7 Biological Augmentation in Rotator Cuff Repair: Scaffolds

Emre Bilgin, Mehmet Kapicioglu, and Kerem Bilsel

7.1 Introduction to scaffolds

Despite the improved implant designs and surgical techniques, the failure rates remain high following rotator cuff (RC) repair. Incidence of re-tears were reported to be 11% in smaller tears but increased up to 94% in massive tears [1, 2]. Hence, studies initially focused on surgical strategies such as the "double row" suture technique to restore the mechanical strength of RC. However, the double row-technique was not found to be superior to the single-row technique based on re-tear rates, and failure of the repair has remained a significant issue in shoulder surgery [3, 4].

The poor healing capacity of RC led to orthopedic research interested in biological augmentation. Thereafter, various approaches have been investigated to improve the healing potential of cuff repair [5, 6]. Cellular tendon augmentation via either allogenic or autogenic sources is determined to be a way of biological augmentation [7]. Allografts from cadaveric Achilles, quadriceps, and patellar tendon were transplanted for massive RC tears. However, improvement of functional scores was not found to be significant compared to the patients with similar conditions who underwent subacromial decompression and RC debridement surgery alone. In addition, increased infection and rejection risk were reported as disadvantages of allograft materials [8].

Augmentation with autologous tenotomized biceps tendon is another way of reinforcement with cellular components. Regarding the decreased possibility of host response and ability of performing readily without secondary incision to harvest the graft, tenotomized long head of biceps seemed to be a useful option [7]. Although biceps-augmented patients showed greater muscle strength and lower structural failure rate, equivalent clinical outcomes were demonstrated in terms of range of motion, pain, and functional scores with non-augmented controls [9].

At date, biological augmentation methods include the use of growth factors, stem cell therapies, and scaffolds or a combination thereof. Scaffolds used in RC surgery are typically classified under three main designations: biological

E. Bilgin
Department of Orthopaedics and Traumatology, Tepecik Training and Research Hospital, Health Science University, İzmir, Turkey

M. Kapicioglu
Faculty of Medicine, Department of Orthopaedics and Traumatology, Bezmialem Vakif University, İstanbul, Turkey

K. Bilsel (✉)
Faculty of Medicine, Department of Orthopaedics and Traumatology, Bezmialem Vakif University, İstanbul, Turkey

Ortopedi ve Travmatoloji Anabilim Dali, Bezmialem Vakif Universitesi Hastanesi, Istanbul, Turkey

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scaffolds (extracellular matrix patches), synthetic scaffolds, or combinations. Extracellular matrix (ECM) scaffolds are manufactured from mammalian tissues. Cell sources can be from porcine small intestinal submucosa (SIS), porcine dermis, bovine dermis, equine pericardium, human dermis, and human fascia lata. By definition, xenografts are ECMs derived from non-human sources, and allografts are ECMs derived from human sources [10–12].

On the other hand, synthetic scaffolds are manufactured from chemical compounds and consist of various polymers including polyester, polypropylene, polyarylamid, Dacron, carbon, silicone, or nylon [13]. The advantages of synthetic scaffolds are that they do not carry a risk of disease transmission and have superior mechanical properties compared with biological scaffolds [12]. Synthetic patches can provide a strong structural environment until the host tissue heals. However, they have a limited biological impact on RC healing in contrast to biological ECM patches [10]. Furthermore, their poor biocompatibility can cause long-term complications such as degeneration of the implants, failure associated with impaired stability, infection, synovitis, foreign body reaction (FBR), osteolysis, and osteoarthritis [13].

As an alternative approach, new generation devices which are synthetic, degradable, and biomimetic polymers have been emerging. These patches provide non-permanent support to the tissues due to their progressively resorbing structure and promote self-healing potential of the repair construct. Enhanced biocompatibility, sufficient mechanical properties, and flexible design are determinant characteristics of these degradable synthetic scaffolds. Poly-L-lactic acid (PLLA), poly-lactic-co-glycolic acid (PLGA), polycaprolactone, and polydioxanone are commonly used members of these implants [14].

7.2 Host Response to Scaffolds

ECM scaffolds are associated with an acute and intensive host response. Cellular components of the augmented scaffolds can be responsible for this antigenicity. Therefore, one goal of the manufacturer is to completely remove or eliminate the cellular components from ECMs for minimizing the risk of host response [10]. Decellularization techniques vary depending on the manufacturer's choice and mainly include physical, chemical, and enzymatic methods. Physical approaches are performed via freezing procedures or mechanical agitation of the harvested tissues. In chemical approaches, the cellular remnants are removed via consecutive washing steps after dissolving the tissue cells with detergents and hypotonic solutions. The enzymatic approach can be performed using a number of enzymes, such as trypsin, to lyse the cellular components [7, 15]. When combined with gamma irradiation, its effect may improve [16]. Each method has distinctive advantages and disadvantages. Hence, a combination of these techniques has been used to achieve complete decellularization.

Besides the cellular components, host response in the recipient may depend on the chemical structure of the scaffold, sterilization method, surgical exposure, and mechanical loading. Architecture of the biomaterial may both affect its degradation characteristics and remodeling potential as well as the recipient immune response. Researches to date reveal that cross-linking is associated with undesirable host response regardless of the ECM type [10, 17].

After implantation, scaffolds are recognized as foreign by the host tissues and induce inflammation defined as FBR. In non-biologic synthetic and modified biologic scaffolds, FBR creates a capsule formation that surrounds the scaffold, and this environment can lead to prolonged inflammatory response. In tissue-engineered scaffolds which are cell embedded, the cells within the patch may respond to this environment and stimulate the migration of inflammatory cells such as macrophages into the scaffolds [18].

The macrophages are known as orchestrators of the FBR. Following the migration they interact with cellular components and manage the inflammatory process through paracrine or juxtacrine signaling mechanisms [18]. Macrophages are classified into two main groups: either M1 or M2 types. The M1 type is associated with a proinflammatory response and typically represents the

inflammatory process associated with FBR. In contrast, the M2 type is associated with the remodeling process and stimulates tissue regeneration [19]. Thus, the macrophage phenotype can be considered as a predictive factor for the outcome of the scaffold augmentation. Currently, it has not been clearly identified yet which factor determines the macrophage type. However, chemically cross-linked scaffolds are prone to cause proinflammatory responses with the M1 type and not cross-linked (rapidly degraded) scaffolds which are more likely to cause a remodeling response with M2 type of macrophages [17].

7.3 Mechanical Properties of Scaffolds

The purpose of scaffold augmentation in RC repair include providing a mechanical support by "off-loading" the surgical repair at time zero and/or a biological environment to enhance the healing potential at the tendon-bone interface. The ECM scaffolds provide more biological advantages rather than the mechanical support. In contrast, synthetic scaffolds can degrade over time and maintain biomechanical support for longer periods depending on its chemistry. Some non-degradable synthetic scaffolds may remain in the tissues till the end of the patient's life. Variable degradation characteristics of ECM or synthetic scaffolds may affect their mechanical performance. On one hand, degradation can elicit impaired mechanical strength, on the other hand host cell integration and remodeling of the implant can concomitantly strengthen the repair construct [10].

Previously, numerous in vitro studies were performed to determine the mechanical characteristics of the various scaffold types to help identify their appropriate clinical usage. Barber et al. [20] biomechanically compared a number of human dermis–derived (GraftJacket, Permacol, TissueMend) and porcine SIS-derived scaffolds (CuffPatch, Restore). They reported that dermis-derived grafts had greater load-to-failure than SIS-derived grafts. GraftJacket Extreme (thicker form of the original patch) demonstrated the highest failure load (229 N). The failure was associated with suture pull-out in almost all cases, except one in which graft tearing occurred.

In another study, ECMs were found to be less elastic than the reported values of the human infraspinatus tendon, which may result in failure of the repair in regard to a decreased load-bearing capacity. SIS-derived patches (Restore, CuffPatch) demonstrated greater elastic modulus than dermis-derived (GraftJacket, TissueMend) patches. In addition, ECM scaffolds required 10–30% stretch before they started to bear significant load. Authors concluded that although ECMs have more biological benefits rather than mechanical, prestretching before the implantation may offer more functional contribution [11].

To better understand the mechanical characteristics of scaffold devices, the following studies used human cadaveric specimens. In one study, the mean load-to-failure in the non-augmented control group was found to be 273 N whereas it was 325 N in the GraftJacket Extreme augmented group in which single-row repair was performed. Failures were observed at the tendon-suture interface in 8 of 10 non-augmented and 6 of 10 augmented repairs. Suture breakage was observed in two and four in non-augmented and augmented repairs, respectively [21]. Omea et al. [22] demonstrated in single-row repaired constructs that the human dermal graft augmented group had significantly higher failure load compared to the non-augmented group (560 N and 345 N, respectively). Failures were observed through three different mechanisms: tendon cut-out ($n = 7$), suture breakage ($n = 3$), and suture anchor pull-out ($n = 3$).

Synthetic scaffolds were also studied in terms of their mechanical properties in human cadaveric shoulders. McCarron et al. [23] reported significantly increased yield load and ultimate failure load but not the initial stiffness of repair construct at time zero after PLLA graft (X-Repair) augmentation.

Recently, Smith et al. [24] investigated a number of synthetic (X-Repair, LARS ligament, Poly-Tape) and biologic ECM scaffolds via comparing their mechanical properties with cadaveric fresh frozen human supraspinatus. Synthetic scaffolds demonstrated greater load-to-failure. Among the scaffolds, LARS and X-Repair were the best performing on the macroscale. However, none of them entirely matched the native tendon in terms of macro- and micro-mechanical proper-

ties, probably because none of these devices were originally designed for RC repair.

Beitzel et al. [25] found that dermis patches (ArthroFlex) augmented on top of the reconstruction and collagen grafts (Mucograft) that are interposed between bone and tendon with double-row repair showed significantly higher load-to-failure (575 N and 573 N, respectively) under cyclic loads whereas interposed dermis patches showed also higher but non-significant load-to-failure (469 N) compared to the non-augmented controls (348 N). Consequently, collagen scaffolds demonstrate more biomechanical advantages when interposed between bone and tendon. However, dermis scaffolds seem to be more effective when augmented on the top of the tendon repair.

The results of previous in vitro studies confirmed that not only the scaffold type, but also the surgical technique including location, number, and type of the sutures as well as the location of the graft may affect the mechanical strength of augmented repair. Moreover, postoperative rehabilitation and existing joint pathology are associated with mechanical performance [10]. Above all, the mechanical strength of the primary tendon-bone reconstruction is the main determinant factor for the overall mechanical performance of the repair construct. The main goal should be to achieve a stable reconstruction of the tendon-bone interface even where scaffold augmentation is intended [26]. One should bear in mind that, however, results of in vitro studies may not entirely represent the in vivo biomechanical characteristic of a scaffold device.

7.4 Specific Scaffold Devices

7.4.1 Biological Scaffolds (Extracellular Matrix Patches)

Currently, more than 20 scaffolds are commercially available for surgical use of RC repair [24] (Tables 7.1 and 7.2). To date, natural ECMs are the most commonly used method to augment RC repair [17] After harvesting, the tissues are processed through various steps including general cleaning, removal of lipids and cellular compounds, cross-linking, and sterilization [27]. Eventually, scaffolds consist of a protein-based

Table 7.1 This table includes a number of commercially available synthetic scaffolds for RC surgery

Synthetic patch	Material	Degradation characteristics	Company
SportMesh	Polyurethane-urea	Partial degradable	Biomet Sports Medicine
X-Repair	Poly-L-lactic acid	Degradable	Synthasome
Poly-tape	Polyethylene terephthalate	Non-degradable	Xiros Ltd, Neoligaments
LARS ligament	Polyethylene terephthalate	Non-degradable	LARS
Biomerix RCR patch	Polycarbonate polyurethane-urea	Non-degradable	Biomerix
BioFiber	Poly-4-hydroxybutyrate	Degradable	Tornier
Gore-Tex patch	Expanded polytetraflouroethylene	Non-degradable	Gore Medical

Table 7.2 This table includes a number of commercially available biological ECM scaffolds for RC surgery

ECM patches	Tissue type	Source	Cross-linked	Company
Xenografts				
Restore Orthobiologic Implant	SIS	Porcine	No	DePuy Orthopaedics
CuffPatch	SIS	Porcine	Yes	Arthrotek
Zimmer Collagen Repair	Dermis	Porcine	Yes	Zimmer
Connexa	Dermis	Porcine	No	Tornier
Arthrex DX Reinforcment Matrix	Dermis	Porcine	No	Arthrex
TissueMend	Dermis	Bovine	No	Stryker Orthopaedics
OrthADAPT Bioimplant	Pericardium	Equine	Yes	Pegasus Biologics
Allografts				
GrafJacket	Dermis	Human	No	Wright Medical Technology
ArthroFlex	Dermis	Human	No	Arthrex
AlloPatch	Dermis	Human	No	MTF

SIS small intestinal submucosa, *MTF* Musculoskeletal Tissue Foundation

ECM, and they contain predominantly type I collagen fibers [11, 12].

The US Food and Drug Administration (FDA) regulation considers ECMs derived from non-human sources (xenografts) as medical devices through the 510(k) application, and these products have been cleared as augmentation devices "for reinforcement of the soft tissues that are repaired by suture or suture anchors during tendon repair including RC surgery." Animal and human studies are not required to prove the efficacy of these devices. However, ECMs derived from human sources (allografts) are classified as human tissue for transplantation, and FDA clearance is not mandatory for their use [10, 17]. Therefore, these devices have been used for augmentation as well as interpositional grafts for bridging the tendon repair (Fig. 7.1).

7.4.1.1 Xenografts

Restore Orthobiologic Implant (DePuy Orthopaedics) is an acellular, structural non-cross-linked porcine SIS. ECM contains over 90% collagen, approximately 5–10% lipids, and small amounts of carbohydrates and growth factors. The patch consists of 10 layers and is dry packaged [11, 12].

Early clinical researches on Restore yielded mixed results. Metcalf et al. [28] reported a 2-year follow up of 12 patients who underwent arthroscopic massive chronic RC repair augmented with porcine SIS. Significant improvement of shoulder range of motion (ROM) in each direction, abduction strength, and functional outcomes were demonstrated. Graft failure with complete resorption was observed in 1 of 12 patients within 12 weeks. Schlamberg et al. [29] evaluated 11 patients with large and massive RC tears treated with open repair. In contrast to former studies, they reported that magnetic resonance (MR) revealed re-tears in 10 out of 11 shoulders. ROM did not change and shoulder pain improved in seven patients postoperatively. However, the lack of non-augmented control groups was an important limitation of these studies.

In a prospective randomized control trial of the Restore implant, Iannoti et al. [30] reported

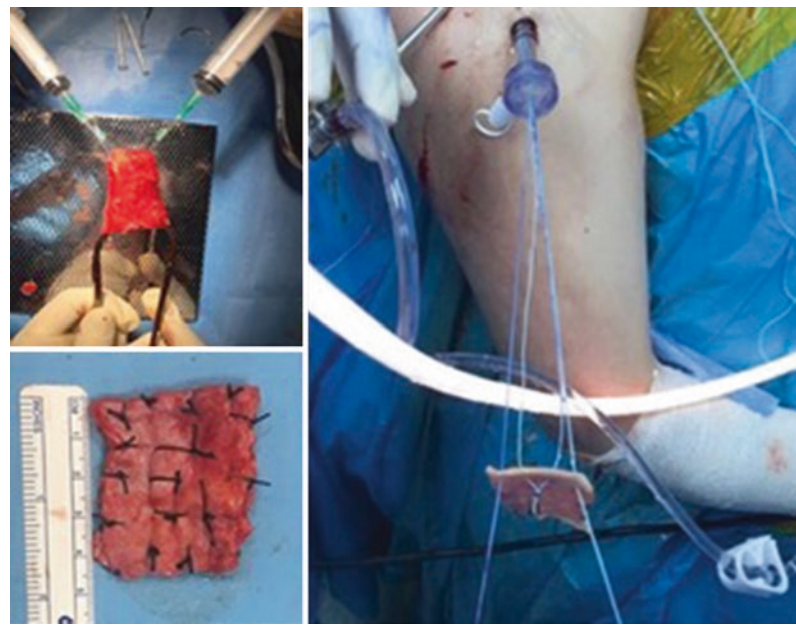

Fig. 7.1 Arthroscopic augmentation of a massive rotator cuff tear with an autologous tensor facia lata graft after preparation according to measured tear size

that RC tears healed in 4 out of 15 patients in the augmented group and in 9 out of 15 patients in the non-augmented group ($p = 0.11$). PENN score was significantly higher in the control group than in the augmented group (83–91, $p = 0.07$). Non-augmented repairs were found to be 7% more likely to heal than those in the control group. The authors concluded that Restore augmentation was insufficient to treat large and massive RC tears. Walton et al. [31] reported impaired muscle strength, greater impingement in external rotation, slower resolution of pain in activity, and longer duration of participation in sports in the Restore augmented group compared to the non-augmented group. At 2-year follow-up, re-tears were comparable between the two groups (6 of 10 in the study group, 7 of 12 in the control group). In the augmented group, four patients underwent open debridement for severe inflammation. Thus, the authors did not recommend the use of Restore as an augmentation graft for RC repairs.

CuffPatch Bioengineered Tissue Reinforcement (Arthrotek) is an acellular, 8–layered, porcine SIS sheet. The product is artificially cross-linked and packaged hydrated [11]. In rats, various types of host responses like multinucleated giant cells, proliferation of blood vessels, and tissue edema were observed at the implantation site [32]. Negligible amounts of porcine DNA were demonstrated inside the CuffPatch [11], and there is limited data on the clinical use and efficacy of the implant. Therefore, the CuffPatch is neither recommended nor contraindicated based on current researches [33].

Zimmer Collagen Repair Patch (Zimmer) is an acellular sheet of cross-linked single layer xenograft derived from porcine dermal tissue also known as the **Permacol Surgical Implant**. It is packaged hydrated [11]. Soler et al. [34] reported the early results of four patients who underwent massive RC repairs with Permacol as a bridging device. The graft failed in all of four patients between 3 and 6 months after the surgery.

The following studies demonstrated more promising results. Badhe et al. [35] evaluated ten patients with a mean age of 66 years where the Zimmer Collagen Patch was used to augment extensive RC tears. At the final follow-up (mean 4.5 years), the mean Constant scores increased from 41 to 62 ($p = 0.0003$). ROM and abduction strength significantly improved postoperatively. Radiologic evaluation revealed intact grafts in 8 of 10 patients and no adverse effect was observed during the follow-up period. Cho et al. [36] reported the results of five patients with massive RC tears who underwent mini-open surgery. Repairs were augmented with Permacol. All the patients showed improved pain relief and functional scores. No intraoperative and postoperative complications were noted. At MRI evaluation, repair was intact in four patients and re-tear was observed in one patient at an average of 8 months postoperatively.

Conexa Reconstructive Tissue Matrix (Tornier) is another ECM scaffold device made from porcine dermis. Gupta et al. [37] reported the augmentation results of 27 RC with massive or two tendon tears with the use of Conexa patch. At an average of 32 months, improved outcomes were reported in terms of active ROM, supraspinatus and external rotation strength, as well as functional scores. The mean American Shoulder and Elbow Surgeons (ASES) score increased from 62.7 to 91.8 ($p = 0.0007$), and Short-Form-12 (SF-12) score increased from 48.4 to 56.6 ($p = 0.044$) postoperatively. Ultrasound evaluations of 22 shoulders were obtained at a minimum of 2 years follow-up. Sixteen shoulders had an intact repair, five had a partially intact repair, and one shoulder had complete disruption at the graft-bone interface.

Arthrex DX Reinforcement Matrix (Arthrex) is also a porcine dermis-derived

ECM. In a recent retrospective comparative trial, Flury et al. [38] concluded that using a porcine dermal xenograft for RC repairs in over 60-year-old patients is insufficient to reduce the re-tear rates and improve the functional outcomes.

7.4.1.2 Allografts

GraftJacket Regenerative Tissue Matrix (Wright Medical Technology) is derived from human skin and composed of mainly collagen, elastin, and proteoglycans. The implant is single layered, not artificially cross-linked, and packaged dry [11]. GraftJacket has been also widely studied in clinical researches.

Bond et al. [39] arthroscopically repaired massive immobile RC tears using GraftJacket as an interpositional bridging graft. At a mean 26.8 months of follow-up period, 15 out of 16 patients were satisfied with their outcome. Significant improvement of Constant (from 53.8 to 84) and UCLA scores (from 18.4 to 30.4) were seen postoperatively. In addition, shoulder pain, forward flexion, and external rotation strength were improved. No complication was noted. MR evaluation revealed that 13 grafts completely incorporated into the native tissue. Failure of the graft was observed in three patients.

Wong et al. [40] reported 45 patients with massive irreparable RC tears arthroscopically treated using GraftJacket with a minimum follow-up of 2 years. Modified UCLA scores increased from 18.4 to 27.5 postoperatively ($p < 0.01$) and no graft rejection was observed. However, one patient who suffered from deep infection underwent arthroscopic debridement.

In a prospective randomized controlled trial, Barber et al. [41] compared the results of two groups of patients with greater than 3 cm, two-tendon tears. The patients in group 1 ($n = 22$) underwent arthroscopic RC repair with GraftJacket augmentation whereas the repairs in group 2 ($n = 20$) were performed without graft augmentation. ASES and Constant scores significantly improved in group 1 ($p = 0.035$, and $p = 0.008$, respectively). At a mean 14.5 months, 85% demonstrated intact cuff on MR evaluation in graft-augmented patients compared with 40% of non-augmented patients.

Similarly, Gupta et al. [42] demonstrated improved ASES scores (from 66.6 to 88.7) after interpositional repair of massive RC tears with GraftJacket. All the 24 patients were satisfied with their clinical result. Moreover, significant improvements were noted in terms of mean active forward flexion and external rotation, mean shoulder abduction, as well as supraspinatus and infraspinatus strength. No infection, inflammatory reaction, or graft rejection was observed. Partial graft re-tear occurred in one case because of patient noncompliance with postoperative rehabilitation.

ArthroFlex (Arthrex) is also a decellularized human dermal allograft (Fig. 7.2). The implant is packaged hydrated and terminally sterilized. Gilot et al. [43] examined the arthroscopic repair of 35 patients with massive RC tear with or without ArthroFlex augmentation. Re-tear incidence was 26.8% in control group (4 of 15) versus 10.4% in augmented group (2 of 20). ASES and SF-12 scores both significantly improved in the augmented group compared with the control group ($p = 0.02$ and 0.031, respectively).

AlloPatch HD (Musculoskeletal Tissue Foundation) is a human skin allograft. Agrawal [44] reported that 12 of 14 patients had intact repair based on MR evaluation after reinforcement with the AlloPatch of massive or previously failed RC repairs at a mean of 16.8 months. Constant score, pain score, scapular plane abduction, and strength were found to be significantly improved postoperatively. The authors concluded that the use of the implant is beneficial for the treatment of massive to large revision RC tears.

Fig. 7.2 Acellular human dermal allograft (ArthroFlex—Arthrex)

7.4.2 Synthetic Scaffolds

Few clinical studies investigated the outcomes of synthetic scaffolds for the treatment of massive RC tears. Encalada-Diaz et al. [45] reported the results of ten patients with full thickness supraspinatus or infraspinatus tears that underwent open repair with the Biomerix RCR Patch (polycarbonate polyurethane-urea) augmentation. Significant improvement in ASES scores, Simple Shoulder Test, ROM, and pain at both 6 and 12 months was observed. MRI and ultrasound evaluation showed 90% of intact repairs at 12 months. No adverse effect was reported.

Proctor [46] evaluated the functional results of X-Repair (PLLA)-augmented large to massive RC repairs. At 12 months, 15 of 18 patients demonstrated intact repair on MRI and ultrasound. At 42 months, intact repairs decreased to 14. Postoperative ASES scores significantly improved from 25 to 71 and 70 at 12 months and 42 months, respectively. In another study which investigated the same scaffold, 13 patients with massive and recurrent RC tears were evaluated [47]. At a mean 1.5 year follow-up, only five patients had an intact repair radiologically despite the significant improvement in ASES and PENN scores postoperatively (from 32.8 to 74.2 and from 50.9 to 77.6, respectively).

Audenaert et al. [48] reported the results of massive RC repairs of 41 patients using a polyester graft at a mean follow-up of 43 months. The mean Constant and Murley scores significantly improved postoperatively (from 25.7 to 72.1). The study group demonstrated significant pain relief and improvement in overhead activities. Nada et al. [49] also reported significantly improved clinical outcomes in terms of Constant score, ROM, and pain in the treatment of massive tears with a polyester patch (Dacron).

The LARS ligament (polyethylene terephthalate) was also used to reinforce the repair of massive RC tears. Petrie and Ismaiel [50] demonstrated significantly increased Oxford Shoulder scores and acromiohumeral distance in 31 shoulders with chronic massive cuff tear after LARS ligament augmentation.

Although these researches display promising results, they lacked a control group. Ciampi et al. [51] clinically compared 152 patients with massive RC tears who underwent surgical repair alone (n = 51) and with bovine pericardium-derived collagen patch (n = 49) or polypropylene patch (n = 51) augmentation. The results showed that

mean UCLA score, shoulder elevation, strength, and re-tear rates were significantly improved in the polypropylene group at 36 months.

7.4.3 Combinations

Recently, novel strategies have been developed such as electrospinning which was predominantly used to closely mimic the native orientation of tendon collagen bundles with structurally aligned synthetic scaffolds. This method provides an opportunity to create combinations via the incorporation of bioactive growth factors or embedding the stem cells into the scaffold devices [6, 14]. In this way, both improved mechanical performance and enhanced cellular activity at the repair site can be obtained simultaneously.

Zahao et al. [52] investigated PLGA and basic fibroblast growth factor (bFGF)-loaded PLGA membranes that are prepared via the electrospinning method. In rats, the authors found that the membranes had excellent biocompatibility and biodegradability. After in vivo RC surgery, bFGF-PLGA significantly improved the collagen organization compared with control and PLGA groups at 2, 4, and 8 weeks. Electrospun membranes demonstrated higher ultimate load-to-failure than the control group.

Yokoya et al. [53] compared control infraspinatus tendon defects in rats with reconstructed tears with poly-glycolic acid (PGA) sheets and autologous cultured mesenchymal stem cell (MSC)-seeded PGA sheet. They found higher volume of type I collagen than type III collagen in the MSC-PGA group compared to the PGA-only group, and besides, regenerated tendons in the MSC-PGA group demonstrated better tensile strength than the PGA-only and control groups at 16 weeks.

Combinations can be prepared via loading growth factors into collagen ECMs. Hee et al. [54] demonstrated higher load-to-failure as well as improved morphologic appearance including tendon-to-bone integration in the repair of ovine infraspinatus tears with augmentation of recombinant human platelet-derived growth factor–loaded bovine collagen matrix compared to the collagen matrix patch alone. Despite promising results in animals, we are not aware of any clinical data based on these novel combinations.

7.5 Summary

Currently, scaffolds have been the most common tissue-engineered approach used to obtain improved outcomes after RC augmentation. The rationale behind the usage of a scaffold device includes mechanical reinforcement of the repair construct as well as the biological enhancement of the healing potential of a RC tear [10].

The ideal scaffold should biomechanically match the physical characteristics of the tendon-bone interface and maintain a support until the healing completes. The implant should be cell-instructive and present with artificially oriented structures to closely mimic native tissue. In addition, it should be biodegradable to enable the new tendon-bone interface to completely integrate and regenerate without causing any side effects because of the degraded material. Finally, the device should artificially permit incorporation of growth factors, stem-cells, or minerals [6, 55]. Future directions may be focused on scaffold devices which meet these demands.

Researches to date have confirmed that porcine SIS-derived xenografts demonstrated higher failure rates with little to no clinical improvement. Because of causing severe inflammatory reactions due to high residual porcine DNA [56], further use of the Restore implant was not recommended for RC repair in humans [31]. Although porcine dermal xenografts and dermal allografts demonstrated more promising results, most of the studies lacked a control group. Moreover, concern still remains that allografts may also create an inflammatory response due to DNA remnants [11, 57].

Synthetic grafts are an alternative approach for the augmentation of RC repair. Several clinical studies demonstrated low complication and decreased re-tear rates and improved outcomes after implantation of various types of synthetic

patches. However, most of them were also unable to compare the study group with a control group (Table 7.3).

Table 7.3 Literature results of ECM and synthetic scaffolds based on clinical researches

Scaffold source	Tissue/material type	Literature results
Porcine	Small intestinal submucosa	Decreased healing potential of RC, high re-tear rates, increased impingement, and shoulder pain, associated with severe inflammatory reaction due to residual DNA content
Porcine	Dermis	Low adverse effect and complication risk, significantly improved functional outcomes. However, ineffective to treat massive tears in >60-year-old patients and when used as a bridging device
Human	Dermis	High satisfaction rates, improved functional scores, decreased re-tear rate, decreased inflammatory reaction, and rejection risk. Safe and useful for augmentation in revision RC surgery
Synthetic	Polycarbonate polyurethane-urea	Improved functional outcomes and 90% intact repair at 12 months. Low complication risk. No observed adverse effect
Synthetic	Poly-L-lactic acid	Improved functional scores and 78% intact repair at 42 months. In contrast, one study reported 62% re-tear rate despite significantly improved functional scores
Synthetic	Polyester	Significantly increased Constant scores. Improved pain and ROM
Synthetic	Polyethylene terephthalate	Successful clinical outcomes, radiologically decreased acromiohumeral distance
Synthetic	Polypropylene	Decreased re-tear rates, improved functional scores, and shoulder elevation at 36 months

Based on the current researches, the data is limited on the use of combination types of scaffolds in humans. There are only a few animal studies available with promising results in the literature. Nevertheless, further clinical studies are required to warrant the reliability and efficacy of these novel tissue-engineered devices.

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