18 Augmenting Rotator Cuff Repairs with Scaffolds

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18.1 Introduction

Rotator cuff pathology is one of the most common musculoskeletal disorders, affecting as many as 17 million people in the United States [1–5] and accounting for more than 4.5 million physician visits per year [6]. Rotator cuff repair (RCR) is one of the most common orthopedic procedures performed. The number of RCRs has steadily increased over the past 2 decades, with between more than 460,000 repairs performed each year in the United States, with an estimated total cost between US$3 billion and US$12 billion [5, 7–12].

Despite the advances in surgical technique, instruments, and implants to repair rotator cuff tendon tears, studies suggest that failure after RCR occurs frequently, early, and with or without an anatomic full-thickness tissue defect [13–17], with the risk of re-rupture ranging from 20% to 60% [18, 19]. While it has been demonstrated that failure of rotator cuff tendons to heal is often associated with acceptable pain relief, most studies have shown higher patient-reported outcome scores, range of motion, and strength when the repair heals [13, 18–28]. It has been suggested that early RCR failures occurring 4–6 weeks postoperatively represent an inability of the surgical construct to mechanically maintain the integrity of the repair site, with biologic factors likely playing a small role in the healing process and thus contributing minimally to the strength of the repair [13]. Mechanical augmentation using extracellular matrix (ECM) materials—namely in the form of a graft of tissue or synthetic material (commonly referred to as a "patch") may be useful in minimizing these early mechanical RCR failures [29].

In contrast, later RCR failures occurring 3–6 months postoperatively likely result from mechanical stresses at the repair site caused by patients' attempts to regain motion and strength. These likely signify a biologic failure to heal [13]. Grafts can also provide a scaffold for delivering biologic therapies (e.g., platelet-rich plasma (PRP) or cell seeding) to augment tendon healing at the operative site while also providing a load-sharing device. This load-sharing and a more organized healing environment is thought to

Note: *Scaffold:* A temporary structure that is put in place to help build a permanent structure; scaffolds are expected to be removed or resorbed through the process they are supporting.
Graft: A segment of tissue or material used to support, or restore missing tissue, usually with favorable biomechanical properties, not expected to be complete resorbed but instead incorporated into the site. A graft can also serve in some capacity as a scaffold.

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prevent scar tissue formation at the tendon-bone interface and encourage growth of functional tissue comprised of tenocytes, chondrocytes, and osteocytes [29, 30].

As a result of the large number of RCRs performed annually and the high rate of structural failure, considerable efforts have been devoted to developing grafts that augment the RCR site by mechanically reinforcing it as well as providing a biological scaffold that can enhance the rate and quality of the healing process [13]. Because the ECM of the graft directly interacts with tissue microenvironments for stem cell proliferation, it is necessary to consider the design of the patch and how it affects cell differentiation [30]. Prior studies have shown that the composition of microenvironments alters cellular adhesion, differentiation, and morphology [30–35]. Since Neviaser et al.'s [36] first use of the interposition allograft for RCR, various graft types have expanded to include synthetic polymers, allograft, autograft, and xenograft materials with varying degrees of clinical success [37]. Common disadvantages to these efforts have included fibrous cartilage formation, strong inflammatory reactions, or rapid degradation of the graft.

The purpose of this chapter is to present the current options and clinical outcomes of synthetic grafts used to augment biological healing in RCR.

18.2 Allografts for Patch Augmentation

Multiple studies have investigated the efficacy of allografts for patch augmentation in RCR, particularly for massive rotator cuff tears. When discussing patch augmentation, it is imperative the surgeon understands the purpose and proper use of the patch. These patches can be used to provide structural integrity to the repair site, increasing the load to failure over a repair of diseased tendon alone, as well as a biological enhancement of the repair to improve healing at the repair site. However, some grafts add little mechanical support and are primarily used as a biological scaffold providing an improved retention of growth factors and cells responsible for the healing cascade. This is an important differentiation, and the surgeon should understand this so that the patch is used in the proper way. Several acellular human dermal matrices are commercially available, with one in particular (GraftJacket; Wright Medical Technology, Arlington, TN) receiving the most attention in the literature. Galvin et al. [38] note that other preliminary studies have investigated an alternative acellular human dermal matrix product, including the Arthroflex patch (Arthrex, Naples, FL), though larger studies are recommended [39]. The human dermal matrices form an acellular collagen ECM scaffold intended to provide an organized framework for host cell infiltration, vascular ingrowth, and later tissue remodeling [38, 40].

Burkhead et al. [41] evaluated 17 patients with massive rotator cuff tears who were treated with a standardized open repair technique with GraftJacket augmentation. At an average follow-up of 1.2 years, the authors reported a 25% retear rate, yet significant improvement in pain scores, UCLA scores, and active forward flexion. Barber et al. [40] found similar results in a randomized, multicenter prospective level II clinical trial comparing 22 patients undergoing GraftJacket augmentation of chronic 2-tendon rotator cuff tears with 20 patients undergoing arthroscopic repair alone. Follow-up at 12 months showed retear rate of 15% in the augmented group and 60% in the control group, as well as significant improvement in outcome scores (American Shoulder Elbow Society, Constant). No adverse reactions were recorded.

Agrawal et al. [42] performed a retrospective case series of the clinical and structural outcomes (1.5 T MRI) of arthroscopic rotator cuff repair with acellular human dermal graft Allopatch HD (MTF Sports Medicine, Edison, NJ) in 14 patients with large, massive, and previously repaired rotator cuff tears. The retear rate was 14.3% and the Constant–Murley score increased from 49.72 to 81.07 ($P = 0.009$). Pain scores improved from 13.57 to 7.73 ($P = 0.008$). Flexilevel scale of shoulder function improved from 53.69 to 79.71.

Despite the clinical successes of some allografts, important disadvantages of this repair modality include difficult accessibility in some regions, location-dependent regulation, concerns regarding sterilization techniques, high costs, as

well as increased technical difficulty in augmenting a repair with a patch when compared to RCR alone. While not reported in many studies, there is also the possibility for rejection of the graft with resorption or increase inflammation and pain.

18.3 Xenografts for Patch Augmentation

Xenograft augmentation of RCRs relies on the premise that acellularized ECM will provide a scaffold to stimulate the host inflammatory response and collagen deposition in order to strengthen tendon healing [38]. Many xenografts have been studied with variable results [43–48].

The porcine small intestine submucosa (Restore Orthobiologic Implant; DePuy, Warsaw, IN) has been thoroughly studied. Iannotti et al. [48] compared the effectiveness of the porcine xenograft augmentation versus a control group without augmentation in 30 shoulders with chronic 2-tendon rotator cuff tears. Results at 1-year follow-up revealed the rotator cuff healed in only 27% (4/15) of augmented shoulders compared to 60% (9/15) in the control group ($P = 0.11$). Clinical outcome scores were worse in the augmentation group and therefore, use of this patch was not recommended for massive rotator cuff tears. Walton et al. [47] performed a similar prospective study confirming these findings.

Bokor et al. [43] demonstrated magnetic resonance imaging (MRI) evidence of partial-thickness rotator cuff tear healing following treatment with a highly porous collagen implant arthroscopically placed over the bursal surface of the supraspinatus tendon. Patients with intermediate- to high-grade bursal, articular, or intrasubstance partial-thickness tears of the supraspinatus tendon demonstrated no tear progression and showed progressive filling in of the defects coupled with improvement in tendon quality through 2-year follow-up. As previously mentioned, the mechanism of action for this healing response is thought to be related to the ability of the collagen implant to induce new host tissue formation and ingrowth over the bursal surface of the tendon [43, 49, 50]. This increase in tendon thickness is thought to improve the local biomechanical environment of the tear by reducing tendon strain and therefore optimizing its healing potential.

Schlegel et al. [50] performed a prospective multicenter trial using a similar protocol in the United States, enrolling 33 patients with chronic, degenerative, intermediate-grade ($n = 12$), or high-grade ($n = 21$) partial-thickness tears (11 articular, 10 bursal, 4 intrasubstance, and 8 hybrid) of the supraspinatus tendon. Following arthroscopic subacromial decompression without repair, the bioinductive xenograft collagen patch was attached over the bursal surface of the tendon. The implant was made from highly purified type I bovine collagen and engineered into a highly oriented, highly porous (85%–90% porosity) scaffold that was approximately 2 mm thick once hydrated. Also included in the repair were polylactic acid tendon staples and polyether ether ketone bone staples (Rotation Medical, Plymouth, MN, USA).

Clinical outcomes were assessed using American Shoulder and Elbow Surgeons and Constant–Murley scores preoperatively and at 3 and 12 months, postoperatively. MRI was performed to assess postoperative tendon healing and thickness at the original tear site [50]. They similarly reported improvements in outcome scores ($P < 0.0001$), no tear progressions, and 94% of patients with either no progression of tears or a reduction in defect size after 1 year. MRI of complete healing was found in 8 patients and a considerable reduction in defect size was shown in 23, whereas 1 lesion remained stable. The authors concluded that arthroscopic implantation of the highly porous and purified type I bovine collagen scaffold is safe and effective for treatment of intermediate-grade to high-grade partial-thickness rotator cuff tears of the supraspinatus tendon [50].

Thon et al. [51] also reported high healing rates (96%) and sufficient functional outcomes following insertion of the same xenograft collagen patch during repair of 23 large and massive rotator cuff tears.

Other studies, however, have demonstrated higher retear rates with different collagen patches. Ciampi et al. [46] demonstrated a retear rate of 51% at 1-year follow-up when using a collagen patch for augmentation. Their findings are more consistent with Muench et al.'s [52] results, as

59% of patients in that study did not meet the substantial clinical benefit criteria for ASES at terminal follow-up and were thus considered clinical failures. Muench et al.'s results should be understood in the context of the study group which was comprised of 40% smokers and 23% diabetics, with all having had at least 1 previously failed cuff repair.

While these results are promising, there are some downsides to xenografts including lack of integration into host tissue, cost and risk of disease transmission. While xenografts have been used for quite some time in other surgical procedures, their use in RCR augmentation is still relatively new and should continue to be studied to determine their long-term benefits.

18.4 Synthetic Grafts for Patch Augmentation

Synthetic grafts for augmentation of RCR are intended to mechanically offload the repair site at surgery and during the initial period of healing after repair. Unlike human-derived ECM grafts, which are considered human tissue for transplantation and thus do not require clearance from the US Food and Drug Administration (FDA) if minimally manipulated and intended for homologous use, synthetic devices must undergo the FDA 510(k) regulatory process [13]. This entails demonstration of equivalence to other devices in performance, biocompatibility, safety, stability, sterility, and packaging.

The theoretical benefit of synthetic patch augmentation of RCRs is that the graft is immune tolerant may provide additional mechanical strength, while still serving as a scaffold for host tissue response and ECM ingrowth [38, 53]. However, given the variety of material composition and morphology of synthetic scaffolds—including size, shape, porosity, and roughness—various immune responses can be elicited [54, 55]. A number of animal, cavaderic, and clinical studies have been performed on graft and scaffolds for RCR.

Van Kampen et al. [49] cultured reconstituted collagen scaffolds made from highly purified type I collagen from bovine tendons (Collagen Matrix, Inc., Oakland, NJ) [56, 57] to the surface of the infraspinatus tendons of 23 adult sheep. Histology demonstrated complete ingrowth with fibrovascular tissue by 6 weeks and by 12 weeks the scaffold had induced the formation of a layer of dense, regularly oriented collagenous tissue which significantly increased the thickness of the native tendon. This new tissue was well-integrated into the host tissues at both the bone interface and along the length of the tendon. At 26 weeks, the scaffold was completely absorbed into the native bone, leaving a stable layer of mature tendon-like tissue over the surface of the host tendon which was still present at 52 weeks. The bony insertion of the new tissue demonstrated evidence of a fibrocartilaginous component that suggested a normal, direct insertion. It was therefore concluded that use of a reconstituted collagen scaffold consistently increased the thickness of a rotator cuff tendon by inducing the formation of a well-integrated and mature tendon-like tissue.

McCarron et al. [58] evaluated a poly-L-lactic acid (X-Repair; Synthasome, San Diego, CA) device for augmentation of repairs in 8 pairs of human cadaveric shoulders. Yield load was 56%–92% higher and ultimate load was 56%–76% higher in augmented repairs. No increase in initial stiffness was found. Failure by sutures cutting through the tendon was reduced, occurring in 17 of 20 non-augmented repairs but only 7 of 20 augmented repairs. These data showed that application of the poly-L-lactic acid device significantly increased the yield load and ultimate load of a primary RCR across all of the supraspinatus tendon and the upper half of the infraspinatus tendon but did not affect initial repair stiffness.

Several studies have evaluated both absorbable and non-absorbable synthetic patch augmentation options. These devices include the poly-L-lactide patch (X-Repair; Synthasome), polypropylene patch (Repol Angimesh, Angiologica BM Srl, Pavia, Italy), and a non-absorbable reticulated polycarbonate polyurethane patch (Biomerix, Fremont, CA). There are variable outcomes after synthetic patch augmentation, with retear rates ranging from 10% to 62% [46, 59–61]. A more comprehensive list of devices and studies are listed in Tables 18.1 and 18.2.

Table 18.1 Commercially available synthetic and biosynthetic scaffolds

Scaffold type	Company	Composition
Synthetic		
BioFiber	Tornier (Edina, MN)	Poly (4-hydroxybutyrate)
Integraft	Hexcel Medical (Dublin, CA)	Carbon fiber tow
LARS ligament	LARS (Arc-sur-Tille, Burgundy, France) Dacron Xiros (Leeds, UK)	Polyethylene terephthalate
Marlex	C.R. Bard (Mullayhill, NJ)	High-density polyethylene
Mersilene mesh	Ethicon, Inc. (Somerville NJ)	Polyethylene terephthalate
Poly-tape	Neoligaments (Leeds, UK)	Polyethylene terephthalate
Repol Angimesh	Angiologica BM Srl (Pavia, Italy)	Polypropylene
Teflon	Dupont Company (Wilmington, DE)	Polytetrafluoroethylene
X-repair	Synthasome (San Diego, CA)	Poly-L-lactic-acid
Nanofiber, unwoven	Atreon Orthopedics. (Columbus, OH)	Polyglycolic acid (PGA) and Polylactide-co-caprolactone (PLCL)
Biosynthetic		
BioFiber-CM	Tornier (Edina, MN)	Poly (4-hydroxybutyrate) + bovine collagen

Table 18.2 Studies Evaluating Outcomes of rotator cuff repair augmentation with synthetic scaffolds

Study	Level of evidence	Inclusion criteria	No. of patients	Surgical technique	Graft used	Retear rate and outcomes	Imaging assessment
Lenart et al. [53]	IV	Large, massive RCTs	Aug: 13	Open	Poly-L-lactic acid (X-repair; Synthasome Inc., San Diego, CA)	62% retear rate. Significant improvement in clinical outcome scores (PENN/ASES)	MRI at 1 year
Proctor [60]	IV	Large, massive RCTs	Aug: 18	Arthroscopic	Poly-L-lactic acid (X-repair; Synthasome Inc., San Diego, CA)	17% retear rate at 1 year, 22% retear rate at 42 months. Significant functional improvement	Ultrasound at 1 year
Ciampi et al. [46]	III	Massive RCTs	Syn aug: 52 Xeno aug: 49 Control: 51	Mini-open	Polypropylene (Repol Angimesh, Angiologica BM Srl, Pavia, Italy)	Retear rates: Synthetic augmentation: 17% Xenographic augmentation: 41% Control: 41% Significant improvement in function, strength at 3-years	Ultrasound at 1 year
Encalada-Diaz et al. [61]	III	Small, medium RCTs	Aug: 10	Mini-open	Polycarbonate polyurethane (Biomerix, Fremont, CA)	10% retear rate Significant improvement in VAS, SST, ASES, & ROM	MRI at 1 year

ASES American Shoulder and Elbow Surgeons score, *Syn* synthetic, *Aug* augmentation group, *Xeno* xenographic group, *RCTs* rotator cuff tears, *ROM* range of motion, *SST* simple shoulder test, *UCLA* University of California, Los Angeles, *VAS* visual analog scale, *MRI* magnetic resonance imaging, *PRP* platelet-rich plasma, *cBMA* concentrated bone marrow aspirate, *SCB* substantial clinical benefit

18.5 Future Directions

Recent attention has been focused on the development of synthetic nanofiber scaffolds for the potential augmentation of the biological component of tendon repair. The scaffold is placed in between the bone and the rotator cuff utilizing the high tensile sutures from the medial row anchors that are passed through the scaffold, then passed through the rotator cuff, and then secured into a lateral row of anchors in a knotless fashion (Figs. 18.1, 18.2, 18.3, and 18.4). Erisken et al.

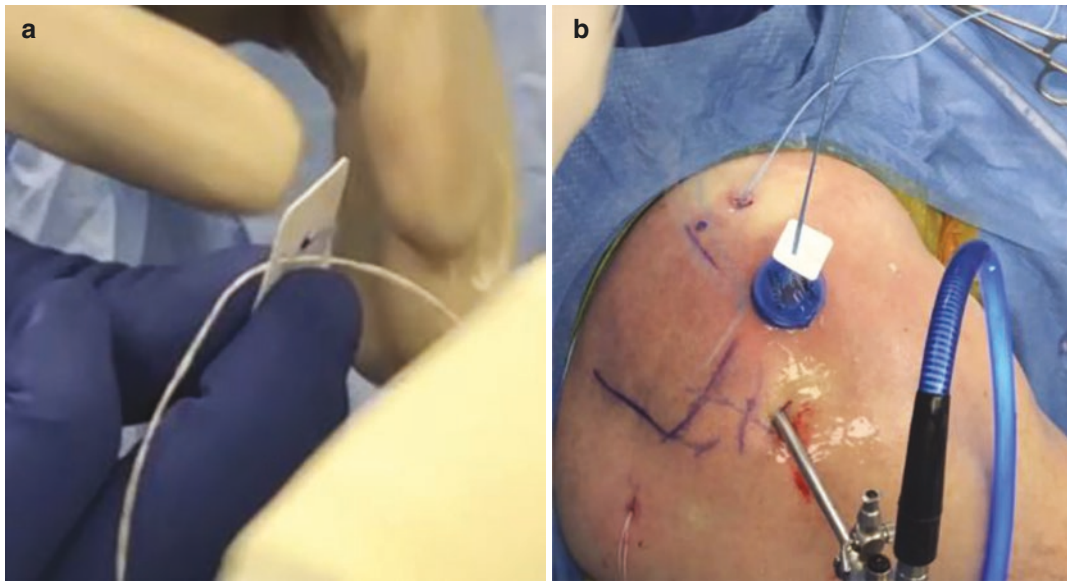

Fig. 18.1 (**a**, **b**) Intraoperative image demonstrating the high tensile suture used in the rotator cuff repair from the medial row anchors placed through the nanofiber scaffold

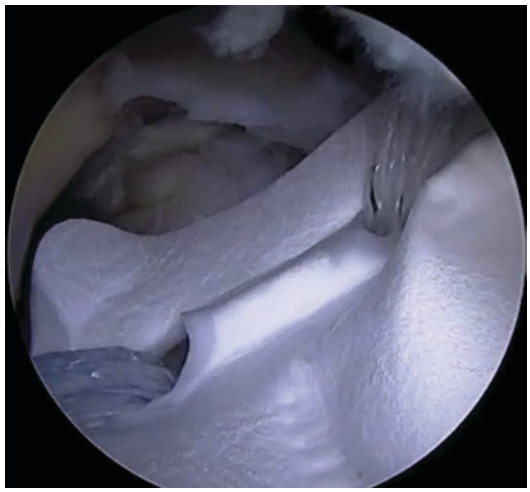

Fig. 18.2 Intraoperative image demonstrating the nanofiber scaffold placed in the shoulder after the high tensile sutures from the medial row anchor have been passed through the scaffold. The sutures will then be passed through the rotator cuff and secured into a lateral row, allowing the scaffold to sit in between the bone and tendon to augment healing

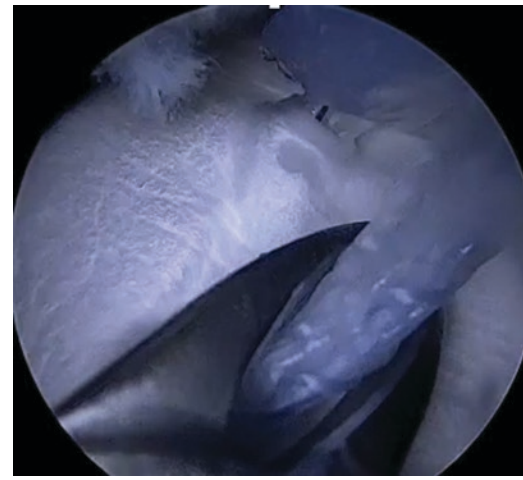

Fig. 18.3 Intraoperative image demonstrating a looped retriever used to grab the high tensile sutures that have been passed through the nanofiber scaffold that will then be passed through the rotator cuff

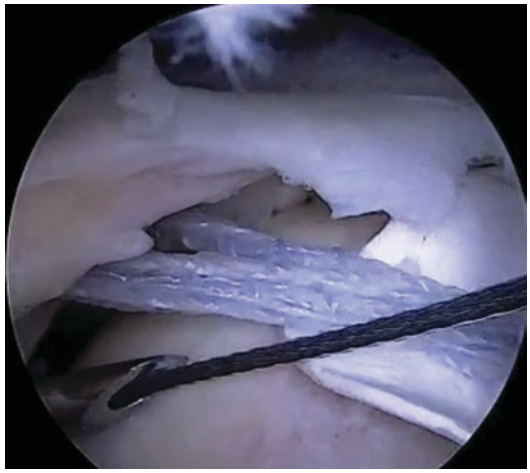

Fig. 18.4 Intraoperative image demonstrating passage of the sutures through the rotator cuff tear that have been previously passed through the nanofiber scaffold

[62] demonstrated that scaffold fiber diameter regulates human tendon fibroblast growth and differentiation. Moreover, this study showed higher cell growth, collagen, and GAG production on nanofibers compared to microfibers, clearly demonstrating the effect of structural properties of scaffolds on cell behavior and delineating the importance of fiber diameter as a design parameter in the fabrication of biomimetic scaffolds. Electrospinning shows enormous potential in the construction of scaffolds with controllable geometric and architectural structures and may enable researchers to design and develop novel scaffolds that more closely mimic the structural environment of the native ECM [63]. Future studies should assess the in vitro and in vivo use of these electrospun nanofiber scaffolds on tendon-to-bone healing.

Using an acute rotator cuff tear model in sheep, a recent study compared the use of a nonwoven nanofiber scaffold to augment rotator cuff repair to a control group of standard RCR and assessed healing at the repair site using biomechanical investigation as well as histological analysis. The scaffold was uniquely placed as an interposition graft between the tendon and the bone. The authors found a significant increase in ultimate failure force at both 6 and 12 weeks when compared to controls. In fact, the nanofiber treatment group force to failure was 47% higher than the control group at 12 weeks. Furthermore, histological assessment demonstrated collagen fiber bundles penetrating into bone in a manner similar to Sharpey's fiber formation. These findings suggest that this nanofiber scaffold may provide benefits in both the early return of mechanical strength of the tendon-to-bone healing site related to the ability of the scaffold to provide a healing environment where Sharpey's fiber formation at the enthesis can occur. The next study will include the same model but use a chronic rotator cuff tear protocol to potentially be more translational to the care of rotator cuff tears in humans.

18.6 Summary

As the number of RCR continues to rise and the healing rates remain stagnant, graft and scaffold augmentation in RCR surgery has become increasingly popular in recent years. Early studies have shown favorable outcomes for several of the devices. Further work is needed to understand the long-term effects and the utility of these grafts and scaffolds to improve the rate of rotator cuff tendon healing to bone.

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