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The Cutting Edge: Bio-inductive Tissue Engineering in ACL Repair

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Introduction

According to the Cleveland Clinic, Americans experience nearly 200,000 anterior cruciate ligament (ACL) tears annually, making it among the most common orthopaedic sports injuries faced by athletes [1]. Functionally, ACL tear treatment requires restoring knee stability to withstand strain during the course of exercise. While more conservative, non-surgical rehabilitation is available for non-athletes and for low-pivot sports, surgery is often the preferred course of treatment to enable an athlete's active return to high-pivot sports. The current standard ACL reconstruction protocol requires surgical intervention, extensive rehabilitation, and a lengthy recovery of up to a year after surgery [2]. In addition, ACL reconstructions are costly and introduce the possibility of other early or late complications, including pain, stiffness, infection, residual instability, re-rupture, and, sometimes, delayed presentation of arthritis years later. Recent developments in the field of bio-inductive tissue engineering introduce resorbable implant-based interventions that can successfully achieve restoration of function in acute ACL injuries. This technique fosters the growth of new, native ACL tissue at the site of injury, which may produce better clinical outcomes for patients.

Across all sports, ACL injuries are most common in high-pivot sports such as basketball and soccer. The ACL tear is especially prevalent among children and young adults, who are at increased risk due to high participation in injury-prone sports that involve rapid movements and the potntial for blunt-force trauma. Female athletes are consistently found to be at significantly higher risk of experiencing an ACL injury, with ACL injury rates in soccer being two times higher and basketball four times higher for female athletes than their male counterparts (2). Research shows ACL injury peak rates in female athletes in their teens and early 40s and in male athletes in their early 20s [4].

Methods

ACL reconstruction, using graft tissue to reconstruct a new ACL, is the current standard of care of the treatment of ACL injuries in athletes. Autograft tissue is typically recognized as having higher levels of efficacy, lower failure rates, and lower procedural costs than allografts. Allografts offer some benefits, including a quicker operation, a less painful recovery, and a lack of donor site morbidity at the source of the graft tissue, but are accompanied by concerns including slower graft incorporation that could cause higher rates of failure, especially in young and active populations [5, 6]. Hamstring tendon (HT) or bone-patellar tendon-bone (BPTP) are the most common choices for donor tissue for ACL reconstruction and have varying failure rates (from 17.35% to 6.13% failure) [7] and varying return to sport rates for athletes [8, 9].

Thus, while a relatively successful procedure exists for athletes with ACL tears, there remains much room for improvement in tissue healing, time of recovery, and long-term failure rates. Advances in tissue engineering have introduced processes that aim to facilitate repairing, rather than replacing, the remaining ACL tissue post-injury. Rather than transplanting graft tissue from a remote site, tissue engineering procedures aim to facilitate the growth of new, native tissue that closely resembles the original ACL by using synthetic materials to augment a repair. The bio-inductive implants used in these procedures follow several common principles that ensure biocompatibility and successfully foster both the initial growth and the long-term viability of new tissue.

Typically, implants are designed with a function similar to scaffolding, such that they provide a structure along which natural tissue may begin to take hold. This speeds up the crucial but often lengthy process of independent cell growth into a structureless area. By serving as a scaffold, implants also provide protection to the young, fragile tissue against threats of injury from the outside world. The gradual incorporation of natural tissue into the scaffold over time provides another form of early short-term and, more importantly,

long-term protection. With artificial, implanted tissue, there is a risk of nascent tissue collapse when undergoing normal physiological stress, whereas, with tissue engineered solutions, a high level of incorporation of new biologic tissue within the scaffold circumvents this structural shortcoming. Thus, the tissue-engineered structure can withstand pressure more consistently and much more closely than the native tissue. New support implants are also designed to be biodegradable over a time period that complements projected native tissue growth. Eventually, the implant itself is biologically resorbed (or absorbed) naturally and replaced by strong native tissue as the collagen grows. This ensures that the initially soft tissue in the wound site is never left without the structural support provided by the scaffold but instead can remain dependent on the hybrid biologic framework as it is slowly replaced by new tissue ingrowth [10, 11].

Results

One such solution is the Bridge-Enhanced ACL Restoration (“BEAR”). Rather than serving solely as a bridge material to connect the remaining ACL remnants, the BEAR implant bridges the gap and also facilitates the primary biologic repair of an acute, fully torn ACL. Serving as a scaffold, the fully resorbable implant occupies this space between ACL fragments. Saturated with blood sampled from the patient (with the normal complement of bio-inductive nutrients and growth factors), it facilitates the growth and expansion of native cells and supporting structures throughout the scaffold. As the implanted scaffold itself slowly dissolves, new ACL tissue is formed in its place. The bio-inductive implant is fully replaced with cells supported by native collagen and blood vessel networks by approximately eight weeks post-operation. Since this process provides the structure necessary to allow the healing of the native ACL rather than transplanting tissue from a different part of the body, ACL treatment by BEAR implant has been shown to produce healthy tissue that more closely resembles native ACL than the aforementioned autograft procedures by the 24-month mark [12].

Conclusion

Further long-term studies on bio-inductive ACL repair to assess rates for post-procedure complications, return to sport, re-rupture, and delayed presentation of arthritis are still needed. However, early studies on tissue-engineered ACL repair are clearly promising, and, as a result, there has been a high early adoption rate amongst surgeons and athletes. Our newfound ability to grow replacement tissue will certainly change the treatment not just of ACL tears today but also of many similar injuries tomorrow.

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