

Current Concepts

Biologic Augmentation of Rotator Cuff Repair

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Rotator cuff tears are a common orthopaedic injury, affecting a substantial proportion of the population. Over the past two decades, surgical management of rotator cuff tears has evolved considerably, resulting in notable improvements in patient outcomes. Despite these advancements, retear rates remain a significant challenge for orthopaedic surgeons, prompting the development of techniques to augment rotator cuff repair (RCR). Using biologic agents, RCR can be augmented to improve long-term outcomes by increasing healing and durability. To evaluate the current landscape of biologic augmentation in RCR, a comprehensive literature review was conducted. This review describes the primary biologic augmentation modalities, including platelet-rich plasma, bone marrow-derived biologics, grafts, and bio-inductive patches, and examines their reported clinical outcomes and limitations to support informed clinical decision-making. Although biologic augmentation has demonstrated promising advancements and improved patient outcomes, further high-quality prospective randomized studies are necessary to standardize practice, given the variability in existing evidence.

INTRODUCTION

Rotator cuff tears are a common orthopaedic injury, affecting nearly 40% of individuals over the age 60.¹ Surgical management is frequently employed, with an estimated 250,000 rotator cuff repairs (RCR) performed annually in the United States.² The widespread adoption of arthroscopic RCR techniques brought improvements in patient outcomes.³ However, despite these technical advances, retear rates remain a challenge, with short-term rates approximately 10-20% and substantially higher rates observed at longer-term follow-up.⁴⁻⁷

Retears following RCR can occur at the bone-tendon interface or more medially at the musculotendinous junction. These failures can be influenced by factors such as age, surgical repair construct, or poor tendon quality from fatty infiltration and muscle atrophy.^{8,9} Postoperative healing is frequently suboptimal, demonstrated by a meta-analysis of approximately 100 studies encompassing more than 8,000 patients, which reported an average retear rate of roughly 26% at two years.¹⁰ Collectively, these findings underscore the limitations of mechanical fixation alone and highlight the need for strategies that enhance the biologic environment at the repair site.

In response to these challenges, biologic augmentation has emerged as an adjunct to RCR to improve tendon healing and long-term durability. Accordingly, the purpose of this review is to provide an overview of contemporary biologic augmentation techniques used in RCR. Specifically, this review will discuss platelet-rich plasma (PRP), bone marrow-derived biologics, grafts, and bio-inductive patches (BP), with an emphasis on their proposed mechanisms, clinical outcomes, and limitations to inform clinical decision-making.

REVIEW

ROTATOR CUFF HEALING BIOLOGY

Biologic augmentation aims to address specific elements of the injury microenvironment. Insight into this microenvironment and the normal healing process guides which strategy may be most appropriate for a given patient. The rotator cuff tendon is mainly type 1 collagen produced by tenocytes, with progressively decreasing vascularity from muscle to tendon.^{11,12} This transition from muscle to tendon and ultimately to the humeral insertion consists of four distinct tissue zones critical for effective load transmission and resistance to tensile forces.¹³

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Following injury, tendon healing occurs through three phases: inflammatory, proliferative (fibroblastic), and remodeling.¹⁴ During the inflammatory phase, platelet activation results in fibrin and fibronectin deposition and the release of growth factors such as insulin-like growth factor-1 (IGF1), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF- β), which recruit neutrophils and macrophages.^{14,15} Macrophages subsequently secrete additional TGF- β , activating myofibroblasts and promoting scar tissue formation. Concurrently, mesenchymal stem cells (MSCs) are recruited and may differentiate into tenocytes or myofibroblasts.¹⁶ The proliferative phase occurs within 2 days up to 6 weeks of the injury and is followed by the remodeling phase, characterized by the gradual replacement of type III for type I collagen for a more organized matrix.¹⁵

Despite this orchestrated healing response, orthopaedic surgeons face baseline tendon-to-bone healing challenges, as the muscle tendon unit is compromised following the cascade of alterations initiated during a full-thickness tear.^{17,18} Fat accumulation and atrophy of the muscle result in musculotendinous retraction and fibrosis, compromising healing potential.^{18,19} Furthermore, the native cellular heterogeneity is disrupted along with its biomechanical properties and replaced with fibrovascular scar tissue. Animal studies demonstrate this concept, as the fibrovascular scar includes a large amount of biomechanically inferior type III collagen and is without the zone of calcified cartilage, making it more prone to failure.²⁰ These alterations likely contribute to the persistently high retear rates reported in the literature, particularly in large, chronic, or revision tears. As a result, biologic augmentation is most commonly considered in these high-risk scenarios.²¹⁻²³

PLATELET-RICH PLASMA (PRP)

Given the central role of growth factors in the early phases of tendon healing, PRP has gained attention as a biologic adjunct to RCR. PRP refers to autologous blood products processed to achieve a higher concentration of platelets. Upon activation, platelets secrete numerous growth factors that may participate in tissue repair.²⁴ These growth factors have been shown to support tissue regeneration by activating stem cells, modulating inflammation, and promoting angiogenesis.²⁵ Additionally, these growth factors have been shown to increase tenocyte proliferation within the rotator cuff and stimulate the synthesis of key extracellular matrix proteins.²⁶

Building on these biological principles, multiple clinical studies have evaluated the effect of PRP augmentation on RCR outcomes. A meta-analysis by *Trantos et al.*, which included 25 clinical trials (16 randomized), reported a 22% reduction in retear risk with PRP augmentation compared to controls.²⁷ Similarly, *Lavoie-Gagne et al.* demonstrated that PRP use in double-row repairs reduced retear risk by 56%.²⁸ A systematic review of 13 meta-analyses further supported these findings, reporting lower retear rates and improved functional outcomes with PRP augmentation.²⁹

However, the influence of tear size on PRP efficacy remains less clear. While *Sánchez-Losilla et al.* found no sig-

nificant difference in either small-to-medium or large-to-massive tears,³⁰ other meta-analyses have reported improved outcomes primarily in smaller tears.^{31,32} In contrast, a randomized controlled trial by *Jo et al.* demonstrated lower retear rates in large tears augmented with PRP (20%) compared with the control group (56%).³³ These conflicting findings highlight the heterogeneity of the existing literature.

Despite encouraging results, no consensus exists regarding the routine use of PRP in RCR.³⁴ The lack of standardization in the processing and administration of PRP presents a unique challenge. Contributing factors to this major limitation include differences in dosing regimens, variability in platelet concentrations, unaddressed clinical characteristics of the patient, as well as differences in reporting of preparation protocols.³⁵

STEM CELLS & BONE MARROW DERIVED BIOLOGICS

Augmentation of RCR with bone marrow-derived biologics aims to enhance healing at the repair site. Through the regenerative potential of MSCs found in the bone marrow, the environment at the tendon-bone interface has the potential to be enhanced.³⁶ Techniques for augmenting RCR with bone marrow-derived biologics have been described through the use of bone marrow stimulation (BMS) or bone marrow aspirate concentrate (BMAC).

BMS can be described as promoting the release of local growth factors and MSCs through creating channels between the bone marrow and tendon footprint.³⁷ The utilization of BMS is practical as the MSCs and growth factors can be released directly from the surgical site. Although technically straightforward, clinical outcomes have been inconsistent. A meta-analysis by *Le Breton et al.* demonstrated that patients who received BMS had significantly lower retear rates and better patient outcomes, as measured by the Constant score, compared with those who did not.³⁸ In contrast, another meta-analysis of randomized clinical studies of BMS reported no difference in patient outcomes or healing rates.³⁹ These discrepancies in results across studies likely reflect the variability in techniques and patient selection.

Similar to BMS, BMAC enhances healing at the tendon-bone interface, which must be harvested. BMAC is harvested from the intramedullary canal of one of three sites (proximal tibia, iliac crest, proximal humerus),⁴⁰ followed by processing of the specimen prior to use. Pre-clinical studies have demonstrated favorable histologic and biomechanical effects.^{41,42} Clinically, *Hernigou et al.* reported improved tendon integrity and significantly lower retear rates in small and medium-sized tears at 10-year follow-up in patients who received BMAC vs the control group (87% vs 44%).⁴³ Similarly, in an analysis of a national database, *Schoch et al.* found that patients who received BMAC during RCR were significantly less likely to undergo revision than those without augmented RCR with BMAC.⁴⁴ In contrast, *Cole et al.* found in a randomized controlled trial that clinical outcomes were not significantly different at 2-year follow-up; however, enhanced tendon integrity was seen

in BMAC augmented RCR on postoperative magnetic resonance imaging.⁴⁵

Practical limitations of BMAC include specimen harvesting and processing, which require a separate procedure and specialized equipment. Furthermore, harvesting the specimen might prove difficult in site-specific locations, such as the proximal humerus, particularly in the elderly population. High-quality evidence studies are still required to determine whether the age-related decline in MSCs affects outcomes in age-stratified populations undergoing RCR.

GRAFTS AND BIO-INDUCTIVE PATCHES

Grafts have emerged as another option to address the high failure rates in RCR. Grafts can be placed by means of interposition for irreparable tears, in which you bridge bone to native tendon, or by means of on-lay for a reparable tear.⁴⁶ The purpose is twofold, as it can enhance mechanical integrity while also serving to supply the framework for new tissue growth; however, it is not to the extent of native tendon development.⁴⁷ Grafts used for on-lay or interposition grafting purposes have been described as either allograft, xenograft, or synthetic. Allografts are derived from human dermis and undergo decellularization, leaving behind an extracellular matrix that provides structural support for soft tissue repair.⁴⁸ Xenografts used have been derived from tissue such as porcine dermis and bovine dermis.⁴⁹ There are different types of commercially available synthetic grafts, while the focus of this paper will remain on biologics.

When used via an on-lay technique, allografts form an acellular extracellular matrix that provides a framework to promote host cell infiltration and vascular ingrowth.⁵⁰ Clinical studies have demonstrated promising results. For example, *Barber et al.* observed a retear rate of only 15% in patients who received an allograft, compared with 60% in patients who received arthroscopic repair alone at 2-year follow-up.⁵⁰ Similarly, *Gilot et al.* demonstrated a retear rate in 10% vs 26% in the control group at roughly 2-year follow-up, along with improved patient outcome scores.⁵¹ However, small patient sample sizes were seen in both of the prospective studies discussed here. Xenografts used for on-lay serve as a scaffold through the acellularized ECM and are proposed to propagate collagen deposition by stimulating the host's inflammatory response.⁴⁹ Variable results have been reported in studies using porcine small intestine submucosa grafts to repair large, massive rotator cuff tears. *Iannotti et al.* and *Walton et al.* reported retear rates of 73% vs 40% and 60% vs 58%, respectively, in the xenograft vs control groups, along with worse outcomes.^{52,53} Whereas a study by *Castagna et al.* reported more favorable findings with porcine acellular dermal matrix, with a retear rate of 21.9% in the xenograft group vs 33.3% in the control group.⁵⁴ However, as demonstrated by *Oettl et al.* in a meta-analysis, xenograft offered no improvement in healing and a threefold increase in complications leading to their disuse.⁵⁵

In contrast to the on-lay technique of grafts, interposition grafts bridge the space between torn rotator cuff and the native insertion on the humerus. The role of allograft

interposition for massive irreparable rotator cuff tears has been studied, with good short-term outcomes. *Wong et al.*, in a randomized controlled trial, found that patients who had large or massive rotator cuff tendon repair with dermal allograft interposition were significantly less likely to retear and showed improvement in patient-reported outcome scores at 2 years compared with maximal repair.⁵⁶ In long-term follow-up of 45 patients, *Modi et al.* observed 39 of those patients to have positive outcomes without requiring revision surgery.⁵⁷ Clinical outcomes vary widely despite the favorable outcomes discussed with acellular dermal allograft interposition.⁵⁸⁻⁶²

Bio-inductive xenografts or BPs are similar to traditional xenografts, which act as structural support, while BPs are processed to actively induce the growth of organized tissue and act as a scaffold that eventually resorbs. Evidence has been presented demonstrating the benefits of highly porous bio-inductive collagen implants used in partial- and full-thickness tears through objective measures, such as increased tendon thickness observed on histology or MRI.⁶³⁻⁶⁶ *Thon et al.* in a case series of 23 patients undergoing RCR for full-thickness tear augmented by bio-inductive collagen patch, observed a 96% healing rate seen on magnetic resonance imaging (MRI) and ultrasound, and recorded a 9% clinical failure rate at 2 years.⁶⁷

Although positive outcomes have been reported among grafts and BPs, the quality of the evidence is limited. Many of the studies have small sample sizes and report variable functional benefits. Additionally, demonstration of improved structural outcomes does not guarantee translation to improved clinical outcomes. The variability in the reported evidence is likely heavily influenced by patient factors that are difficult to account for, such as tendon quality, chronicity, and tear size. These challenges underscore the need for improved patient stratification and higher-quality evidence.

INDICATIONS & DECISION-MAKING IN CLINICAL PRACTICE

Given the variability in outcomes across biologic augmentation strategies, no formal guidelines exist for their routine use in RCR. Instead, augmentation techniques should be considered on a case-by-case basis, dependent on factors such as tear size, chronicity, tendon quality, and risk factors for failure. Development of algorithms to identify patients at high risk for failure, versus those for whom primary repairs may heal without augmentation, should be established to assist surgeons in decision-making. The major biologic augmentation strategies discussed in this review are summarized in [\[Table 1\]](#).

CONCLUSION

Biologic augmentation of RCR is a rapidly evolving and multifaceted field with demonstrated potential to improve tendon healing and clinical outcomes. Both hematologic and structural biologic strategies have shown promise, with human dermal allografts emerging as one of the more con-

Table 1. Summary of Biologic Augmentation Strategies in Rotator Cuff Repair

Modality	Proposed Mechanism	Clinical Outcomes	Limitations
Platelet-Rich Plasma (PRP)	Autologous platelet concentrate releasing growth factors (e.g., PDGF, TGF- β , IGF-1) that promote tenocyte proliferation, angiogenesis, and extracellular matrix synthesis.	Modest improvements in functional scores and reduced retear risk reported in systematic reviews; benefits may be greater in smaller tears.	Lack of standardization in preparation, platelet concentration, and delivery; heterogeneous study designs limit consensus.
Bone Marrow Stimulation (BMS)	Microfracture or channeling at the rotator cuff footprint to release marrow-derived MSCs and growth factors to enhance tendon-bone healing.	Mixed findings; some meta-analyses report improved Constant scores while others show no significant difference compared with standard repair.	Variability in surgical technique and patient selection; inconsistent clinical evidence regarding healing and functional improvement.
Bone Marrow Aspirate Concentrate (BMAC)	Concentrated MSCs and biologic factors harvested from bone marrow and applied to repair site to enhance tendon-bone regeneration.	Long-term studies report reduced retear rates and lower revision surgery rates; however, some randomized trials show no difference in functional outcomes.	Requires additional harvesting and processing; increased in operative time and cost; potential variability in MSC yield, particularly in older patients.
Allograft	Decellularized extracellular matrix scaffold that provides mechanical reinforcement and facilitates host cell infiltration, neovascularization, and collagen deposition.	Improved patient-reported outcomes and lower retear rates in several small prospective studies.	Limited by small sample sizes and heterogeneity of studies; cost considerations; long-term outcomes remain limited.
Xenograft	Acellular biologic scaffold intended to stimulate host inflammatory response and collagen deposition while reinforcing repair.	Clinical outcomes inconsistent, with some studies demonstrating worse outcomes and higher complication rates.	Higher complication rates reported in meta-analyses; inconsistent healing outcomes; largely fallen out of favor in current practice.
Bio-inductive Patch	Highly porous collagen scaffold designed to induce formation of organized tendon-like tissue.	Early studies demonstrate favorable clinical scores and low failure rates at short-term follow-up.	Evidence largely limited to small case series and short-term follow-up; need for larger comparative studies to determine long-term benefit.

sistently favorable options. However, widespread adoption is limited by heterogeneity in study designs, biological preparations, and patient-related variables. Future research should focus on large, multicenter randomized controlled trials with standardized biologic definitions and long-term follow-up to more clearly define the role of biologic augmentation in RCR.

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