Early Clinical and Radiologic Outcomes After Arthroscopic Rotator Cuff Repair Augmented With A Demineralized Bone Fiber Implant

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Abstract: (1) Background: Tendon-to-bone healing is a challenge after rotator cuff repair. This study reports early radiological and clinical outcomes following arthroscopic repair of rotator cuff tears augmented with a novel demineralized bone fiber (DBF) implant at the footprint to enhance the enthesis; (2) Methods: Retrospective review of patients who underwent arthroscopic rotator cuff repair with DBF augmentation was conducted. Pain, range of motion (ROM), isometric strength of rotator cuff, and patient-reported outcome measures were evaluated preoperatively and at 6, 12, and 24 months postoperatively. Magnetic resonance imaging at 6 months postoperatively was assessed for tendon thickness, healing, and quality (Sugaya Classification). A matched control group without augmentation was used for comparison; (3) Results: Thirty-one patients were included in each group. At mean follow-up of 8 months, pain, ROM, and strengths were comparable between the two groups. DBF-augmented group had significantly better ASES, Constant, and UCLA scores. While tendon quality and thickness did not differ significantly, qualitative MRI analysis showed obvious encroachment of tendon onto bone with greater surface coverage on the footprint; (4) Conclusions: DBF augmentation in rotator cuff repair shows promising early signs of enhanced enthesis and superior patient-reported outcomes. Long-term studies with larger patient population are needed to confirm these preliminary findings.

Keywords: rotator cuff repair; rotator cuff healing; retear; enthesis; tendon-to-bone healing; demineralized bone fiber implant; demineralized bone matrix

1. Introduction

Rotator cuff repair is a widely performed procedure for symptomatic rotator cuff tears. It has been estimated that approximately 250,000 rotator cuff repairs are being performed per year in the United States [1], with the rates steadily increasing because of the aging population. However, despite this high volume and efforts, rotator cuff repairs are still reported to fail at a high rate, especially in massive, retracted rotator cuff tears. Retear rate after repair of these tears can be as high as 94% [2]. Failure after a cuff repair is multifactorial. Both patient and surgical variables play a role in increasing the risk of retear. These include age, size of tear, fatty infiltration, tendon quality, presence of osteoporosis, diabetes, and smoking status. All these factors ultimately affect the healing of rotator cuff tendons onto bone. Despite advancements in surgical techniques, healing after rotator cuff repair, particularly of massive, retracted rotator cuff tears, has been a challenge. Achieving robust tendon-to-bone healing at the enthesis, even in smaller cuff tears, has consistently been a weak link and a source of failure. The enhancement of biologic integration at this bone-tendon interface is crucial to improve healing rates after rotator cuff repair and decreases the risk of retears. The enthesis is a specialized transitional zone where the rotator cuff attaches to bone.

Due to tendon and bone having different stiffness properties, this interface is crucial for effective load transfer. A healthy enthesis features a fibrocartilage region with gradations in not only mechanical properties, but also cell phenotype, matrix composition and tissue organization. It consists of a four-zone structure, involving bone, mineralized and unmineralized fibrocartilage, and tendon [3]. However, the enthesis has poor healing potential, and true biological healing at this interface has often failed with traditional repair methods using sutures, anchors, and even overlay patches. These methods frequently result in the formation of disorganised scar tissue, which is biomechanically inferior to native tissue [3-5]. Incomplete healing and gap formation commonly occur at the enthesis, increasing the risk of retears and clinical failure, which most

commonly occurs within the initial 6 to 26 weeks following arthroscopic repair (mean 19.2 weeks) [6,7]. Apart from improving on surgical techniques to address the risk of retear, recent advancements include biologic approaches to improve healing at the enthesis after rotator cuff repair. A novel 100% demineralized cortical bone implant (Enfix®, Tetrous Inc., Los Angeles, CA) has been developed to augment rotator cuff repair at the footprint with the aim of improving the enthesis. This interpositional, all-in-bone implant is designed to be easily incorporated into the surgeon's current technique and is placed in the bone extending between the bone and the tendon. The underlying rationale is that the demineralized bone fiber (DBF) technology can trigger endochondral ossification, leading to the formation of healthy and strong new tissue with continuity from the bone through the enthesis and into the tendon, which has been demonstrated in several preclinical studies [8,9]. This DBF technology has been implemented successfully in bone grafting applications in spine surgery [10]. The EnFix family of implants (including EnFix RC™, TAC-O™, and TAC-T™) aims to uniquely offer biological enhancement of the re-attachment of bone to tendon, differentiating it from traditional methods and addressing the persistent point of failure in rotator cuff repair. This study aims to present the early radiological and clinical outcomes after arthroscopic repair of rotator cuff tears augmented with the Enfix RC DBF implant at the footprint. The primary objective was to evaluate the initial impact of this augmentation technique on tendon healing and clinical outcomes at a minimum of 6 months postoperatively in comparison to a matched cohort that did not receive the augmentation. This interim analysis of prospectively collected data provides early insights into the potential benefits of this novel approach in improving the quality of tendon healing following rotator cuff repair and its impact on clinical outcomes.

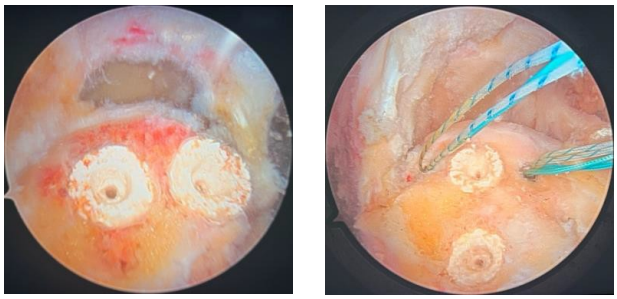
2. Materials and Methods

2.1. Study Design

This is a retrospective review of prospectively collected data of patients who underwent arthroscopic rotator cuff repair for posterosuperior rotator cuff tears augmented with Enfix RC DBF implant in a single center performed by a single shoulder subspecialist (AG) from August 2023 to October 2024 (augmented group). A matched control group based on age, sex, repaired tendons, tear characteristics, and follow-up period was selected from the database of patients who underwent rotator cuff repair without augmentation prior to the availability of Enfix RC. Patients with repairable subscapularis tears were not excluded from the cohort. Patients with follow-up of less than 6 months and with no postoperative magnetic resonance imaging (MRI) were excluded from the study. Ethical approval was received from the Ramsay Health Care QLD Human Research Ethics Committee (Protocol No. 2024/ETH/0050) and informed consents were obtained from all patients.

2.2. Surgical Technique

The senior surgeon's indications for the use of Enfix RC DBF implant during arthroscopic rotator cuff repairs include large to massive rotator cuff tears, tears with poor tendon quality, and in revision surgeries. All surgeries are performed in a beach chair position under combined general anaesthetic and interscalene nerve block. Standard diagnostic arthroscopy using standard posterior and anterior portals is performed to assess rotator cuff tear and other concomitant pathologies. After diagnostic arthroscopy, adequate releases are performed. Whenever appropriate, muscle slide and advancement with suprascapular nerve release are performed especially for the large and massive retracted rotator cuff tears to ensure tension-free repair [11,12]. Once tension-free reduction of the rotator cuff tendons to the footprint is achieved, Enfix RC is inserted onto the footprint, adjacent to the planned anchor placement near the medial row or between the medial and lateral rows (Figure 1). Standard double row repair technique is performed. For delaminated tears, separate repair of the deep and superficial layers is done using the double layer Lasso loop technique [13]. All repairs are performed using 5.5-mm polyether ether ketone (PEEK) Quattro X medial row anchors (Zimmer Biomet, Warsaw, IN) and 5.5-mm PEEK Quattro Link Knotless lateral row anchors (Zimmer Biomet, Warsaw, IN). The same technique and implants were utilized for the control group, with the exception that no Enfix RC insertion was carried out.



(a) (b)

Figure 1. Shoulder arthroscopy of the right shoulder viewed from the lateral portal showing Enfix RC inserted (a) side-by-side and (b) adjacent to the medial row anchors and between medial and lateral rows.

2.3. Postoperative Rehabilitation

Patients are placed in an abduction sling for 6 weeks. Gentle passive ROM is begun on day 1 postoperatively, progressed to active-assisted ROM at 2 weeks and to active ROM at 6 weeks. Strengthening is generally commenced at 12 weeks postoperatively.

2.4. Clinical Outcomes

As part of standard clinical practice, pain, active range of motion (ROM), isometric strength of rotator cuff muscles, patient-reported outcome measures (PROMs), and satisfaction were collected preoperatively and at 6 months, 12 months, and 24 months after surgery using Akunah PROMs (Akunah Medical Technology, Brisbane, Australia). Pain was evaluated using visual analogue scale (VAS). Active ROM included forward flexion (FF), lateral elevation (LE), external rotation at 0° abduction (ER1), external rotation, internal rotation to the back (IR1), and internal rotation at 90° abduction (IR2). Functional external rotation, as described by Constant et al. [14], involved a combination of external rotation, frontal, and lateral elevation. This movement included positioning the hand behind or above the head, with elbows directed either forward or back. Isometric strength of the rotator cuff was obtained using handheld dynamometer (Commander Echo MMT; JTECH Medical, Midvale, UT). Subscapularis strength was measured in the bear hug position. Supraspinatus strength was measured in the empty can position. Infraspinatus strength was measured in the ER1 position. Strength of lateral elevation was also measured with the shoulder at 90 degree abduction. Relative strength was calculated as a percentage of the strength of the operated shoulder in comparison to the contralateral shoulder. Hence, patients who had pathology on the contralateral shoulder were not included in the analysis of relative strengths. PROMs included the American Shoulder and Elbow Surgeons (ASES) Shoulder score, Constant score, University of California Los Angeles (UCLA) Shoulder score, and satisfaction.

2.5. Radiologic Assessment

MRI arthrogram scans with 3.0-T machine were routinely obtained preoperatively to assess the degree of tendon retraction, the severity of fatty infiltration, and the length of the remaining tendon stump. Supraspinatus, infraspinatus, and teres minor tendon retraction was classified using the Patte classification [15]. Subscapularis tears were graded according to the Lafosse classification [16]. Fatty infiltration was initially classified on T1-weighted sagittal oblique sequence using the Goutallier classification modified by Fuchs et al. [17,18] and then simplified to low-grade fatty infiltration (Goutallier 0-2) and high-grade fatty infiltration (Goutallier 3-4). Noncontrast MRI scans were repeated at 6 months postoperatively to assess tendon healing and quality using the Sugaya classification [19]. Tendon thickness was measured on the T2-weighted coronal oblique sequence, measuring perpendicular to the thickest portion of the tendon at the footprint near the repair site where the anchors are visible (Figure 2). All radiographic evaluation was assessed by two fellowship-trained shoulder surgeons.

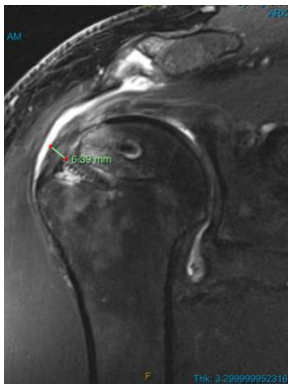


Figure 2. Tendon thickness measurement at the footprint near the repair site on T2-weighted coronal oblique sequence.

2.6. Statistical Analysis

Descriptive statistics were presented as means, standard deviations, ranges, and percentages. Comparisons of variables between groups were made using t-test or Mann-Whitney U-test depending on data normality. There was no adjustment for multiple testing. Comparisons between categorical variables were made using Fishers Exact test and Chi-squared test. P value <.05 was considered significant. Minimal clinical important differences (MCID) for the different variables were established from published data to determine the clinical significance of findings and statistical analysis [20,21]. A change in the mean score that exceeded MCID for a specific variable was considered clinically significant.

3. Results

3.1. Patient Demographics and Rotator Cuff Tear Characteristics

A total of 31 patients from the augmented group and 31 patients from the matched control group with mean age of 54.8 years were included in the study. The mean follow-up period was 8 months. Both groups were comparable in terms of age, sex distribution, follow-up period, and preoperative tear characteristics (Table 1). Majority of the patients have at least two-tendon tears with Patte 2 to 3 retraction and low-grade fatty infiltration (Goutallier 0 to 2) with comparable distribution between the two groups.

Table 1. Patient Demographics and Rotator Cuff Tear Characteristics

Variables	Augmented Group	Control Group	*P value*
Age at surgery, y Mean (SD, range)	54.8 (6.1, 40-65)	54.8 (6.2, 42-64)	p=1.000
Sex (Male : Female)	24 (77.4%) : 7 (22.6%)	23 (74.2%) : 8 (25.8%)	p=0.767
Follow-up time, months Mean (SD, range)	7.8 (3.4, 6-14)	8.4 (3.4, 6-18)	p=0.388
Affected tendons based on Collin Classification			
Type A	1 (3.2%)	1 (3.2%)	
Type B	2 (6.5%)	1 (3.2%)	
Type C	6 (19.4%)	4 (12.9%)	
Type D	15 (48.4%)	12 (38.7)	
Type E	2 (6.5%)	6 (19.4%)	p=0.617
Type B+D§	3 (9.7%)	2 (6.5%)	
Type C+E§	0 (0%)	1 (3.2%)	
Type B+E§	0 (0%)	2 (6.5%)	
Isolated supraspinatus	2 (6.5%)	2 (6.5%)	
Fatty Degeneration*			
SSC			
Goutallier 0-2	10/12 (83.3%)	11/11 (100%)	p=0.478
Goutallier 3-4	2/12 (16.7%)	0/11 (0%)	
SSP			
Goutallier 0-2	27/31 (87.1%)	27/31 (87.1%)	p=1.000
Goutallier 3-4	4/31 (12.9%)	4/31 (12.9%)	
Goutallier 0-2	24/26 (92.3%)	25/27 (92.6%)	p=1.000
Goutallier 3-4	2/26 (7.7%)	2/27 (7.4%)	
TM			
Goutallier 0-2	2/2 (100%)	9/9 (100%)	N/A
Goutallier 3-4	0/2 (0%)	0/9 (0%)	
Tendon Retraction			
Patte 1	13 (41.9%)	10 (32.3%)	
Patte 2	4 (12.9%)	6 (19.4%)	p=0.662
Patte 3	14 (45.2%)	15 (48.4%)	

SD, standard deviation; *SSC*, subscapularis; *SSP*, supraspinatus; *ISP*, infraspinatus; *TM*, teres minor.

§Not in the original Collin classification but the types have been combined to depict involved tendons.

*Only includes cases with tears

3.2. *Patient-Reported Outcome Measures (PROMs)*

Preoperative PROMs were comparable between the two groups, except for preoperative pain which was significantly worse in the augmented group (p=0.048) (Table 2). Postoperatively, the patients in the augmented group showed significantly better Constant, ASES, and UCLA scores. The improvement in scores from preoperative to postoperative was also greater in the augmented group but was only statistically significant for VAS (p=0.016) and ASES (p=0.018). The mean change in PROMs for both groups exceeded the MCID of 1.5, 4.6, 11.1, and 6 for VAS, Constant, ASES, and UCLA scores, respectively, suggesting clinically significant improvements [20,21]. A greater percentage of patients from the augmented group reached the MCID but this difference did not reach statistical significance. Postoperative satisfaction rate was also similar in both groups (p=0.612). At six months postoperatively, 83.9% in the augmented group were able to return to work and sport/hobby completely, while 54.8% in the control group were able to return to work completely and 51.6% in the control group were able to return to sport/hobby completely.

Table 2. Preoperative and Postoperative Patient-Reported Outcome Measures (PROMs)

Variables	Augmented	Control	*P Value*
VAS Mean (SD, range)			
Preoperative	4.3 (2.5, 0-9)	3.0 (2.6, 0-8)	p=0.048
Postoperative	0.4 (0.9, 0-4)	0.9 (1.5, 0-7)	p=0.094
Change	-3.9 (2.5, -9.0-0.0)	-2.1 (2.7, -6.0-7.0)	p=0.016
n(%)≥ MCID of 1.5 [20]	25/31 (80.6%)	18/31 (58.1%)	p=0.054
Constant Score Mean (SD, range)			
Preoperative	55.4 (16.5, 13-81)	50.7 (18.0, 4-75)	p=0.375
Postoperative	80.4 (6.1, 62-92)	70.6 (12.0, 37-88)	p<0.001
Change	25.0 (17.1, 0-66.0)	19.8 (17.4, -10-64)	p=0.248
n(%) ≥ MCID of 4.6 [21]	26/30 (86.7%)	25/31 (80.6%)	p=0.525
ASES Score Mean (SD, range)			
Preoperative	55.8 (20.8, 22-100)	60.5 (19.5, 10-90)	p=0.368
Postoperative	95.2 (8.9, 63-100)	87.9 (12.3, 55-100)	p=0.001
Change	39.3 (21.0, 0-78)	27.4 (17.4, -23-60)	p=0.018
n(%) ≥ MCID of 11.1 [21]	29/31 (93.5%)	26/31 (83.9%)	p=0.425
UCLA Score Mean (SD, range)			
Preoperative	18.9 (6.9, 8-35)	16.4 (5.9, 7-29)	p=0.207
Postoperative	33.1 (2.8, 25-35)	27.3 (7.5, 10-35)	p<0.001
Change	14.1 (7.0, 0-26)	10.9 (8.5, -14-23)	p=0.206
n(%) ≥ MCID of 6.0 [20]	26/30 (86.7%)	25/31 (80.6%)	p=0.525
Satisfaction Frequency (%)			
Preoperative	3/31 (9.7%)	0/31 (0%)	p=0.238
Postoperative	30/31 (96.8%)	28/31 (90.3%)	p=0.612
Return to Work			
Complete	83.9%	54.8%	
Partial	16.1%	38.7%	p=0.034
Unable	0%	6.5%	
Return to Sport/Hobby			
Complete	83.9%	51.6%	
Partial	16.1%	38.7%	p=0.016
Unable	0%	9.7%	

VAS, Visual analogue scale. *ASES*, American Shoulder and Elbow Surgeons. *UCLA*, University of California-Los Angeles

3.3. Active Range of Motion

Preoperative active ROM in all planes were comparable between the two groups (Table 3). Postoperatively, there was no significant difference in active ROM between the two groups. The improvement in active ROM from preoperative to postoperative was also not statistically different between the two groups.

3.4. *Strength*

Preoperative absolute and relative strengths of the rotator cuffs were comparable between the two groups. On the other hand, the preoperative relative strength of LE was significantly greater in the augmented group (p=0.004) (Table 4). Postoperatively, there was no significant difference in absolute strengths between the two groups, while the improvement in absolute strengths from preoperative to postoperative was comparable as well. Postoperative relative strengths of the rotator cuff were greater in the augmented group, while the lateral elevation relative strength was greater in the control group. However, these differences did not reach statistical significance. Both groups achieved at least 90% of the strength of the contralateral normal shoulder postoperatively, except for supraspinatus strength of the control group, which was 87%. There was greater improvement in relative strength from preoperative to postoperative in the control group, but this did not reach statistical significance.

Table 3. Preoperative and Postoperative Active Range of Motion

Variables	Augmented	Control	*P Value*
Forward Elevation Mean, degrees (SD, range)			
Preoperative	143 (44, 30-180)	141 (47, 0-180)	p=0.710
Postoperative	170 (12, 120-180)	171 (15, 100-180)	p=0.377
Change	27 (45, -20-150)	30 (44, -10-180)	p=0.610
Lateral Elevation Mean, degrees (SD, range)			
Preoperative	137 (49, 20-180)	129 (47, 0-180)	p=0.268
Postoperative	161 (29, 70-180)	161 (17, 100-180)	p=0.225
Change	24 (45, -50-130)	33 (38, -10-170)	p=0.226
ER1[*] Mean, degrees (SD, range)			
Preoperative	52 (16, 20-80)	52 (22, 0-80)	p=0.536
Postoperative	63 (14, 20-80)	60 (12, 30-80)	p=0.190
Change	11 (22, -30-50)	9 (21, -30-60)	p=0.629
Functional ER[∇] Frequency (%)			
Preoperative	4/0/5/5/17 (12.9/0/16.1/16.1/54.8)	3/1/5/9/13 (9.7/3.2/16.1/29/41.9)	p=0.589
Postoperative	0/0/0/3/27 (0/0/0/10/90)	0/0/0/1/6/24 (0/0/3.2/19.4/77.4)	p=0.339
IR1[◊] Frequency (%)			
Preoperative	0/4/8/9/9/1 (0/12.9/25.8/29/29/3.2)	2/3/5/5/13/2 (6.7/10/16.7/16.7/43.4/6.7)	p=0.413
Postoperative	0/0/2/10/16/2 (0/0/6.7/33.3/53.3/6.7)	0/0/3/9/14/5 (0/0/9.7/29/45.2/16.1)	p=0.647
IR2[§] Mean, degrees (SD, range)			
Preoperative	55 (22, 0-90)	53 (21, 0-80)	p=0.785
Postoperative	68 (17, 30-90)	64 (14, 30-80)	p=0.141
Change	13 (27, -40-80)	11 (21, -30-65)	p=0.744

[*]External rotation at 0° abduction

[∇]Functional external rotation: hand to the back of the head with elbow forward/ hand to the back of the head with elbow back/ hand to the top of the head with the elbow forward/ hand to the top of the head with the elbow back/ full elevation

[◊] Internal rotation to the back: lateral thigh/buttock/lumbosacral junction/waist/T12 vertebrae/interscapular area

[§]Internal rotation at 90° abduction

Table 4. Preoperative and Postoperative Absolute and Relative Strengths

Absolute Strength Kg, mean (SD, range)	Augmented n=31	Control n=31	*P Value*
Lateral Elevation			
Preoperative	3.7 (1.6, 0-6.4)	3.1 (1.5, 0-7.0)	p=0.584
Postoperative	4.7 (1.7, 2.7-10.0)	4.4 (2.1, 1.7-11.3)	p=0.515
Change	1.0 (2.0, -2.8-5.2)	1.3 (2.2 (-3.4-7.7)	p=0.486
Supraspinatus			
Preoperative	3.3 (1.6, 0-7.7)	3.4 (1.9, 0-9.1)	p=0.820
Postoperative	4.4 (1.7, 1.8-8.8)	4.5 (2.1, 1.4-10.9)	p=0.834
Change	1.1 (1.9, -3.6-5.4)	1.1 (2.3, -2.3-7.0)	p=0.981
Infraspinatus			
Preoperative	4.0 (1.5, 0-6.4)	3.9 (2.0, 0-8.2)	p=0.779
Postoperative	4.8 (1.3, 2.9-7.5)	5.2 (2.5, 1.4-15.0)	p=0.664
Change	0.7 (1.8, -2.5-5.0)	1.3 (2.5, -2.7-10.0)	p=0.462
Subscapularis			
Preoperative	5.4 (2.4, 0-11.6)	6.1 (3.3, 0-14.5)	p=0.376
Postoperative	6.5 (2.3, 2.9-14.7)	7.6 (3.4, 4.1-18.6)	p=0.267
Change	0.9 (2.6, -4.6-6.4)	1.6 (3.6, -5.4-10.2)	p=0.419

Relative Strength* %, mean (SD, range)	Augmented n=29	Control n=26	*P Value*
Lateral Elevation			
Preoperative	71.9 (25.3, 0-108.5)	53.3 (21.4, 16.9-100)	p=0.002
Postoperative	90.9 (15.6, 47.7-123.7)	91.3 (25.1, 38.9-148.1)	p=0.515
Change	20.0 (32.8, -36.7-94.1)	38.0 (29.2, -39.5-99.0)	p=0.038
Supraspinatus			
Preoperative	65.8 (31.4, 0-118.5)	57.9 (20.5, 26.5-95.1)	p=0.288
Postoperative	90.4 (22.4, 42.6-161.5)	87.2 (22.9, 31.1-133.3)	p=0.601
Change	26.1 (39.4, -68.5-105.1)	31.5 (22.0, -10.4-69.5)	p=0.549
Infraspinatus			
Preoperative	81.5 (37.7, 0-213.3)	68.1 (25.2, 23.7-117.4)	p=0.133
Postoperative	97.6 (16.9, 72.9-140.4)	90.2 (20.2, 34.1-115.4)	p=0.340
Change	16.5 (42.0, -113.3-105.9)	22.1 (23.6, -19.3-76.2)	p=0.554
Subscapularis			
Preoperative	75.1 (28.8, 0-153.5)	72.0 (23.9, 0-106.7)	p=0.672
Postoperative	97.9 (19.3, 57.6-148.8)	95.2 (18.1, 60.0-135.6)	p=0.610
Change	22.3 (38.8, -59.2-126.7)	23.2 (27.5, -19.8-85.6)	p=0.918

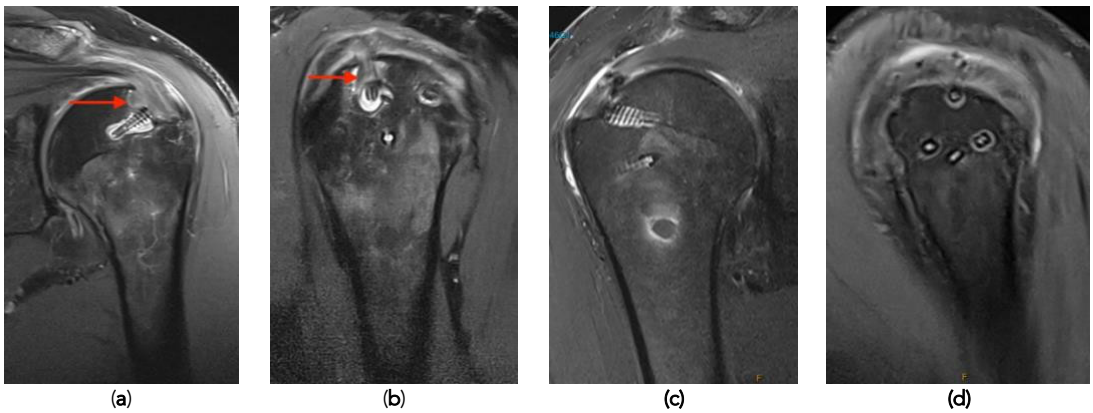
*Relative strength is the strength of the affected shoulder compared with the contralateral normal shoulder as a percentage. Patients with pathology in the contralateral shoulder preoperatively and on follow-up were excluded from this analysis.

3.5. *Radiographic* Outcomes

Twenty-seven patients (27) and twenty-nine patients (29) from the augmented group and control group, respectively, had MRI scans at 6 months postoperatively. There were no re-tears in either group, with a healing rate of 100%. The distribution of patients having Sugaya type I, II, and III was similar in both groups (p=0.985), with most patients having Sugaya type II tendon quality. The tendon at the footprint was noted to be thicker in the augmented group, but the difference did not reach statistical significance (p=0.464) (Table 5). Qualitative observation of the MRI scans of the patients in the augmented group, however, showed more robust tendons, with obvious encroachment of tendon onto bone and bigger surface area of coverage on the footprint as seen in Figure 3.

Table 5. Radiographic Outcomes

Variables	Augmented Group n=27	Control Group n=29	*P value*
Tendon thickness at footprint mm, mean (SD, range)	5.3 (1.9, 2.1-11.2)	4.9 (1.8, 1.6-8.7)	p=0.464
Healing Frequency (%)	27 (100%)	29 (100%)	p=0.985
Sugaya Classification Frequency (%)			
Type I	1 (3.7%)	1 (3.4%)	
Type II	20 (74.1%)	21 (72.4%)	
Type III	6 (22.2%)	7 (24.1%)	
Type IV	0 (0%)	0 (0%)	
Type V	0 (0%)	0 (0%)	



(a) (b) (c) (d)

Figure 3. Six-month postoperative noncontrast MRI: (**a**) Coronal and (**b**) sagittal T2-weighted images of a patient in the augmented group showing obvious encroachment of tendon onto bone with greater surface coverage at the footprint (red arrow), which is not visible in the non-augmented repair (**c-d**).

4. Discussion

This study presents the early outcomes of a novel DBF implant (Enfix RC) used in the augmentation of arthroscopic rotator cuff tear repairs. Radiologic assessment at 6 months postoperatively demonstrated complete healing with a trend towards more robust tendon quality and greater surface area of tendon encroachment onto bone in the augmented group compared to the non-augmented group. Neither group experienced any re-tears during this period. Furthermore, the improvements in the clinical outcomes of pain, function, active ROM, and strength were comparable between the cohorts, with promising early results of significantly better ASES, Constant, and UCLA scores, with a trend of achieving greater rotator cuff relative strengths in the group with DBF augmentation. DBF, which is a form of demineralized bone matrix (DBM), promotes healing and integration at the enthesis following rotator cuff repair through both osteoconductive and osteoinductive properties, and providing a structural scaffold. Bone collagen is the primary constituent and they also contain bone morphogenetic proteins (BMPs), as well as other growth factors known to facilitate healing. These BMPs are primarily responsible for stimulating the differentiation of mesenchymal stem cells (MSCs) into osteoblasts and chondrocytes, thereby promoting osteoinduction [22-24]. Thus, the recreation of the four-zone fibrocartilaginous structure of the native enthesis is achieved [25-27]. Furthermore, collagen deposition, neovascularisation, and infiltration of host cells occurs through the porous structure of the DBF which functions as a scaffold. This osteoconductive property enables cells necessary for tissue repair to migrate to the area and provides a framework for new tissue formation at the enthesis [28-30]. By allowing for the organization of the newly formed extracellular matrix and guiding the regeneration of the neo-enthesis, DBF is thought to give additional support to the initial tendon repair [3,31]. Numerous preclinical studies have demonstrated that instead of just forming fibrous scar tissue, the use of DBM at the tendon-bone interface can lead to the development of a more functional four-zone enthesis. DBM aims to enhance integration between the bone and tendon through soft tissue and osseous ingrowth into the matrix in order to more evenly distribute tensile forces and reduce stress concentrations. The ultimate goal being to improve the mechanical properties of the repair and potentially decrease retear rates. The early clinical findings observed in the augmented group support the efficacy of the use of DBF in rotator cuff repairs and are consistent with preclinical animal studies, which have demonstrated improved tendon-bone healing with better histological and biomechanical characteristics. Sundar et al. [9] produced strips of demineralized allogeneic bone and used them in a sheep model of tendon enthesis healing. The DBM- treated group experienced fewer early failures compared to the control group, and histological analysis at 12 weeks showed reformation of the enthesis in the DBM group, which was not observed in the control group. In another bovine study using a patellar tendon defect model, allogenic DBM resulted in significantly higher functional weight- bearing compared to xenogenic DBM at 6, 9, and 12 weeks [26]. The allograft DBM also had greater remodelling into tendon-like tissue and a significantly more mature neo-enthesis with the characteristic four zones [26]. Heuberer et al. [25] showed less scar tissue and more physiologic enthesis morphology in sheep 4 weeks following injection with DBM powder. The growth factors, including the BMPs found in DBM, have also shown promising results in rotator cuff healing. Rodeo et al. [7] used a mixture of osteoinductive growth factors in a collagen type I sponge in a sheep model, reporting improved biomechanical properties. Smith et al. [30] studied rotator cuff healing in a dog model using a demineralized cancellous sponge loaded with platelet-rich plasma (PRP). They demonstrated improved histology, MRI scores, and repair strength at 12 weeks in the DBM-PRP group compared to the direct repair group. MRI and histology scores were significantly better, and biomechanical testing showed significantly improved strength at various displacements and for ultimate failure load in the DBM-PRP repairs. Lovric et al. [32] demonstrated that DBM powder introduced into the bone tunnel of an ACL repair in a rodent model demonstrated increased graft strength at 4 and 6 weeks. The tendon-bone interface had considerably more woven bone formation and statistically higher peak load to failure, potentially due to higher levels of BMPs. Moreover, Lee et al. [31] compared rotator cuff repair with and without DBM augmentation in a rabbit model. Histological analysis revealed that the DBM group had a more organized tendon midsubstance with densely arranged collagen fibers and a tendon-bone interface consisting of organized collagen fibers with large quantities of fibrocartilage and mineralized fibrocartilage, which was less pronounced in the control group. Other studies involving rabbit models have also demonstrated promising histological results with the use of DBM [33,34]. In contrast, another study in rats with chronic rotator cuff degeneration found that allogenic DBM was not associated with improved histological remodelling compared to nonaugmented repair or repair with dermal matrix [35]. There is limited clinical literature specifically analysing the outcomes of DBM augmentation at the enthesis in rotator cuff repair. A systematic review by Hexter et. al. [36] highlighted that the efficacy of DBM in augmenting healing at the enthesis in humans lacks clinical studies, with most evidence being

preclinical. However, some studies have examined DBM augmentation in general. Wellington et al. [28] reported on DBM (Flexigraft, Arthrex, Naples, FL, USA) augmented with PRP and concentrated bone marrow aspirate (cBMA) for chronic full thickness rotator cuff tears. MRI demonstrated supraspinatus failure in 50% of complex rotator cuff tears – a failure rate similar to that previously described for such repairs. The study acknowledged limitations such as the lack of a control group and the concomitant use of PRP and cBMA, making it difficult to isolate the effect of DBM alone. While further research is required to define the clinical benefits of the DBF in rotator cuff repair, there are several advantages. This method addresses the weak link by targeting the enthesis, which is described as a persistent point of rotator cuff repair failure. Furthermore, the notion that it triggers biological regeneration in this area is well supported in preclinical literature as described previously. The DBM technology is also safe for clinical use and has been used extensively in other orthopaedic operations, particularly in spinal surgery as a bone void filler and graft material [10]. While this is the case, DBM is most commonly used in powder form, putties, paste, or cancellous chips. Hence, its handling and use during arthroscopic rotator cuff repairs would be challenging or impossible, as well as it lacks osteoconductivity. The advantage of the DBF technology is that it utilizes the biologic potential of DBM in a form that has better handling characteristics and osteoconductivity, providing ease of use during arthroscopic rotator cuff repairs. Because Enfix implants are shaped similar to suture anchors, their insertion during surgery aligns with the current techniques performed during arthroscopic rotator cuff repairs. The use of augmentation strategies to improve healing at the tendon-bone interface is an active area of research. While various materials and techniques have been proposed (e.g. fenestrated anchors and open coils), interpositional DBF implants like Enfix RC represent a direct and distinct approach to biological enhancement at the enthesis. Although studies have indicated lower failure rates with similar interpositional implants as compared to onlay-augmented repairs, they often lacked control groups, rendering direct comparisons challenging [37-39]. Our study attempts to address this with a matched non-augmented cohort. Although both cohorts demonstrated comparable postoperative outcomes across most clinical variables, the augmented group showed superior postoperative PROMs and a trend toward rotator cuff strengths more closely resembling that of the non-operated shoulder at a mean follow-up of 8 months. Correlating this to the radiologically observed structural improvement in enthesis, it is possible that this allows patients to regain strength earlier in the postoperative period as compared to the non-augmented group, subsequently allowing patients to achieve better function earlier as well. While the findings outlined in this study contribute to initial human data and show promising results, these represent early data with a mean follow-up of 8 months. Nevertheless, the current findings show clinical significance as supported by the scores exceeding MCIDs. Future research should initially prioritize longer follow-up of this cohort to monitor trends in clinical and radiological outcomes as well as re-tear rates. Given that rotator cuff healing and retear risk are influenced by factors such as patient age, tear size, diabetes mellitus and smoking status, future studies with a larger patient cohort should consider such variables and include a univariate/subgroup analysis. Moreover, future studies can also focus on purely massive, retracted tears, as these are the ones that have higher risk of retears which would ideally need biologic augmentations.

5. Conclusions

The use of demineralized bone fiber implant to augment arthroscopic rotator cuff repairs demonstrates promising early radiological signs of improved healing at the enthesis and better ASES, Constant, and UCLA scores. Although early data on other clinical variables are comparable to repairs without augmentation, investigation through extended follow-up and larger patient cohort is warranted given the potential for improved long-term structural integrity and better clinical outcomes.

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References

1. Mather, R.C., 3rd; Koenig, L.; Acevedo, D.; Dall, T.M.; Gallo, P.; Romeo, A.; Tongue, J.; Williams, G., Jr. The societal and economic value of rotator cuff repair. *J Bone Joint Surg Am* **2013**, *95*, 1993-2000, doi:10.2106/JBJS.L.01495.
2. Routledge, J.C.; Saber, A.Y.; Pennington, N.; Gupta, N. Re-Tear Rates Following Rotator Cuff Repair Surgery. *Cureus* **2023**,*15*, e34426, doi:10.7759/cureus.34426.
3. Zumstein, M.A.; Ladermann, A.; Raniga, S.; Schar, M.O. The biology of rotator cuff healing. *Orthop Traumatol Surg Res* **2017**,*103*, S1-S10, doi:10.1016/j.otsr.2016.11.003.
4. Kovacevic, D.; Rodeo, S.A. Biological augmentation of rotator cuff tendon repair. Clin Orthop Relat Res 2008, 466, 622-633, doi:10.1007/s11999-007-0112-4.
5. Carpenter, J.E.; Thomopoulos, S.; Flanagan, C.L.; DeBano, C.M.; Soslowsky, L.J. Rotator cuff defect healing: a biomechanical and histologic analysis in an animal model. *J Shoulder Elbow Surg* **1998**, *7*, 599-605, doi:10.1016/s1058-2746(98)90007-6.
6. Iannotti, J.P.; Deutsch, A.; Green, A.; Rudicel, S.; Christensen, J.; Marraffino, S.; Rodeo, S. Time to failure after rotator cuff repair: a prospective imaging study. *J Bone Joint Surg Am* **2013**, *95*, 965-971, doi:10.2106/JBJS.L.00708.
7. Rodeo, S.A.; Potter, H.G.; Kawamura, S.; Turner, A.S.; Kim, H.J.; Atkinson, B.L. Biologic Augmentation of Rotator Cuff Tendon-Healing with Use of a Mixture of Osteoinductive Growth Factors*. *JBJS* **2007**, *89*, 2485-2497, doi:10.2106/jbjs.C.01627.
8. Reddi, A.H.; Anderson, W.A. Collagenous bone matrix-induced endochondral ossification hemopoiesis. *J Cell Biol* **1976**, *69*, 557-572, doi:10.1083/jcb.69.3.557.
9. Sundar, S.; Pendegrass, C.J.; Blunn, G.W. Tendon bone healing can be enhanced by demineralized bone matrix: a functional and histological study. *J Biomed Mater Res B Appl Biomater* **2009**, *88*, 115-122, doi:10.1002/jbm.b.31157.
10. Shepard, N.A.; Rush, A.J., 3rd; Scarborough, N.L.; Carter, A.J.; Phillips, F.M. Demineralized Bone Matrix in Spine Surgery: A Review of Current Applications and Future Trends. *Int J Spine Surg* **2021**, *15*, 113-119, doi:10.14444/8059.
11. Gupta, A.; Ker, A.M.; Maharaj, J.C.; Veen, E.J.D.; Cutbush, K. All-Arthroscopic Muscle Slide and Advancement Technique to Repair Massive Retracted Posterosuperior Rotator Cuff Tears. Arthrosc Tech 2021, 10, e1439-e1446, doi:10.1016/j.eats.2021.02.009.
12. Gupta, A.; Italia, K.; Jomaa, M.N.; Ker, A.M.; Pareyon, R.; Tok, A.E.; Maharaj, J.; Whitehouse, S.L.; Cutbush, K. All-Arthroscopic Supraspinatus and Infraspinatus Muscle Advancement Leads to High Healing Rate and Excellent Outcomes in Patients With Massive, Retracted Rotator Cuff Tears, Even in Patients With Pseudoparalysis. Arthroscopy 2024, 40, 2801-2811, doi:10.1016/j.arthro.2024.03.041.
13. Opsomer, G.J.; Gupta, A.; Haeni, D.L.; Schubert, T.; Lejeune, E.; Petkin, K.; Maharaj, J.; Lafosse, L. Arthroscopic Double-Layer Lasso Loop Technique to Repair Delaminated Rotator Cuff Tears. Arthroscopy 2018, 34, 2943-2951, doi:10.1016/j.arthro.2018.06.024.
14. Constant, C.R.; Gerber, C.; Emery, R.J.; Sojbjerg, J.O.; Gohlke, F.; Boileau, P. A review of the Constant score: modifications and guidelines for its use. J Shoulder Elbow Surg 2008, 17, 355-361, doi:10.1016/j.jse.2007.06.022.
15. Patte, D. Classification of rotator cuff lesions. Clin Orthop Relat Res 1990, 81-86.
16. Lafosse, L.; Jost, B.; Reiland, Y.; Audebert, S.; Toussaint, B.; Gobezie, R. Structural integrity and clinical outcomes afterarthroscopic repair of isolated subscapularis tears. *J Bone Joint Surg Am* **2007**, *89*, 1184-1193, doi:10.2106/JBJS.F.00007.
17. Goutallier, D.; Postel, J.M.; Bernageau, J.; Lavau, L.; Voisin, M.C. Fatty muscle degeneration in cuff ruptures. Pre- and postoperative evaluation by CT scan. *Clin Orthop Relat Res* **1994**, 78-83.
18. Fuchs, B.; Weishaupt, D.; Zanetti, M.; Hodler, J.; Gerber, C. Fatty degeneration of the muscles of the rotator cuff: assessment by computed tomography versus magnetic resonance imaging. J Shoulder Elbow Surg 1999, 8, 599-605, doi:10.1016/s1058-2746(99)90097-6.
19. Sugaya, H.; Maeda, K.; Matsuki, K.; Moriishi, J. Functional and structural outcome after arthroscopic full-thickness rotator cuff repair: single-row versus dual-row fixation. Arthroscopy 2005, 21, 1307-1316, doi:10.1016/j.arthro.2005.08.011.
20. Kim, D.M.; Kim, T.H.; Kholinne, E.; Park, J.H.; Shin, M.J.; Kim, H.; Park, D.; Jeon, I.H.; Koh, K.H. Minimal Clinically

Important Difference, Substantial Clinical Benefit, and Patient Acceptable Symptomatic State After Arthroscopic Rotator Cuff Repair. Am J Sports Med 2020, 48, 2650-2659, doi:10.1177/0363546520943862

21. Cvetanovich, G.L.; Gowd, A.K.; Liu, J.N.; Nwachukwu, B.U.; Cabarcas, B.C.; Cole, B.J.; Forsythe, B.; Romeo, A.A.; Verma, N.N. Establishing clinically significant outcome after arthroscopic rotator cuff repair. J Shoulder Elbow Surg 2019, 28, 939-948, doi:10.1016/j.jse.2018.10.013.

22. Li, Y.; Fu, G.; Gong, Y.; Li, B.; Li, W.; Liu, D.; Yang, X. BMP-2 promotes osteogenic differentiation of mesenchymal stem cells by enhancing mitochondrial activity. J Musculoskelet Neuronal Interact 2022, 22, 123-131.

23. Urist, M.R.; Strates, B.S. Bone Morphogenetic Protein. *Journal of Dental Research* **1971**, *50*, 1392-1406, doi:10.1177/00220345710500060601.

24. Urist, M.R. Bone: formation by autoinduction. *Science* **1965**, *150*, 893-899, doi:10.1126/science.150.3698.893.

25. Heuberer, P.; Lovric, V.; Russell, N.; Goldberg, J.; Walsh, W. DEMINERALISED BONE MATRIX AUGMENTED TENDON BONE HEALING. *Orthopaedic Proceedings* **2014**, *96-B*, 157-157, doi:10.1302/1358-992x.96bsupp_11.Cors2013-157.

26. Thangarajah, T.; Shahbazi, S.; Pendegrass, C.J.; Lambert, S.; Alexander, S.; Blunn, G.W. Tendon Reattachment to Bone in an Ovine Tendon Defect Model of Retraction Using Allogenic and Xenogenic Demineralised Bone Matrix Incorporated with Mesenchymal Stem Cells. *PLoS One* **2016**, *11*, e0161473, doi:10.1371/journal.pone.0161473.

27. Elnikety, S.; Pendegrass, C.J.; de Godoy, R.F.; Holden, C.; Blunn, G.W. Augmentation and repair of tendons using demineralised cortical bone. *BMC Musculoskelet Disord* **2016**, *17*, 483, doi:10.1186/s12891-016-1323-1

28. Wellington, I.J.; Muench, L.N.; Hawthorne, B.C.; Uyeki, C.L.; Antonacci, C.L.; McCarthy, M.B.; Connors, J.P.; Kia, C.; Mazzocca, A.D.; Berthold, D.P. Clinical Outcomes following Biologically Enhanced Demineralized Bone Matrix Augmentation of Complex Rotator Cuff Repair. J Clin Med 2022, 11, doi:10.3390/jcm11112956.

29. Gruskin, E.; Doll, B.A.; Futrell, F.W.; Schmitz, J.P.; Hollinger, J.O. Demineralized bone matrix in bone repair: history and use. Adv Drug Deliv Rev 2012, 64, 1063-1077, doi:10.1016/j.addr.2012.06.008.

30. Smith, M.J.; Pfeiffer, F.M.; Cook, C.R.; Kuroki, K.; Cook, J.L. Rotator cuff healing using demineralized cancellous bone matrix sponge interposition compared to standard repair in a preclinical canine model. J Orthop Res 2018, 36, 906-912, doi:10.1002/jor.23680.

31. Lee, W.Y.; Kim, Y.M.; Hwang, D.S.; Shin, H.D.; Joo, Y.B.; Cha, S.M.; Kim, K.H.; Jeon, Y.S.; Lee, S.Y. Does Demineralized Bone Matrix Enhance Tendon-to-Bone Healing after Rotator Cuff Repair in a Rabbit Model? Clin Orthop Surg 2021, 13, 216-222, doi:10.4055/cios20099.

32. Lovric, V.; Chen, D.; Yu, Y.; Oliver, R.A.; Genin, F.; Walsh, W.R. Effects of Demineralized Bone Matrix on Tendon-Bone Healing in an Intra-articular Rodent Model. The American Journal of Sports Medicine 2012, 40, 2365-2374, doi:10.1177/0363546512457648.

33. Kiliçoğlu, Ö.; Dikmen, G.; Koyuncu, Ö.; Bilgiç, B.; Alturfan, A.K. Effects of demineralized bone matrix on tendon-bone healing: an in vivo, experimental study on rabbits. *Acta Orthop Traumatol Turc* **2012**, *46*, 443-448, doi:10.3944/aott.2012.2748.

34. Hsu, S.L.; Wang, C.J. The use of demineralized bone matrix for anterior cruciate ligament reconstruction: a radiographic, histologic, and immunohistochemical study in rabbits. *J Surg Res* **2014**, *187*, 219-224, doi:10.1016/j.jss.2013.09.025.

35. Thangarajah, T.; Henshaw, F.; Sanghani-Kerai, A.; Lambert, S.M.; Blunn, G.W.; Pendegrass, C.J. The effectiveness of demineralized cortical bone matrix in a chronic rotator cuff tear model. *J Shoulder Elbow Surg* **2017**, *26*, 619-626, doi:10.1016/j.jse.2017.01.003.

36. Hexter, A.T.; Pendegrass, C.; Haddad, F.; Blunn, G. Demineralized Bone Matrix to Augment Tendon-Bone Healing: A Systematic Review. *Orthop J Sports Med* **2017**, *5*, 2325967117734517, doi:10.1177/2325967117734517.

37. Krupp, R.; Frankle, M.; Nyland, J.; Baker, C.E.; Werner, B.C.; Pierre, P.S.; Tashjian, R. Interpositional scaffold anchor rotator cuff footprint tear repair: excellent survival, healing, and early outcomes. *Knee Surgery, Sports Traumatology, Arthroscopy* **2023**,*31*, 2670-2680, doi:10.1007/s00167-023-07383-2.

38. Mandalia, K.; Mousad, A.; Welborn, B.; Bono, O.; Le Breton, S.; MacAskill, M.; Forlizzi, J.; Ives, K.; Ross, G.; Shah, S. Scaffold-and graft-based biological augmentation of rotator cuff repair: an updated systematic review and meta-analysis of preclinical and clinical studies for 2010-2022. *Journal of Shoulder and Elbow Surgery* **2023**, *32*, 1784-1800, doi:https://doi.org/10.1016/j.jse.2023.03.031.

39. Seetharam, A.; Abad, J.; Baessler, A.; Badman, B.L. Use of a nanofiber resorbable scaffold during rotator cuff repair: Surgical technique and results after repair of small-to medium-sized tears. *Orthopaedic Journal of Sports Medicine* **2022**, *10*, 23259671221094848.