquisition of data, analysis, and interpretation of data.

GK, KS, KY, NN: article drafting and revising for critically important intellectual.

NN: Final article approval before publishing.

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