Augmentation of a Transosseous-Equivalent Repair in Posterosuperior Nonacute Rotator Cuff Tears With a Bioinductive Collagen Implant Decreases the Retear Rate at 1 Year: A Randomized Controlled Trial

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Purpose: To determine whether the addition of a bioinductive collagen implant (BCI) over a transosseous equivalent (TOE) repair of medium-to-large posterosuperior rotator cuff tears improves the healing rate determined by magnetic resonance imaging (MRI) at 12-month follow-up. **Methods:** A Level I randomized controlled trial was performed in 124 subjects with isolated, symptomatic, reparable, full-thickness, medium-to-large posterosuperior nonacute rotator cuff tears, with fatty infiltration $\leq$2. These were randomized to 2 groups in which an arthroscopic posterosuperior rotator cuff tear TOE repair was performed alone (Control group) or with BCI applied over the TOE repair (BCI group). The primary outcome was the retear rate (defined as Sugaya 4-5) determined by MRI at 12 months of follow-up. Secondary outcomes were characteristics of the tendon (Sugaya grade and thickness of the healed tendon) and clinical outcomes (pain levels, EQ-5D-5L, American Shoulder and Elbow Surgeons, and Constant–Murley scores) at 12 months of follow-up. **Results:** Of the 124 randomized patients, 122 (60 in the BCI group and 62 in the Control group) were available for MRI evaluation 12.2 $\pm$ 1.02 months after the intervention. There were no relevant differences in preoperative characteristics. Adding the BCI reduced the retear rate (8.3% [5/60] in the BCI group vs 25.8% [16/62] in the Control group, $P = .010$; relative risk of retear of 0.32 [95% confidence interval 0.13-0.83]). Sugaya grade was also better in the BCI group ($P = .030$). There were no differences between groups in the percentage of subjects who reached the MCID for CMS (76.7% vs 81.7%, $P = .654$) or American Shoulder and Elbow Surgeons (75% vs 80%, $P = .829$), in other clinical outcomes or in complication rates at 12.4 $\pm$ 0.73 (range 11.5-17) months of follow-up. **Conclusions:** Augmentation with a BCI of a TOE repair in a medium-to-large posterosuperior rotator cuff tear reduces the retear rate at 12-month follow-up by two-thirds, yielding similar improvements in clinical outcomes and without increased complication rates. **Level of Evidence:** Level I, randomized controlled trial.

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Rotator cuff tears often cause pain and dysfunction, and arthroscopic rotator cuff repair (ARCR) is a successful surgical procedure with good clinical outcomes that is increasingly performed.[1] However, structural failure of the repair is not uncommon, affecting 10% to 75% of repairs.[2-4] Despite the

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introduction of advanced arthroscopic techniques, the clinical and structural outcomes of ARCR have not dramatically improved since the 1990s.[5]

During rotator cuff repair, both mechanical and biological factors should be considered to obtain healing. From a mechanical standpoint, it is necessary that the tendon is kept in close contact with the bone long enough to heal,[6] and double-row and transosseous equivalent (TOE) technologies were developed to address this issue, albeit with limited success in improving healing rates.[7] It is increasingly clear that the main issue is biological. There are 2 main challenges: first, tendon-to-bone healing is notably difficult to achieve, and failure to heal at the footprint (a type 1 failure according to Cho et al.[8]) is not uncommon.[9] Second, as the tendon tissue is often diseased, failure medial to the repair (a type 2 failure) is also relatively frequent, ranging from 24% to 92% of tendon failures.[9-11] Different biological alternatives, such as bone marrow stimulation, platelet-rich plasma, and stem cells, have been proposed to try to improve outcomes.[9,12] Augmentation of the repaired tendon with different grafts (allogenic dermal tissue or fascia lata, or xenogenic dermal matrix) is another alternative that has shown to have some benefit, in particular reducing the retear rate.[13] Recently, a bioinductive collagen implant (BCI) of bovine origin has been used to supplement ARCR.[14,15] This implant is progressively infiltrated by cells from the native tendon and incorporates into it, increasing its quality and thickness.[14,16,17] Good preliminary outcomes have been reported when used to supplement an ARCR, with retear rates of 11% in mid-sized tears[18] and 9% in large and massive tears,[19] but no high level of evidence data is available.

The purpose of this randomized controlled trial (RCT) was to determine whether the addition of a BCI over a TOE repair of medium-to-large posterosuperior rotator cuff tears improves the healing rate determined by magnetic resonance imaging (MRI) at 12-month follow-up. The hypothesis was that patients treated with BCI augmentation would have lower retear rates, increased tendon thickness, and better clinical outcomes at 12-month follow-up.

Methods

Trial Design

This was a 2-arm, multicentric, triple blinded (patient, outcome assessor, and data analyst-blinded), parallel-group, pragmatic, randomized, superiority trial with 12 months of follow-up. The study (called the MALLAMANGUITO01 clinical trial) was approved by the institutional review board of Hospital Universitario Ramón y Cajal (in Madrid, Spain. Protocol code MALLAMANGUITO01, approved June 8, 2020. A copy of the approval letter is included as Appendix Figure 1, available at www.arthroscopyjournal.org). All patients received information orally and in writing about the study, and written consent was obtained. The detailed protocol was preregistered in ClinicalTrials.gov (NCT04444076) and is available there. The study was performed between June 2020 and April 2023.

Participants

Eight orthopaedic surgeons with at least 10 years' experience in ARCR from 4 surgical centers (2 university hospitals: Hospital Universitario Ramón y Cajal and Hospital Universitario HM Sanchinarro, both in Madrid, Spain; and 2 workers' compensation hospitals: Hospital Maz Zaragoza in Zaragoza, Spain, and Hospital Asepeyo Coslada in Madrid, Spain) participated in the study. Patients scheduled for primary elective posterosuperior cuff repair were eligible for inclusion. The inclusion criteria were (1) age $\geq$18 years; (2) nonacute symptomatic (>3 months of symptoms) full-thickness posterosuperior cuff tear with an intraoperative anterior–posterior size between 1 and 4 cm; and (3) fully repairable tear (>80% footprint coverage without tension confirmed during surgery). The exclusion criteria were (1) pregnancy or risk of pregnancy; (2) retraction larger than 3 cm; (3) Goutallier-Fuchs[20,21] grade 3-4 fatty infiltration in any rotator cuff tendon in a preoperative MRI evaluation performed <6 months before the surgery; (4) any subscapularis tendon tear that required repair during the surgical procedure; and (5) previous surgery or fracture in the index shoulder.

Interventions

After informed consent was obtained, the participants were brought to the surgical theater and operated under general anesthesia and an interscalene nerve block. The tear was debrided and the tear pattern was defined (according to Davidson and Burkhart[22]), and size and retraction were measured using a graduated probe. The footprint was debrided, gently decorticated and microfractured, and its surface measured with a probe. Biceps tenotomy was performed if the supraspinatus tear extended to the bicipital groove anteriorly or there were inflammatory or degenerative signs of the tendon. No biceps tenodesis were performed. Acromioplasty was rarely performed. After proper debridement of the tendon, capsular and subacromial releases were performed as needed. The reparability of the tendon was confirmed, ensuring it could cover the footprint without undue tension. A TOE repair was done with 1 to 3 medial row anchors (HEALICOIL REGENESORB loaded with a tape and a suture; Smith & Nephew, Andover, MA) placed in the medial edge of the footprint; all limbs of the sutures and tapes were passed

through the medial tendon and tied. The tapes were brought laterally over the tied sutures in a rip-stop configuration, then secured into 1 or 2 lateral anchors (MULTIFIX; Smith & Nephew) placed 10 to 20 mm distal to the edge of the footprint. If the footprint was not fully covered, the uncovered surface was measured again.

After completion of the repair and confirmation of eligibility criteria, randomization proceeded: (1) In the Control group, the procedure was finished; (2) in the BCI group the implant (REGENETEN BIOINDUCTIVE IMPLANT, Smith & Nephew, large size) was used as per the instructions for use: placed over the repaired tendon, stretching 5- to 10-mm lateral to the footprint, and fixed to the tendon with 5-8 absorbable anchors and to the bone with 1 to 3 PEEK (polyether ether ketone) anchors (Fig 1). The BCI used is made of highly purified type I collagen obtained from bovine calcaneal tendons. The collagen fibers are processed to create a highly porous (85%-90% porosity) and highly oriented collagen scaffold (20-mm wide, 30-mm long, and 2-mm thick). The BCI is freeze-dried after processing and rehydrated during surgery.[14]

Both groups used the same postoperative protocol: the arm was placed in a sling for 6 weeks; passive range of motion exercises were allowed after the first 3 weeks and active assisted exercises were allowed after 6 to 8 weeks. Full active exercises were started at the ninth week, and strengthening exercises were started at the 10th week.

Randomization and Blinding

A random list of numbers was computer generated with an allocation rate of 1:1 using block sizes of 10 and 150 opaque envelopes were prepared by a researcher independent from the study. Ten-envelope blocks were randomly assigned to each team with further blocks assigned as needed. Envelope-opening was performed after the TOE rotator cuff repair was completed and the inclusion and exclusion criteria were confirmed. The surgeon was not blinded to assignation. The patients were blinded to the group they were assigned and remained blinded until after the 12-month follow-up evaluation. Outcome assessment of the participants was done by one surgeon who did not participate in the surgical procedure and was unaware of the group assignment. For MRI assessment, all images were stripped of personal data before evaluation by the assessors. Blinded MRI assessment was possible, as the BCI integrates into the tendon during the first 6 months postoperatively,[16] without any remnants of the collagen implant in 6-month biopsies[16,17] and is no

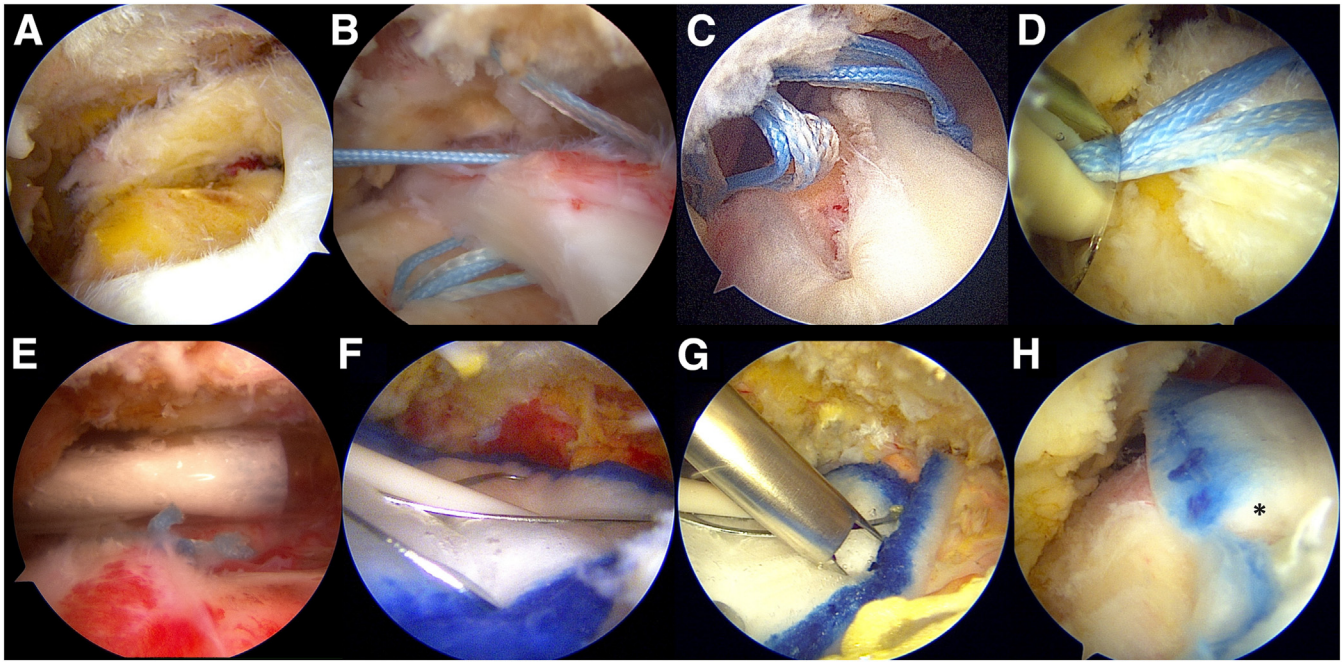

Fig 1. The repair technique using the bioinductive collagen implant. An arthroscopic view of the subacromial space of a patient with a medium-sized, full-thickness tear in the left shoulder (A). The tear is repaired using a transosseous equivalent (TOE) technique with 2 medial-row anchors with sutures and tapes passed through the medial tendon (B) and tied (C). The tapes are brought laterally in a rip-stop configuration over the tied sutures and secured into one lateral anchor (D). The Bioinductive Collagen Implant (BCI) is inserted through the lateral portal (E) and adjusted to cover the repair (F). It is fixed medially to the tendon with 5 to 8 absorbable anchors (G) and laterally to the bone with 1 or 2 PEEK anchors (*) that are placed so as not to collide with the lateral row anchors, distally to them if possible, as seen here (H). The final BCI covers the repair starting 5 to 10 mm distal to the lateral edge of the repair and reaching the tendon 5 to 15 mm proximal to the medial sutures.

longer apparent in MRI studies at 12-month follow-up.[23,24] The statistician who performed the data analysis was blinded to the group assignments.

Outcomes

The primary outcome was the retear rate evaluated in an MRI performed 12 months after the procedure. MRI scans were performed in each institution as per the local standard of care. Tendon continuity was assessed using the Sugaya classification[25] (considering grades ≤ 3 as healed and grades ≥ 4 as retears). Three surgeons and a radiologist independent from the study, each with more than 20 years' experience in shoulder radiology, examined separately all blinded MRIs. After that, in a second round of assessment, all 4 examiners reviewed together each MRI in which a disagreement was observed and resolved those by consensus between them.

Some secondary outcomes were assessed in the final MRI: (1) structural continuity using the 5-grade Sugaya classification.[25] (2) Retear location: either at the footprint (type 1) or medial to the repair (type 2).[26] (3) In the healed tendons (Sugaya 1-3), supraspinatus tendon thickness in a T2-coronal view, at the center of the repair, in 3 zones (medial edge of the footprint, 10 mm, and 20 mm medial to it, Fig 2). The measurements were made with the Radiant DICOM viewer (version 2021.2; Poznam, Poland) that has a nominal precision of 0.1 mm. The in-plane spatial resolution of the MRI studies was between 0.2 and 0.5 mm. (4) Fatty infiltration according to the Goutallier-Fuchs classification in the supraspinatus and infraspinatus muscles.

The rest of the clinical secondary outcomes were assessed preoperatively and at 3, 6, and 12 months of follow-up: (5) pain levels using questions 3 to 6 of the Brief Pain Inventory (a self-administered questionnaire that assess maximum, minimum, mean and actual pain in the last 24 hours in a 0-10 discrete scale) (6) Constant–Murley score (CMS), American Shoulder and Elbow Surgeons (ASES) score and EQ-5D-5L self-rated general health questionnaire; and (7) time to return to work. The minimally clinical important difference (MCID) for the CMS and ASES values were calculated using half the standard deviation of the delta as suggested by Harris et al.[27] Further baseline information was also recorded (Table 1).

Statistical Analysis

Sample size estimation was done using the primary outcome. A baseline healing rate of 70% was assumed.[7,9] To identify a potential difference between groups of at least 20% with an α-error = 0.05 and a power $(1 - \beta) = 0.8$, 54 subjects per arm of the study were considered necessary. After considering a loss of follow-up of 10%, this was adjusted to 60 subjects per group. An adaptative design was used with an interim analysis planned when the first 60 subjects were available for assessment at 1 year. The significance parameters were adjusted as suggested by Haybittle and Peto[28] ($\alpha = 0.002$ for interim analysis, $\alpha = 0.05$ for the final analysis).

Continuous variables were tested for normality using the Kolmogorov–Smirnoff test. The χ^2 test was used to compare dichotomous and qualitative variables. The Student *t* test was used to compare quantitative variables. The Mann–Whitney *U* test was used to compare Sugaya grades. Outcome analysis was performed "per protocol". The statistical threshold for significance was established at $P < .05$. To assess the robustness of the study, the fragility index, defined as the minimum number of subjects whose status would have to change from a nonevent to an event in order to convert a statistically significant result of the

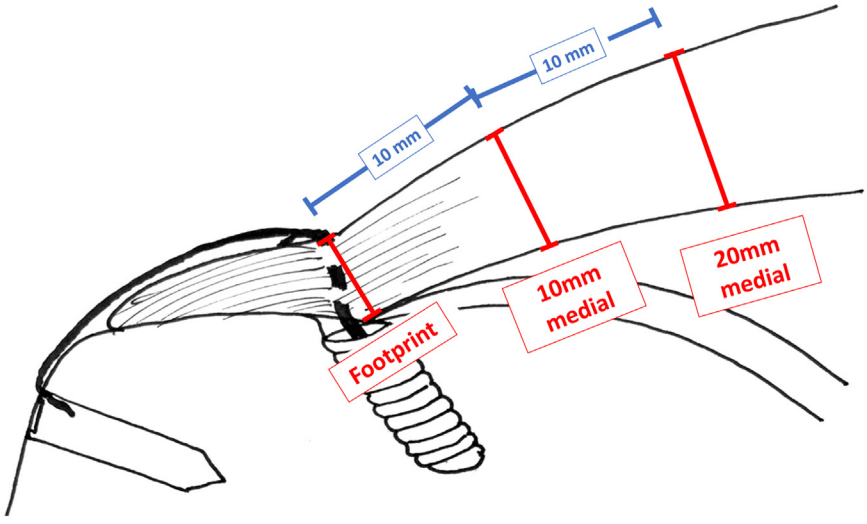

Fig 2. Diagram showing the tendon thickness measurement technique. For the 101 healed tendons (Sugaya 1-3) a T2-coronal view of the center of the repair was selected (based on the number of medial and lateral anchors). The medial edge of the footprint was identified and the thickness measurements were made at this level and also 10 mm and 20 mm medial to it.

Table 1. Baseline Demographic, Clinical Characteristics, and Surgical Data for Each Group

	Bioinductive Collagen Implant (n = 61)	Control (n = 63)	*P* Value
Demographic data			
Age, y	56.6 ± 6.86	58.7 ± 8.39	.140
Sex (male:female)	31:30	30:33	.722
Weight, kg	77.1 ± 14.6	77.0 ± 18.6	.987
Height, cm	166 ± 8.8	164.8 ± 13.7	.429
BMI, kg/m^2	27.8 ± 4.69	27.2 ± 4.07	.501
Ethnicity			
(White/Hispanic/other)	52/9/0	55/7/1	.521
Comorbidities			
Diabetes	7 (11.5%)	8 (12.7%)	.834
Tobacco use	14 (22.9%)	16 (25.4%)	.751
Hypercholesterolemia	21 (34.4%)	15 (23.8%)	.192
Steroid injections in the last 6 mo	7 (11.5%)	10 (15.9%)	.481
Number of previous injections	1.3 ± 0.49	1.6 ± 0.84	.391
Time from injection to surgery, mo	2.17 ± 0.98	2.7 ± 1.70	.498
Labor force status			.458
Active	50 (82.0%)	46 (73.0%)	
Not working	4 (6.6%)	5 (7.9%)	
Retired	7 (11.5%)	12 (19.0%)	
Workers' compensation	31 (50.8%)	29 (46.0%)	.284
Tear characteristics			
Side (right:left)	44:17	42:21	.509
Tear shape			.180
Crescent	31 (75.8%)	39 (61.9%)	
L-shaped	8 (13.1%)	11 (17.5%)	
Inverted-L	6 (9.8%)	6 (9.53%)	
U-shaped	16 (26.2%)	7 (11.1%)	
Tear size, mm	20.4 ± 6.83	19.7 ± 6.39	.541
10-19.9	29 (47.5%)	28 (44.4%)	.582
20-29.9	24 (39.3%)	29 (46.0%)	
30-40	9 (14.8%)	6 (9.5%)	
Tear retraction, mm	16.5 ± 8.78	13.8 ± 7.22	**.040**
Fatty infiltration in preoperative MRI			
SE (0:I:II)	50:11:0 (81.9%:18.1%:0%)	47:15:1 (74..6%:23.8%:1.6%)	.267
IE (0:I:II)	56:4:1 (88.8%:6.5%:1.6%)	55:8:0 (87.3%:12.7%:0%)	.323
Functional			
Preoperative pain levels			
Maximum	6.7 ± 2.1	7.1 ± 2.3	.312
Minimum	2.4 ± 2.2	2.5 ± 2.5	.818
Mean	4.9 ± 2.1	5.0 ± 2.9	.763
Now	4.0 ± 2.7	4.6 ± 2.9	.306
Preoperative CMS	45.7 ± 16.9	45.6 ± 14.3	.980
Pain	4.1 ± 3.7	4.7 ± 3.7	.358
Functional	9.4 ± 3.8	9.6 ± 3.4	.821
ROM	28.8 ± 10.0	29.1 ± 8.1	.859
Strength	3.3 ± 5.8	2.2 ± 4.4	.241
Preoperative ASES	44.6 ± 16.4	42.6 ± 16.5	.476
EQ-5D-5L scores			
Health index (TTO)	2.43 ± 0.53	2.31 ± 0.58	.227
Health level (VAS)	68.1 ± 21.9	64.4 ± 19.7	.343
Surgical technique			
Duration of surgery, min	90.5 ± 19.9	76.6 ± 17.6	**<.0001**
Associated procedures			
Acromioplasty	1 (1.67%)	2 (3.17%)	.578
Biceps tenotomy	60 (98.4%)	62 (98.4%)	.476

NOTE. Values are given as mean ± standard deviation for quantitative variables and number (percentage of total) for quantitative variables. Variables with *P* values <.05 are presented in bold. The statistical analysis results comparing both groups for each variable is presented in the right column.

ASES, American Shoulder and Elbow Surgeons; BMI, body mass index; BPI, Brief Pain Inventory; CMS, Constant–Murley scores; IE, infraspinatus; MRI, magnetic resonance imaging; ROM, range of motion; SE, supraspinatus; TTO, time trade-off; VAS, visual analog score.

study into a nonsignificant result, was calculated.[29,30] The S-index was also calculated.[31,32]

Results

Patients

Between June 2020 and February 2022, 592 ARCRs were performed in the 4 participating institutions. Of these, 165 subjects preliminarily met the inclusion and exclusion criteria before surgery, gave informed consent to participate in the study, and were considered for inclusion (Fig 3). After ARCR, 124 were randomized (61 to BCI and 63 to Control). Recruitment was stopped after randomizing the estimated required number of participants. The 124 subjects included were distributed quite evenly between the 4 participating centers (34, 34, 32, and 24 subjects for each center). The baseline data for each group can be seen in Table 1. The only differences between groups in the epidemiologic, preoperative clinical, preoperative MRI, and surgical data were tendon retraction (greater in the BCI group, mean difference 2.7 mm, $P = .040$) and surgery duration (13.9 minutes longer in the BCI group, an 18% increase in surgical time, $P < .0001$). Platelet-rich plasma was not used in any patient at any time. Two subjects were lost to follow-up: one was not willing to complete the study and withdrew from the study at 5-months' follow-up; another, a 61-year-old female smoker with diabetes, died 8 months after surgery due to a worsening of a previous cardiac insufficiency complicated with an ischemic event; this incident was considered unrelated to the study after a full clinical autopsy. The remaining 122 (98.4%) subjects (BCI group, n = 60; Control group, n = 62) were available for MRI assessment (Fig 4). Two subjects (both in the control group) presented poor functional outcomes and persistent pain at 5- and 6-months' follow-up. An MRI showed a clear retear and both underwent revision ARCR. These 2 patients were included in the primary variable analysis (MRI outcomes) but were excluded from the clinical assessment, leaving 120 (96.8%) subjects for secondary clinical variable assessment. All 122 remaining patients were considered to be compliant with the rehabilitation protocol by their physical therapists.

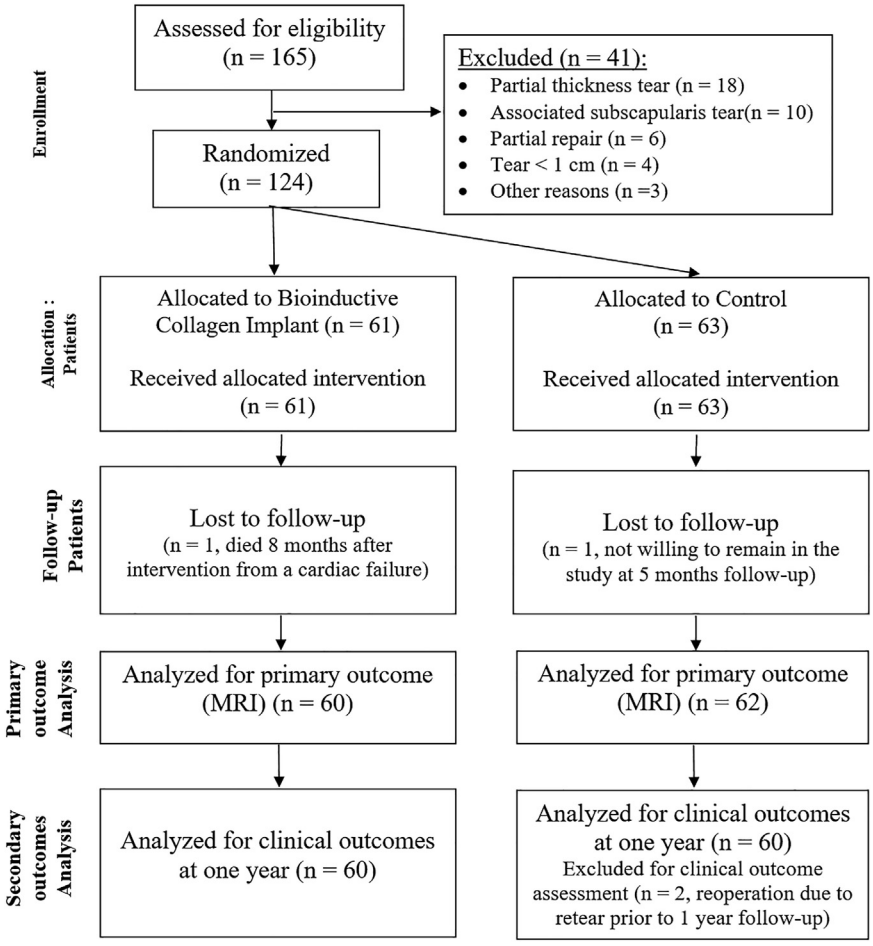

Fig 3. CONSORT flow diagram of the study. (CONSORT, Consolidated Standards of Reporting Trials.)

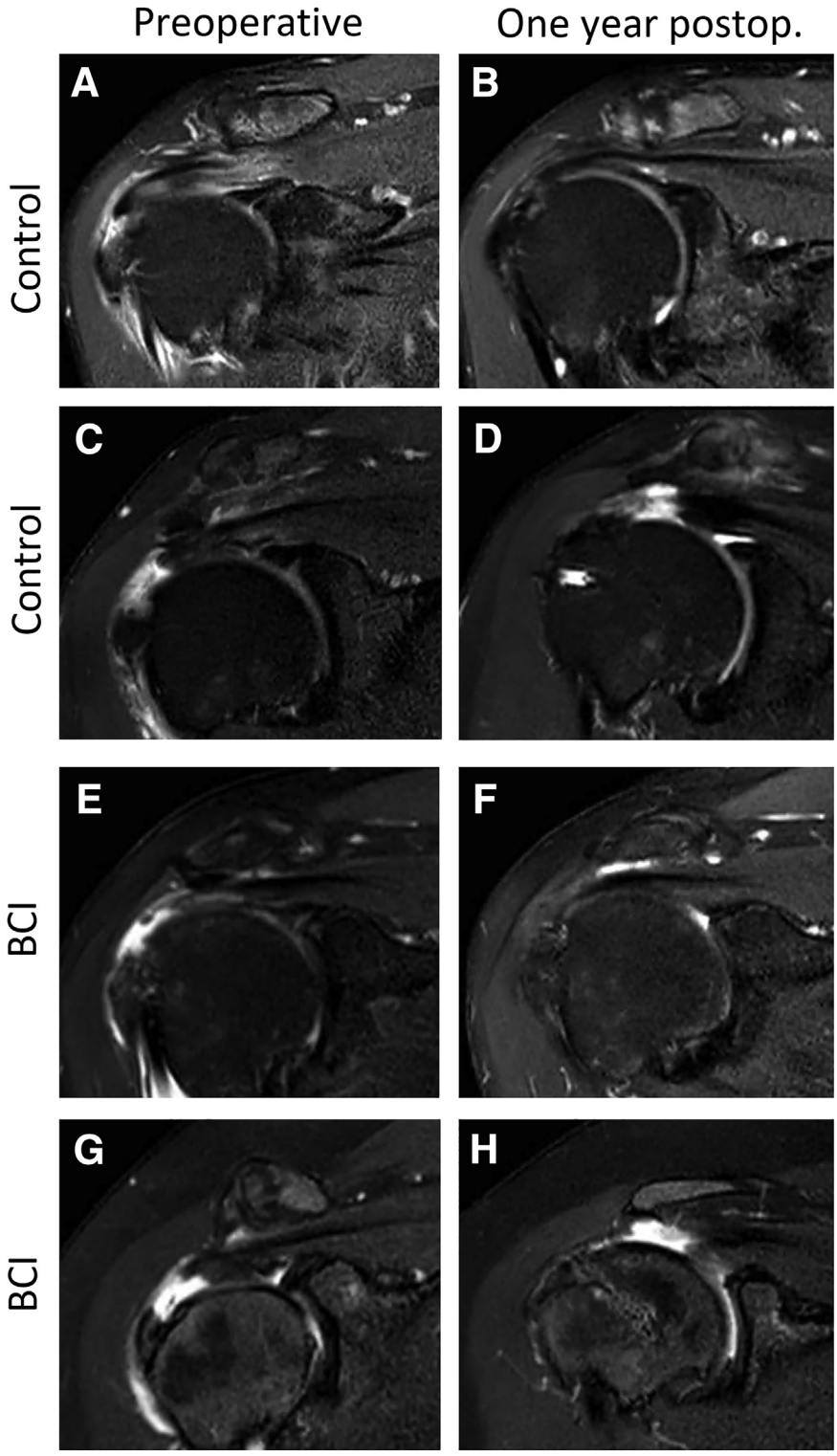

Fig 4. Oblique coronal T2-weighted magnetic resonance imaging of 4 representative cases. Preoperative images (A, C, E, G) can be seen side by side to 12-month follow-up images (B, D, F, H). Two cases belong to the control group (A-B and C-D) and 2 to the bioinductive collagen implant (BCI) group (E-F and G-H). Cases A-B and E-F (one from each study group) show complete healing and were classified as Sugaya grade 1. Case C-D shows a failure in the control group that was considered a Sugaya grade 4 with a type 2 (medial) failure. Case G-H shows a failure in the BCI group that was considered a Sugaya grade 5 with a type 1 (footprint) failure.

Primary Outcome

The MRI studies of 122 subjects performed 12.2 ± 1.02 months after surgery were assessed. Initial agreement between all four examiners was obtained in 72% of cases and all disagreements were resolved in the second round of assessment. There was a decreased retear rate in the BCI group: in the Control group, there were 16 retears in 62 subjects (25.8%,

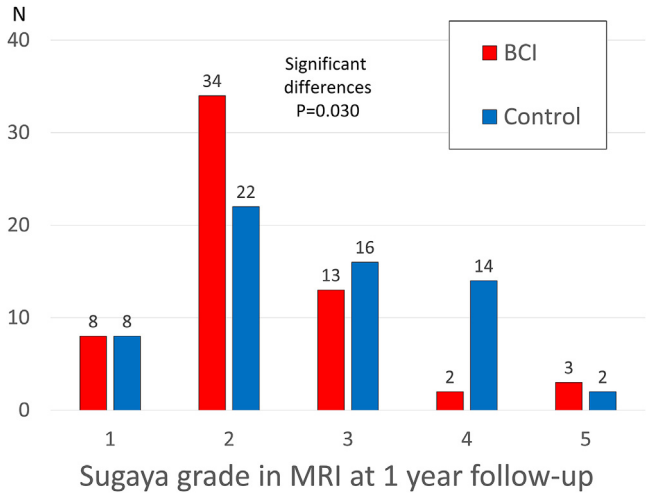

Fig 5. Assessment of rotator cuff integrity in the 12-month magnetic resonance imaging using the Sugaya Classification of the 122 tendon repairs.

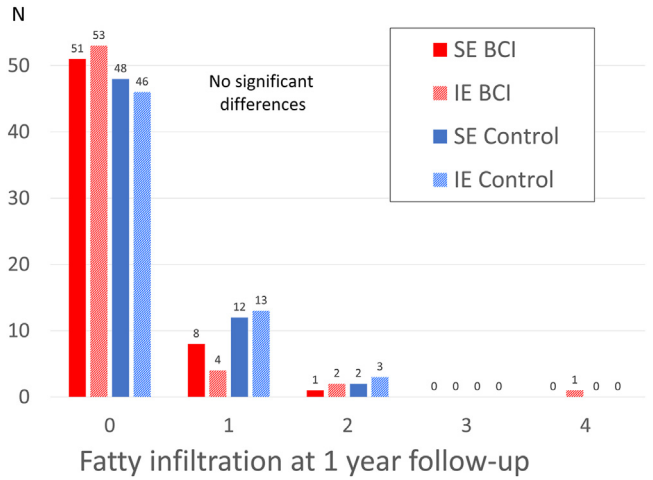

Fig 6. Degree of fatty infiltration of the supraspinatus (SE) and infraspinatus (IE) muscles according to Goutallier-Fuchs in the 122 magnetic resonance imaging (MRI) scans analyzed from the Control group and the bioinductive collagen implant (BCI) group in the 12-month MRI.

95% confidence interval [CI] 16.6%-37.9%) and, in the BCI, there were 5 retears in 60 subjects (8.33%, 95% CI 3.61%-18.1%); these differences were significant ($\chi^2 = 6.53$, $P = .0106$) with an odds ratio of 0.261 (CI 0.093-0.745). The absolute reduction in retear risk was 0.174 (95% CI 0.304-0.045). The relative retear risk was 0.323 (95% CI 0.126-0.826). The number of subjects needed to treat with the BCI to avoid a retear was 5.7 (95% CI 3.3-22.5). The fragility index of these results was 3. The S-value was 6.56.

Secondary Outcomes

In the MRIs performed 12 months after surgery, the structural continuity of the repaired tendon according to Sugaya was better in the BCI group ($P = .030$, Fig 5). In the 21 cases with a retear, a type-1 failure (Fig 4H) was found in 4 cases (2 in each group, $P = 1.0$), but the 17 type-2 retears (Fig 4D) developed mainly in the Control group (14 in the Control group vs 3 in the BCI group, $P = .0051$). There were no differences in the degree of fatty infiltration between groups ($P = .879$ for supraspinatus and $P = .169$ for infraspinatus, Fig 6) at the final MRI. The tendon thickness in the 101 healed tendons was greater in the BCI group in 2 of the 3 measured zones (Fig 7). The standard error of measurement for tendon thickness measurements was 0.29 mm. Detailed analysis of these 101 MRI studies did not show the presence of any distinguishable remaining BCI over the tendon.

Clinical assessment was performed 12.4 ± 0.73 (range 11.5-17) months after surgery (12.5 ± 0.70 [range 11.8 to 17] months in the BCI group and 12.4 ± 0.75 [range 11.5-17] months in the Control group, differences not significant, $P = .295$). There were general improvements of all secondary clinical variables compared with baseline data in both groups, but no differences were found between groups during the follow-up in the pain levels (Table 2), CMS (Fig 8), ASES score (Fig 9), or EQ-5D-5L (Fig 10) at any time point. It should be noted that the 2 patients who required a second surgical procedure, both from the control group, were excluded in this analysis. Compared with baseline, maximum, mean and "now" pain levels improved early in the first postoperative month. Minimum pain levels were similar in the 1- and 3-month follow-up but improved

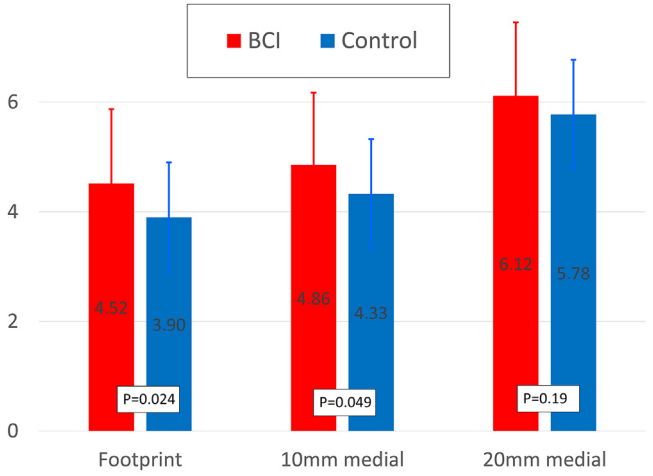

Fig 7. Tendon thickness (in mm) of the 101 healed tendons measured in the 12-month MRI scans from the Control group and the bioinductive collagen implant (BCI) group at the medial edge of the footprint (Footprint), and 10 and 20 mm medial to it.

Table 2. Pain Levels of Both Groups During the First Year After Surgery

	Preoperative			1 Month			3 Months			6 Months			1 Year		
Pain Levels	BCI	Control	*P* Value	BCI	Control	*P* Value	BCI	Control	*P* Value	BCI	Control	*P* Value	BCI	Control	*P* Value
Maximum pain	6.72 ± 2.11	7.13 ± 2.32	.311	**5.02 ± 2.20**	**4.84 ± 2.67**	.691	**4.74 ± 2.31**	**4.67 ± 2.72**	.875	**2.90 ± 2.30**	**2.98 ± 2.66**	.853	**2.05 ± 2.46**	**2.17 ± 2.78**	.809
Minimum pain	2.41 ± 2.20	2.51 ± 2.53	.818	**1.51 ± 1.79**	**1.67 ± 2.43**	.680	1.69 ± 2.04	1.87 ± 2.32	.639	**1.32 ± 1.91**	**1.28 ± 1.69**	.908	**0.92 ± 1.63**	**0.82 ± 1.79**	.749
Mean pain	4.90 ± 2.09	5.02 ± 2.11	.762	**3.07 ± 1.93**	**3.17 ± 2.33**	.776	**3.02 ± 2.00**	**3.35 ± 2.32**	.394	**2.08 ± 1.97**	**2.18 ± 2.10**	.794	**1.50 ± 2.07**	**1.52 ± 2.27**	.966
Pain now	4.03 ± 2.74	4.56 ± 2.92	.306	**2.26 ± 2.37**	**2.35 ± 2.85**	.854	**2.57 ± 2.61**	**2.89 ± 2.74**	.513	**1.98 ± 2.13**	**1.93 ± 2.34**	.904	**1.38 ± 2.15**	**1.48 ± 2.27**	.869

NOTE. The subjects answered 4 questions of the Brief Pain Inventory preoperatively, 1, 2, 3, 6, and 12 months' postoperatively. The values are given as mean ± standard deviation. Numbers in bold indicate significant differences from preoperative values at $P < .01$. *P* values are for differences between the 2 groups at each time point.

BCI, bioinductive collagen implant.

at 6- and 12-month follow-up. In the 120 assessed subjects the MCID for Constant was established as 11.2 and for ASES at 12.8. In total, 79% reached the MCID for CMS and 76.7% for ASES. There were no differences in these rates between both study groups for the CMS (76.7% for BCI vs 81.7% for Control, $P = .654$) or for the ASES (75% for BCI vs 80% for Control, $P = .829$). Of the 96 patients who were in the active working population at the beginning of the study, 92 were able to return to work 6.8 ± 3.4 months after surgery (BCI: 6.86 ± 3.38 months; Control: 6.87 ± 3.76 months, $P = .99$); 4 subjects (2 from each group, $P = 1.0$) had not returned to work at the latest follow-up.

A post-hoc analysis of the factors correlated to retear was done. Apart from the addition of the BCI, no preoperative or intraoperative variables correlated with an increased risk of retear at 12-month follow-up. Regarding secondary clinical outcomes, none of these were different between the patients with a healed tendon and those with a torn tendon at 12-month follow-up.

Complications

There were complications in 10 subjects (Table 3). Five had major complications: 2 (one from each group, 1.6% of total) suffered postoperative deep infections with positive cultures that required surgical debridement (the BCI implant was left in place in the BCI case), and prolonged antibiotic treatment, but at 12-month follow-up both tendons had healed successfully (with Sugaya scores of 1 and 2) and the subjects had clinical improvements over twice the MCID for both ASES and CMS. The other 3 major complications were previously mentioned: 2 reinterventions due to early failure of the repair and 1 death. No patient required a revision procedure for stiffness at 1-year follow-up, and no relevant postoperative inflammatory episodes were recorded.

Regarding minor complications, 2 patients (one from each group) suffered superficial infections that were treated with local debridement and antibiotic therapy; one case, from the control group, suffered a superficial skin burn adjacent to the portals that healed uneventfully. Two minor complications were found in the 12-month MRI assessment: (1) one patient from the BCI group had an 8 × 2 × 4-mm (64 mm^3) mass consistent with partially encapsulated foreign body in the subacromial recess, posterior to the repair zone; it was considered to be probably a displaced piece of BCI; and (2) in another patient from the control group, one lateral row anchor had partially extruded 4 mm into the subacromial space. In both cases the tendon had healed successfully, the patients were asymptomatic at 12 months and were subsequently followed with serial ultrasounds at 18 and 24 months, with no further action required.

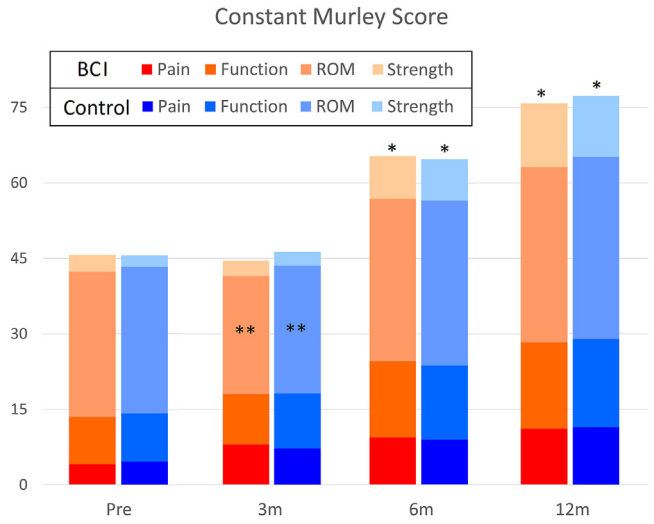

Fig 8. Evolution of the Constant–Murley scores (CMS) of the 120 patients available during the study. *$P < .001$ for total CMS score and every subscale compared with baseline (Pre) at 6- and 12-months follow-up. **$P = .001$ for the range of motion subscale when compared to baseline (Pre) at 3 months' follow-up.

Discussion

This RCT shows that the addition of a BCI to the repair of a medium to large posterosuperior cuff tear reduces the retear rate in the 12-month postoperative MRI. The BCI also improves the structural quality of the repaired tendon and increases marginally the thickness of the healed tendon. Despite these differences, at 1-year follow-up, there is no significant impact in pain levels or clinical outcomes. The complication rate is similar between groups.

The MRI failure rates and the clinical outcomes obtained in this study were similar to previous studies. The general retear rate in our study was 17% (26% in the control group and 8% in the BCI group), comparable with a retear rate of 17% found by Kim et al.[33] in 82 supraspinatus tears slightly smaller than those from our study, and smaller than the 43% rate found in the UKuff RCT, that included mostly small and medium sized tears.[34] Hein et al.,[7] in a meta-analysis including data from 920 posterosuperior tears with sizes ranging between 1 and 5 cm, found a pooled retear rate of 20.3%. In our study, the failures developed mostly (17/21, 81%) medial to the repair; this is in line with the results of other studies in which a TOE ARCR was performed: Cho et al.[8] found type 2 retears in 20 of 27 (74%) of failures in a retrospective review of 96 cases treated with a TOE ARCR; Ruiz Iban et al.[9] in a RCT found that 5 of 7 (71%) failures were type 2 in 36 cases treated with a repair technique very similar to the one presented here; to finish Shibata et al.[10] in another RCT found that 12 of 13 (92%) of failures were type 2.

There are some preliminary case series that analyze the effect of the addition of a BCI in the retear rate after a rotator cuff repair and show results in line with our data: Thon et al.[19] found a retear rate of 9% at 2 years of follow-up in 23 large and massive rotator cuff tears repaired with the addition of a BCI. Bushnell et al.,[18] in a larger prospective multicenter study of 91 medium-to-large tears with an TOE-ARCR supplemented with a BCI, found a retear rate of 11% at 12-month follow-up. Regarding other potential augmentation alternatives, a recent RCT did not find any effect on tear rates with the use of a human dermal allograft patch at 12 months' follow-up, although this was admittedly a pilot study.[35]

The results of this RCT indicate that adding a BCI to an ARCR of a posterosuperior medium-to-large cuff tear results in lower retear rates at 12-month follow-up. This is due mainly to a reduction of type 2 retears. These findings are also supported by the data on improvement of the structural quality (measured with Sugaya grade) and the marginally increased tendon thickness found at the locations in which the BCI was placed over the tendon. All this can help to speculate on a possible mechanism of action: first, as subjects with healed cuffs, when supplemented with the BCI, had tendons that had better structural quality (improved Sugaya scores) the BCI might indeed be infiltrated by cells from the native tendon and incorporate over the tendon as confirmed by previous pathology studies performed both in animal models[14] and human subjects.[16,17] Second, the BCI seemed to work preventing mostly type 2 retears (at the medial edge of the repair) and not type 1 retears (at the footprint), which makes sense as the BCI is placed over the tendon, in close contact with the zone in which medial retears develop,

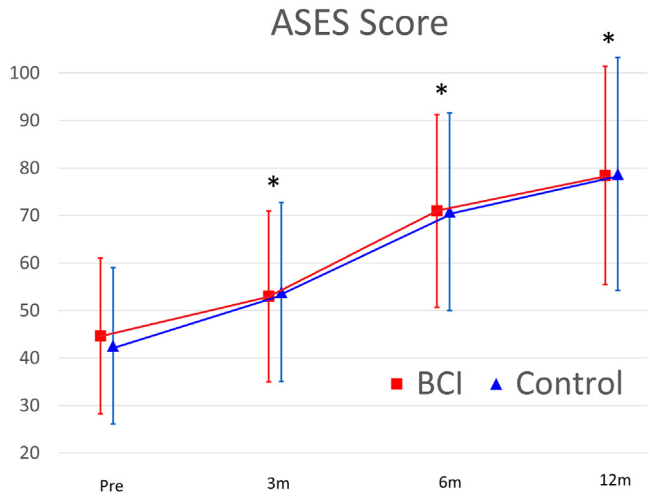

Fig 9. Evolution of the ASES score of the 120 patients available during the study. *$P < .01$ compared with baseline (Pre) at 3, 6, and 12 months' follow-up. (ASES, American Shoulder and Elbow Society)

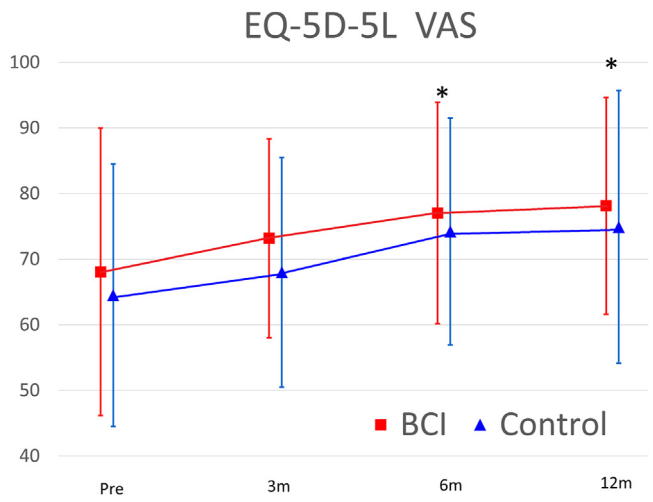

Fig 10. Evolution of the EQ-5D-5L VAS score of the 120 patients available during the study. *$P < .01$ compared with baseline (Pre) at 6 and 12 months' follow-up. (VAS, visual analog scale.)

but it is separated by the repaired tendon from the bone–tendon interface.

We did not find any other predictors of anatomical failure apart from the addition or not of the BCI. It is well established that older age, fatty infiltration, and increased tear size are associated with increased risk of repair failure, but these were not found to be significant in our study. This might be due to the relatively uniform characteristics of our sample, with no or very limited, fatty infiltration (only 5 subjects [4%] had preoperative grade 2 infiltration in any tendon) and a small range of tear sizes (between 1 and 4 cm and retraction smaller than 3 cm). There was a small difference in the tendon retraction parameter between the two study groups: tears included in the BCI had a mean of 2.7 mm more retraction than those in the control group. This difference, although statistically significant, is objectively small and might not have a clear relevance regarding outcomes or surgical technique.

There is also some recent concerns about the statistical robustness of RCT studying rotator cuff repair,[36,37] specifically when dealing with biologic augmentation,[38] as most recent studies have fragility indexes that are close to zero or smaller than the number of subjects lost to follow-up (a threshold proposed for robustness of a RCT[29,36,37]). The results presented here are relatively robust, with a Fragility Index[30] of three, which is larger than the number of subjects lost to follow-up (n = 2) but anyway suggest some caution when considering the results as completely definitive.

With respect to clinical outcomes, the subjects included in the study experienced clinically relevant improvements of around 30 points in the CMS and 24 points in the ASES score with dramatic pain level reductions (Table 2), again in line with those found by previous authors.[39] However, no clinical differences between groups were found, despite the clear radiologic improvement offered by the addition of the BCI. In fact, in a post hoc analysis, we could not find significant clinical differences between subjects with a radiological retear at 1 year and those with an intact tendon irrespective of the randomization group, although the 2 patients who had an early reoperation from the control group were not included in this analysis. This lack of clinical efficacy could be explained by the short follow-up, that is acceptable for MRI assessment of retear rates,[40] but that might cloud the real clinical relevance of a retear. Many studies have found little impact of a retear in the short term, and differences are found only when pooling results from different studies.[41,42] Anyway, analyzing short-term retear rates is a good indicator of long term loss of function and quality of life, as it is clear that longer follow-up better defines the poorer outcomes of patients with a retear: with time patients with a repair failure will have poorer CMS,[43,44] increased fatty infiltration[45] and greater reoperation rates that range from 25% to 48%.[46,47] This is further supported by the AAOS Clinical Practice Guideline on the management of rotator cuff injuries that states that "*Moderate evidence supports that healed rotator cuff repairs*

Table 3. Complications in Both Study Groups During the Twelve-Month Follow-Up

	Total (n = 124)	BCI (n = 61)	Control (n = 63)	*P* Value
Total complications	10 (8.06%)	4 (6.56%)	6 (9.52%)	.744
Minor complications	5 (4.03%)	2 (3.28%)	3 (4.76%)	1
Superficial infection	2 (1.61%)	1 (1.64%)	1 (1.59%)	1
Local skin burn	1 (0.81%)	0 (0%)	1 (1.59%)	1
Foreign body on MRI	1 (0.81%)	1 (1.64%)	0 (0%)	.492
Anchor protrusion	1 (0.81%)	0 (0%)	1 (1.59%)	1
Serious complications	5 (4.03%)	2 (3.28%)	3 (4.76%)	1
Deep infection	2 (1.61%)	1 (1.64%)	1 (1.59%)	1
Reintervention due to retear	2 (1.61%)	0 (0%)	2 (3.17%)	.496
Death (unrelated to study)	1 (0.81%)	1 (1.64%)	0 (0%)	.492

NOTE. Values are given as absolute number (percentage).
BCI, bioinductive collagen implant; MRI, magnetic resonance imaging.

show improved patient reported and functional outcomes compared to (…) unhealed rotator cuff repairs."[48]

Limitations

We acknowledge several limitations. First, some clinical parameters such as whether the tears were traumatic or not, duration of symptoms, acromial anatomy or tension of the repair, were not assessed specifically. These issues were partially addressed in two ways that would control for small differences in these parameters between groups: first, the randomization routine, with patients only randomized after the repair was performed and was considered correct and tension-free; and second, the large sample size relative to other RCT on rotator cuff repair (for example in the systematic review by Hein et al. only 6% of RCT on rotator cuff repair had samples sizes over 125 subjects[7]). Second, this study uses MRI data as the primary outcome at 12-month follow-up and a longer follow-up focused in MCID or Substantial Clinical Benefit of patient-reported outcomes measures might be better. This limitation is partially offset by the MRI data at 12-month follow-up as anatomical success is an established predictor of better clinical outcomes[48] and repair failure is eventually associated with poorer clinical outcomes[41,43,44,46]; furthermore, MRI data at this time threshold is helpful as most retears develop along the first postoperative year[40,49] and many other high-quality RCT have used MRI data at this time point.[9,50,51] Third, the data on increased thickness of the tendon in the BCI group should be interpreted with caution, as there was no preoperative data on tendon thickness and the differences found were sub-millimetric, close to the standard error of measurement and might have limited clinical relevance. Fourth, as this study was powered to healing rate and not PROM or MCID, the lack of difference in clinical outcomes may be due to a type II error. Fifth, a potential possibility of bias or unblinding in the final MRI assessment was present as the PEEK lateral anchors used to fix the BCI in place are nonabsorbable and are sometimes seen in the MRI, but they were not consistently visible and this was partially mitigated by having an assessor independent from the study involved in the analysis. To finish, a proper economic analysis was not performed; as the BCI has a relatively high cost, this would be interesting. A recent study has already suggested reasonable cost effectiveness of the BCI using retear rates closely resembling our own data,[52] specifically due to the increased risk of costlier surgical procedures after a postoperative retear.

Conclusions

Augmentation with a BCI of a TOE repair in a medium-to-large posterosuperior rotator cuff tear reduces the retear rate at 12-month follow-up by two-thirds, yielding similar improvements in clinical outcomes and without increased complication rates.

Disclosures

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References

1. Yanik EL, Chamberlain AM, Keener JD. Trends in rotator cuff repair rates and comorbidity burden among commercially insured patients younger than the age of 65 years, United States 2007-2016. *JSES Rev Rep Tech* 2021;1:309-316.
2. Tsuchiya S, Bois AJ, Matthewson G, Oiwa S, More KD, Lo IKY. The relationship between preoperative Goutallier stage and retear rates following posterosuperior rotator cuff repair: A systematic review. *J Shoulder Elbow Surg* 2023;32:435-443.
3. Orozco E, Dhillon J, Keeter C, Brown TD, Kraeutler MJ. Rotator cuff repair with patch augmentation is associated

with lower retear rates for large tears: A systematic review of randomized controlled trials. *Arthroscopy* 2024;40:1300-1308.
4. Longo UG, Carnevale A, Piergentili I, et al. Retear rates after rotator cuff surgery: A systematic review and meta-analysis. *BMC Musculoskelet Disord* 2021;22:749.
5. McElvany MD, McGoldrick E, Gee AO, Neradilek MB, Matsen FA 3rd. Rotator cuff repair: Published evidence on factors associated with repair integrity and clinical outcome. *Am J Sports Med* 2015;43:491-500.
6. Huegel J, Williams AA, Soslowsky LJ. Rotator cuff biology and biomechanics: A review of normal and pathological conditions. *Curr Rheumatol Rep* 2015;17:476.
7. Hein J, Reilly JM, Chae J, Maerz T, Anderson K. Retear rates after arthroscopic single-row, double-row, and suture bridge rotator cuff repair at a minimum of 1 year of imaging follow-up: A systematic review. *Arthroscopy* 2015;31:2274-2281.
8. Cho NS, Yi JW, Lee BG, Rhee YG. Retear patterns after arthroscopic rotator cuff repair: single-row versus suture bridge technique. *Am J Sports Med* 2010;38:664-671.
9. Ruiz Iban MA, Sanchez Alepuz E, Diaz Heredia J, et al. Footprint preparation with nanofractures in a supraspinatus repair cuts in half the retear rate at 1-year follow-up. A randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2021;29:2249-2256.
10. Shibata T, Izaki T, Miyake S, Shibata Y, Yamamoto T. Efficacy of bone marrow stimulation for arthroscopic knotless suture bridge rotator cuff repair: A prospective randomized controlled trial. *J Shoulder Elbow Surg* 2023;32:909-916.
11. Bedeir YH, Schumaier AP, Abu-Sheasha G, Grawe BM. Type 2 retear after arthroscopic single-row, double-row and suture bridge rotator cuff repair: A systematic review. *Eur J Orthop Surg Traumatol* 2019;29:373-382.
12. Charles MD, Christian DR, Cole BJ. The role of biologic therapy in rotator cuff tears and repairs. *Curr Rev Musculoskelet Med* 2018;11:150-161.
13. de Andrade ALL, Garcia TA, Brandao HS, Sardeli AV, Mouraria GG, Belangero WD. Benefits of patch augmentation on rotator cuff repair: A systematic review and meta-analysis. *Orthop J Sports Med* 2022;10:23259671211071146.
14. Van Kampen C, Arnoczky S, Parks P, et al. Tissue-engineered augmentation of a rotator cuff tendon using a reconstituted collagen scaffold: A histological evaluation in sheep. *Muscles Ligaments Tendons J* 2013;3:229-235.
15. Washburn R 3rd, Anderson TM, Tokish JM. Arthroscopic rotator cuff augmentation: Surgical technique using bovine collagen bioinductive implant. *Arthrosc Tech* 2017;6:e297-e301.
16. Arnoczky SP, Bishai SK, Schofield B, et al. Histologic evaluation of biopsy specimens obtained after rotator cuff repair augmented with a highly porous collagen implant. *Arthroscopy* 2017;33:278-283.
17. Camacho-Chacon JA, Cuenca-Espierrez J, Roda-Rojo V, et al. Bioinductive collagen implants facilitate tendon regeneration in rotator cuff tears. *J Exp Orthop* 2022;9:53.
18. Bushnell BD, Connor PM, Harris HW, Ho CP, Trenhaile SW, Abrams JS. Two-year outcomes with a bioinductive collagen implant used in augmentation of arthroscopic repair of full-thickness rotator cuff tears: Final results of a prospective multicenter study. *J Shoulder Elbow Surg* 2022;31:2532-2541.
19. Thon SG, O'Malley L 2nd, O'Brien MJ, Savoie FH 3rd. Evaluation of healing rates and safety with a bioinductive collagen patch for large and massive rotator cuff tears: 2-year safety and clinical outcomes. *Am J Sports Med* 2019;47:1901-1908.
20. Goutallier D, Postel JM, Bernageau J, Lavau L, Voisin MC. Fatty muscle degeneration in cuff ruptures. Pre- and postoperative evaluation by CT scan. *Clin Orthop Relat Res* 1994;304:78-83.
21. Fuchs B, Weishaupt D, Zanetti M, Hodler J, Gerber C. Fatty degeneration of the muscles of the rotator cuff: assessment by computed tomography versus magneticresonance imaging. *J Shoulder Elbow Surg* 1999;8:599-605.
22. Davidson J, Burkhart SS. The geometric classification of rotator cuff tears: A system linking tear pattern to treatment and prognosis. *Arthroscopy* 2010;26:417-424.
23. Bushnell BD, Connor PM, Harris HW, Ho CP, Trenhaile SW, Abrams JS. Retear rates and clinical outcomes at 1 year after repair of full-thickness rotator cuff tears augmented with a bioinductive collagen implant: A prospective multicenter study. *JSES Int* 2021;5:228-237.
24. Schlegel TF, Abrams JS, Bushnell BD, Brock JL, Ho CP. Radiologic and clinical evaluation of a bioabsorbable collagen implant to treat partial-thickness tears: A prospective multicenter study. *J Shoulder Elbow Surg* 2018;27:242-251.
25. 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.
26. Trantalis JN, Boorman RS, Pletsch K, Lo IK. Medial rotator cuff failure after arthroscopic double-row rotator cuff repair. *Arthroscopy* 2008;24:727-731.
27. Harris JD, Brand JC, Cote M, Waterman B, Dhawan A. Guidelines for proper reporting of clinical significance, including minimal clinically important difference, patient acceptable symptomatic state, substantial clinical benefit, and maximal outcome improvement. *Arthroscopy* 2023;39:145-150.
28. Haybittle JL. Repeated assessment of results in clinical trials of cancer treatment. *Br J Radiol* 1971;44:793-797.
29. Dettori JR, Norvell DC. How fragile are the results of a trial? The fragility index. *Global Spine J* 2020;10:940-942.
30. Feinstein AR. The unit fragility index: An additional appraisal of "statistical significance" for a contrast of two proportions. *J Clin Epidemiol* 1990;43:201-209.
31. Shannon CE. The mathematical theory of communication. 1963. *MD Comput* 1997;14:306-317.
32. Mansournia MA, Nazemipour M, Etminan M. P-value, compatibility, and S-value. *Glob Epidemiol* 2022;4:100085.
33. Kim YS, Lee HJ, Jin HK, Kim SE, Lee JW. Conventional en masse repair versus separate double-layer double-row repair for the treatment of delaminated rotator cuff tears. *Am J Sports Med* 2016;44:1146-1152.
34. Carr A, Cooper C, Campbell MK, et al. Effectiveness of open and arthroscopic rotator cuff repair (UKUFF): A randomised controlled trial. *Bone Joint J* 2017;99-B:107-115.
35. Snow M, Kuiper JH, James S, Keeling E, Rich S, Amit P. A pilot randomised controlled trial assessing standard

versus dermal patch-augmented rotator cuff repair found no adverse effects and suggest future trials need a minimum of 150 patients. *Knee Surg Sports Traumatol Arthrosc* 2023;31:2654-2661.
36. Fackler NP, Ehlers CB, Callan KT, et al. Statistical fragility of single-row versus double-row anchoring for rotator cuff repair: A systematic review of comparative studies. *Orthop J Sports Med* 2022;10:23259671221093391.
37. Imbergamo C, Sequeira SB, Patankar A, Means KR Jr, Stein JA. The statistical fragility of studies on rotator cuff repair with graft augmentation. *J Shoulder Elbow Surg* 2023;32:1121-1125.
38. Parisien RL, Ehlers C, Cusano A, Tornetta P 3rd, Li X, Wang D. The statistical fragility of platelet-rich plasma in rotator cuff surgery: A systematic review and meta-analysis. *Am J Sports Med* 2021;49:3437-3442.
39. Millett PJ, Warth RJ, Dornan GJ, Lee JT, Spiegl UJ. Clinical and structural outcomes after arthroscopic single-row versus double-row rotator cuff repair: A systematic review and meta-analysis of level I randomized clinical trials. *J Shoulder Elbow Surg* 2014;23:586-597.
40. Miller BS, Downie BK, Kohen RB, et al. When do rotator cuff repairs fail? Serial ultrasound examination after arthroscopic repair of large and massive rotator cuff tears. *Am J Sports Med* 2011;39:2064-2070.
41. Holtedahl R, Boe B, Brox JI. The clinical impact of retears after repair of posterosuperior rotator cuff tears: A systematic review and meta-analysis. *J Shoulder Elbow Surg* 2023;32:1333-1346.
42. Yang J Jr, Robbins M, Reilly J, Maerz T, Anderson K. The clinical effect of a rotator cuff retear: A meta-analysis of arthroscopic single-row and double-row repairs. *Am J Sports Med* 2017;45:733-741.
43. Zumstein MA, Jost B, Hempel J, Hodler J, Gerber C. The clinical and structural long-term results of open repair of massive tears of the rotator cuff. *J Bone Joint Surg Am* 2008;90:2423-2431.
44. Collin P, Betz M, Herve A, et al. Clinical and structural outcome 20 years after repair of massive rotator cuff tears. *J Shoulder Elbow Surg* 2020;29:521-526.
45. Paxton ES, Teefey SA, Dahiya N, Keener JD, Yamaguchi K, Galatz LM. Clinical and radiographic outcomes of failed repairs of large or massive rotator cuff tears: Minimum ten-year follow-up. *J Bone Joint Surg Am* 2013;95:627-632.
46. Shah NS, Suriel Peguero E, Umeda Y, Crawford ZT, Grawe BM. Long-term outcomes of massive rotator cuff tear repair: A systematic review. *HSS J* 2022;18:130-137.
47. Parikh N, Martinez DJ, Winer I, Costa L, Dua D, Trueman P. Direct and indirect economic burden associated with rotator cuff tears and repairs in the US. *Curr Med Res Opin* 2021;37:1199-1211.
48. American Academy of Orthopaedic Surgeons. Management of Rotator Cuff Injuries. Evidence-Based Clinical Practice Guideline. 2020. Accessed January 6, 2023, www.aaos.org/rccpg
49. Chona DV, Lakomkin N, Lott A, et al. The timing of retears after arthroscopic rotator cuff repair. *J Shoulder Elbow Surg* 2017;26:2054-2059.
50. van Deurzen DFP, Auw Yang KG, Onstenk R, et al. Long head of biceps tenotomy is not inferior to suprapectoral tenodesis in arthroscopic repair of nontraumatic rotator cuff tears: A multicenter, non-inferiority, randomized, controlled clinical trial. *Arthroscopy* 2021;37:1767-1776.e1761.
51. Snow M, Hussain F, Pagkalos J, et al. The effect of delayed injection of leukocyte-rich platelet-rich plasma following rotator cuff repair on patient function: A randomized double-blind controlled trial. *Arthroscopy* 2020;36:648-657.
52. McIntyre LF, Nherera LM, Schlegel TF. Resorbable bioinductive collagen implant is cost effective in the treatment of rotator cuff tears. *Arthrosc Sports Med Rehabil* 2023;5:e367-e374.