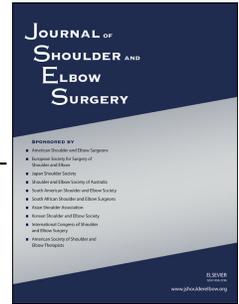# Journal Pre-proof

An isolated bioinductive repair vs. sutured repair for full-thickness rotator cuff tears: 2-year results of a double blinded, randomized controlled trial

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**Title:** An isolated bioinductive repair vs. sutured repair for full-thickness rotator cuff tears: 2-year results of a double blinded, randomized controlled trial

**Running title:** An isolated bioinductive implant for rotator cuff tears

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Institutional review board approval was received from Comité de Ética de la Investigación de la Comunidad de Aragón (CEICA), number C.I. PI21/144.

1 **Title:** An isolated bioinductive repair vs. sutured repair for full-thickness rotator cuff tears: 2-year

2 results of a double blinded, randomized controlled trial

3 Abstract

4 Background: Partial-thickness rotator cuff tears treated with an isolated bioinductive repair (IBR)

5 in lieu of a completion-and-repair have shown complete healing. This treatment option is afforded

6 by the remaining tendon's structural integrity, which is similar to that present in small/medium

7 full-thickness tears (FTTs) when the rotator cable remains intact. This randomized controlled trial

8 (RCT) investigated whether an IBR for small/medium FTTs resulted in superior healing and

9 patient-reported outcomes (PROs) compared with a sutured repair.

10 Methods: This prospective, double blinded (patients and outcome assessors), single-center RCT

11 enrolled patients ≥18 years with a small/medium (≤2.5cm) full thickness supraspinatus tear and

12 intact rotator cable. Patients were randomized and blinded to arthroscopic transosseous-equivalent

13 repair (control, n = 30) or IBR (n = 30). The primary outcome was tendon quality on biopsy at 6

14 months. Secondary outcomes were PROs (American Shoulder and Elbow Surgeons [ASES],

15 Constant-Murley Shoulder [CMS], and pain visual analogue scale scores) and tendon thickness

16 and healing measured via MRI at 6, 12, and 24 months; satisfaction at 12 and 24 months; and time

17 to return to work.

18 Results: Baseline demographic, tear, and surgical characteristics were comparable between the

19 groups (IBR: mean age, 54.2 years, 14 male; control: mean age, 56.4 years, 16 male). Measured

20 via 6 month biopsy, highly organized, parallel bundles of collagen, without inflammation, were

21 present in all IBR patients, whereas poorly organized, non-parallel collagen fibers were present in

22 24/30 (80%) of control patients ($P < .0001$), with 28/30 having minimal to mild inflammation. The

23  increase in tendon thickness measured via MRI at 6 months from baseline was greater in the IBR

24  group (2.0 mm) than in the control group (0.8 mm) ($P < .0001$). All IBR patients had 100% healing

25  on MRI at 12 and 24 months. Compared with the control group, the IBR group had higher ASES

26  and CMS scores at each evaluation, less pain at 6 and 12 months, and greater satisfaction at 12 and

27  24 months ($P < .0003$). The IBR group returned to work significantly faster (median 90 days [IQR,

28  25] vs. median 163.5 days [IQR, 24]; $P < .0001$) than the control group.

29  Conclusion: Compared with a sutured repair, the IBR treatment resulted in superior tendon quality,

30  patient outcomes, satisfaction, and return to work. The IBR enabled a robust healing response

31  evident through MRI and biopsy evaluation, demonstrating superior tendon quality and healing.

32  Word count: 389

33  Level of Evidence: Level I; Randomized Controlled Trial; Treatment Study

34  Keywords: bioinductive collagen implant; rotator cuff; rotator cuff tear; full-thickness rotator cuff

35  tear; rotator cuff repair; augmented rotator cuff repair; isolated bioinductive repair; rotator cable

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39  Rotator cuff tears are a common cause of shoulder pain and often compromise upper extremity

40  function and decrease quality of life. Conservative treatment such as physical therapy is the first-

41  line option to improve clinical outcomes, but it is not always effective at reducing pain or

42  preventing tear progression and associated functional decline.[28] In patients who fail conservative

43  treatment, surgical repair of the rotator cuff tear may be necessary to alleviate pain and improve

44  function.[29] Surgical repair for full-thickness tears entails suturing the torn tendon and generally

45  yields improvements in long-term clinical outcomes.[32] Despite these long-term benefits, sutured

46  repair is associated with a risk of retear; a rate that varies broadly across the literature and depends

47  on tear size and repair technique.[17] Sutured repair is also associated with significant morbidity and

48  lengthy rehabilitation.[2, 16]

49      The goal of any sutured repair of a rotator cuff tear is to reestablish the structural integrity

50  of the tendon. However, in some tears, such as small to medium-sized, posterosuperior crescent-

51  shaped tears, the structural integrity of the tendon may be maintained by an intact rotator cable.[8,

52  21, 24, 27] The rotator cable is a semicircular ligamentous tissue that runs perpendicular to fibers of

53  the supraspinatus and infraspinatus tendons, attaching anteriorly to the lesser tuberosity and

54  coracohumeral ligament.[8, 30] The primary purpose of the rotator cable is to support the

55  posterosuperior rotator cuff through its stress-shielding and load-bearing properties, ensuring

56  structural integrity and proper function of the shoulder. Therefore, if a rotator cuff tear doesn't

57  disrupt the rotator cable, a treatment strategy focused on biologic tendon healing could be more

58  appropriate than sutured repair.

59      Over the past decade, studies of a bioinductive collagen implant (BCI) have consistently

60  demonstrated its ability to promote biologic tendon healing.[4, 9-11, 23, 25, 26, 33] Animal and human

61  studies have demonstrated that the BCI stimulates ingrowth of host tissue, which matures into

62  well-organized, parallel bundles of type I collagen capable of functional loading.[3, 5, 37] The BCI

63  has been used either as an augment to a sutured repair or as an isolated treatment.[9, 11] In rotator

64  cuff tears that disrupt the rotator cable, a sutured repair is performed to restore tendon structure,

65  and then the BCI is used as an augment to support the biologic healing.[3, 4, 10, 11, 25, 26, 36] With the

66  maintained structural integrity of the tendon in a partial-thickness tear, an isolated bioinductive

3

67  repair (IBR), in which the BCI is used without a sutured repair, provides a robust healing response

68  that decreases tear size[5, 11, 33] and improves clinical outcomes.[5, 9, 11, 13, 25] Although the IBR has

69  been successfully used in partial thickness tears, it has not been evaluated in smaller full-thickness

70  tears in the presence of an intraoperatively confirmed intact rotator cable.

71       Therefore, the purpose of this randomized controlled trial (RCT) was to compare tendon

72  healing and patient outcomes between patients with small to medium-sized full-thickness rotator

73  cuff tears treated with an IBR or conventional sutured repair. We hypothesized that patients treated

74  with an IBR would achieve better tendon quality at 6 months and superior clinical outcomes at 24-

75  month follow-up than those treated with conventional sutured repair.

76

77

78  **Materials and Methods**

79  *Trial design*

80  A prospective, single-center, parallel-arm RCT of patients with chronic degenerative rotator cuff

81  tears was conducted between November 2020 and April 2023 by a single surgeon in a specialty

82  surgical center. Consecutive patients who met the inclusion criteria were enrolled in the study and

83  randomized in 1:1 ratio into either the IBR (Regeneten; Smith & Nephew, Inc; Andover, MA,

84  USA) arm or the conventional sutured repair arm (control group). An individual not involved in

85  the surgical treatment of the patients provided a software-generated simple, random allocation

86  sequence (SPSS Statistic Version 21; IBM; Armonk, NY, USA) and prepared opaque, sealed

87  envelopes with treatment allocation. Group assignment was performed intraoperatively following

88  study inclusion confirmation, when a randomization envelop was received and opened by study

89  personnel outside the sterile field. This study was approved by the Comité de Ética de la

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90    Investigación de la Comunidad de Aragón (CEICA) with number C.I. PI21/144. Written informed

91    consent was obtained from each patient in the study. Patients were blinded to treatment group and

92    notified of the treatment group assignment upon completion of the study. This report follows the

93    latest available version of the CONSORT (Consolidated Standards of Reporting Trials)

94    guideline.[35]

95        Inclusion criteria were full-thickness tear of the supraspinatus tendon as assessed on

96    preoperative magnetic resonance imaging (MRI) and confirmed intraoperatively;[14, 15] age ≥18

97    years; failure of conservative treatment (analgesics, anti-inflammatory medication, and physical

98    therapy) after 6 months; absence of previous surgeries; consent for surgical intervention and the

99    performance of percutaneous biopsy 6 months after surgery; absence of infectious complications

100   after arthroscopy; tear size that did not exceed 2.5 cm and could be covered by a medium BCI (20

101   mm x 26 mm). Exclusion criteria were known hypersensitivity to bovine collagen; rheumatic

102   disease; recent steroid use; insulin-dependent diabetes; heavy smoking; genetic collagen disease;

103   chronic inflammatory disease; significant subscapularis tear requiring repair; a posterosuperior

104   tear size that exceeded the size of the implant in the anterior-posterior plane; post-traumatic tear;

105   tear pattern requiring significant side-to-side tendon repair; absence or damage of the rotator cable;

106   large U-shaped tear; intra-articular pathology, such as superior labrum from anterior to posterior,

107   Bankart, or chondral lesions; grade 3 or greater chondromalacia; and previous rotator cuff surgery.

108

109   *Surgery and rehabilitation*

110   During surgery under general anesthesia, the patient was placed in the lateral decubitus position,

111   and the glenohumeral joint was assessed arthroscopically. At that point, the integrity of the rotator

112   cable was verified. After subacromial bursectomy, acromioplasty and decompression were

5

113  performed as needed, defined as a reduction in the thickness of the acromion of approximately 2

114  mm with a burr (Acromionizer Burr; Smith & Nephew, Inc; Andover, MA, USA), and an

115  evaluation of the rotator cuff pathology was performed, which included the assessment of tear

116  size.[14] For the IBR group, the tear was débrided and the BCI was placed on top of the tear,

117  overlapping the bone-tendon junction. The BCI was secured with tendon anchors and two bone

118  anchors. For the control group, the tear was débrided and the tendon was repaired using an

119  equivalent transosseous repair, with medial and lateral suture anchors (Healicoil Regenesorb

120  anchors with non-resorbable suture Ultratape; Smith & Nephew, Inc; Andover, MA, USA). For

121  all patients, the biceps tendon was inspected and tenodesis or tenotomy was performed at the

122  discretion of the surgeon.

123       Rehabilitation was performed according to a previously published protocol by a therapist

124  blinded to the study arm assignment.[11] Rehabilitation protocol was identical for both study arms,

125  including recommendations to use a sling for 2 weeks and begin passive range of motion exercises

126  immediately after surgery. This physical therapy program allowed for patients to progress as

127  tolerated, including shortening sling time, depending on pain.

128  *Outcomes*

129  The primary outcome of this study was histological characteristics assessed via biopsy at 6 months.

130  Secondary outcomes were tendon healing, measured as gap fill-in, and tendon thickness on MRI

131  at 6, 12, and 24 months; patient-reported outcome measures (PROMs), including pain visual

132  analogue scale (VAS-Pain), the standardized American Shoulder and Elbow Surgeons (ASES),

133  and Constant-Murley Shoulder (CMS) scores at 6, 12, and 24 months; satisfaction at 12 and 24

134  months; overall sling time, defined as the number of days the patient used a sling; number of

135  completed physical therapy visits; and time to return to work, as well as any changes in the

6

136  employment status. All outcomes were obtained at the specialty surgical center where the surgeries

137  were performed.

138      Ultrasound-guided biopsy with histology was performed according to previously published

139  protocol.[11] The surgeon who performed rotator cuff repair also performed the biopsy; hence, that

140  person was not blinded to the treatment arm assignment. Pathologist who performed biopsy

141  evaluation was independent of the study, and thus treatment arm blinding was maintained. To

142  ensure extraction consistency during biopsy, lateral anchors were used in the control group and

143  bone anchors in the IBR group to define the extraction location. The donor site was located under

144  ultrasound control by selecting the intermediate portion of the neotendon located between the two

145  bone anchors anchored in the anterior and posterior middle area of the implant. Histological

146  visualization of necrosis, fibrosis, inflammation, and collagen was performed. The quality of

147  newly formed collagen was graded according to a previously published system (Grade 0, poorly

148  organized fibroplasia with loose, disorganized collagen; Grade 1, abundant poorly organized

149  fibroplasia, with non-parallel collagen fibers; Grade 2, equal amounts of poorly organized fibrosis

150  and well-organized polarized collagen; Grade 3, minimal poorly organized fibrosis, with typical

151  wavy collagen pattern; Grade 4, tightly packed, organized parallel bundles of collagen with normal

152  crimping).[1]

153      Each patients underwent MRI evaluation prior to surgery and at 12 and 24 months post

154  operation. An independent musculoskeletal radiologist was consulted to maintain treatment arm

155  blinding during MRI evaluation. Preoperative tendon thickness was measured at the lateral edge

156  of the supraspinatus tendon, medial to the articular margin of the supraspinatus insertion.

157  Postoperatively, tendon thickness was measured in the middle portion of the tendon, just lateral to

158  the articular margin of the supraspinatus insertion.[4]

159     PROMs were assessed preoperatively and at three postoperative visits as described above.

160     Clinical significance of improvement from baseline in ASES and CMS scores was measured as

161     the minimal clinically important difference (MCID). The MCIDs for ASES and CMS scores were

162     drawn from the literature and defined as 15.5 and 10.4, respectively.[19] Assessors of PROMs, who

163     administered the questionnaire, were blinded to the treatment arm assignment.

164

165     *Statistical analysis*

166     All calculations were made using the SAS software (SAS Institute; Cary, NC, USA). Continuous

167     variables were reported as either means with standard deviations (SD) or medians with

168     interquartile ranges (IQR), depending on the distribution of the data. Categorical variables were

169     reported as frequencies with percentages.

170     Visual inspections and tests for normality were conducted. Data were found to be

171     nonparametric, so Wilcoxon tests were used to analyze continuous variables and Fisher's exact

172     tests were used to analyze categorical variables. Power analysis was not performed due to the

173     novelty of this patient population for the IBR procedure. Sample size was determined by the

174     number of patients that could be enrolled between November 2020 and April 2021. A post-hoc

175     Bonferroni correction was applied to account for the multiple comparisons and the statistical

176     significance was set at $P < 0.002$ (0.05/26)**.** All $P$ values refer to comparisons between the

177     treatment groups.

178     **Results**

179     *Patient demographics and surgical characteristics*

8

180    Patients were enrolled between November 2020 and April 2021 and completed 2-year follow-up

181    between December 2022 and April 2023. Patient enrollment, randomization, follow-up, and

182    analysis numbers are presented in Figure 1. No patients withdrew from the trial or were lost to

183    follow-up. Baseline patient characteristics did not differ significantly between the groups (Table

184    1). The groups were also well matched in terms of tear and surgical characteristics (Table 2).

185

186    *Histological assessment of postoperative tendon quality and immune response*

187    Postoperative tendon evaluation via biopsy at 6 months revealed highly organized, parallel bundles

188    of collagen, without inflammation, for all IBR patients, whereas biopsies of patients in the control

189    group displayed poorly organized, non-parallel collagen fibers in 24/30 (80%) patients ($P <$

190    0.0001), with 28/30 having minimal to mild inflammation (Table 3).

191

192    *MRI assessment of tendon thickness and healing*

193    Tendon thickness on MRI was similar between the groups at baseline (Table 4). Tendon thickness

194    increased from baseline in both groups at 6 months and then increased slightly throughout the

195    remainder of the follow-up period. Tendon was significantly thicker at 6 months in the IBR group

196    compared with the control group, and this was maintained throughout the follow-up period.

197         In the IBR group at 6 months, 27 (90%) patients had 100% tendon gap fill-in, 2 (6.7%) had

198    80% fill-in, and 1 (3.3%) had 35% fill-in. By 12 months, all 30 (100%) patients had 100% gap fill-

199    in, which was sustained at 24 months postoperatively. Because the gap in the tendon was closed

200    surgically during sutured repair, these data are not available for the control group.

201

202    *PROMs and patient satisfaction*

9

203  Pre- and postoperative PROMs were deemed to be nonparametric, therefore, medians and IQRs

204  for each treatment group are presented in Table 5, with *P* values determined through Wilcoxon

205  tests. Baseline ASES and VAS-Pain scores did not differ between the groups, but the CMS score

206  was significantly higher in the IBR group. Postoperatively, all PROMs were significantly higher

207  in the IBR group throughout the entire follow-up period, except VAS-Pain, which no longer

208  differed between the groups at 24 months. To allow for better comparison with the literature, the

209  means and standard deviations for pain are presented here for descriptive purposes only for

210  baseline and 6, 12, 24 months postoperative are as follows: IBR 6.8 (0.6), 0.2 (0.5), 0.2(0.5),

211  0.2(0.5); Control 6.6 (0.8), 1.3(0.8), 0.7(0.7), 0.3(0.5).

212      The MCID for the ASES score was met by 100% and 96.7% of IBR and control group

213  patients, respectively, by 6 months. The MCID for the CMS score was met by 100% and 16.7%

214  of IBR and control group patients, respectively, by 6 months. All 60 patients met the MCID at 12

215  and 24 months (Table 5). Patients in the IBR group were also significantly more satisfied at both

216  12 and 24 months compared with the control group (Figure 2).

217

218  *Rehabilitation outcomes and return to work*

219  Patients in the IBR group spent significantly fewer days in a sling and returned to work

220  significantly faster compared with the control group (Table 6). There was no difference in the type

221  of work performed pre- or postoperatively.

222      Complications in the postoperative period were limited to post-surgical arthrofibrosis (1

223  patient in the IBR group and 2 patients in the conventional control group), which resolved with

224  physical therapy.

225

**Discussion**

226

227        The purpose of this double blinded RCT was to compare the postoperative tendon quality

228   and clinical outcomes in patients with stable small to medium full-thickness rotator cuff tears

229   treated with IBR or the conventional sutured repair. This study revealed that patients treated with

230   an IBR, compared with patients treated with a sutured repair, had superior tendon quality and

231   tendon thickness, a reduced sling time, faster return to work, and greater improvement in PROMs.

232   The results of this study support the performance of an IBR instead of the conventional sutured

233   repair for smaller full-thickness supraspinatus tendon tears, when an intact rotator cable is present

234   to provide structural support to the tendon.

235        Due to its anatomical structure and mechanical function, the rotator cable is described as

236   acting like a cable for a "suspension bridge" that transfers load from the cuff tendons to the humeral

237   bone and mechanically shields the thinner and weaker avascular rotator crescent region of the cuff

238   that is distal to the rotator cable.[8, 30] Several biomechanical and clinical studies have demonstrated

239   that a patient with an intact rotator cable can have a rotator cuff that is "biomechanically intact"

240   even when the tendon is "anatomically deficient" with a tear in the crescent region;[7, 8, 27, 30] the

241   region where partial-thickness rotator cuff tears most commonly occur.[24] For high-grade partial-

242   thickness tears within the rotator crescent, previous evaluations have demonstrated the

243   effectiveness in healing and improvements in PROMs when using an IBR, relying on the intact

244   tendon stability, instead of a sutured repair.[5, 6, 9, 11, 13, 25, 33] Those results included complete gap fill-

245   in or a reduction in tear size,[5, 11] an increase in tendon thickness by approximately 2 mm,[6, 11, 33] and

246   improved PROMs compared with baseline,[5, 9, 11, 13, 25, 33] with ≥90% of patients meeting the MCID

247   by 24 months.[9, 33] The evidence for IBR demonstrates the ability for complete healing of partial-

11

248   thickness tears and suggests that a more invasive sutured repair is not required to add structural

249   integrity to the torn tendon.

250        In contrast to partial-thickness tears, small to medium-sized full-thickness tears may have

251   been assumed to lack the structural integrity needed for proper healing and, hence, requiring

252   sutured repair. The current study questions this dichotomy by considering the integrity of the

253   rotator cable instead of the tear type as the main factor that determines structural integrity of the

254   tendon and, consequently, eligibility for an IBR. Similar to previous results on partial-thickness

255   tears,[5, 6, 9, 11, 13, 25, 33] patients in the current study treated with an IBR achieved full gap fill-in by

256   12 months and had significantly greater tendon thickness throughout the postoperative evaluations,

257   resulting in superior patient satisfaction and PROMs compared with patients in the control group.

258   Notably, the IBR group had substantial improvement in the early postoperative phase as the ASES

259   score at 24 months in the control group was comparable to the ASES score at 6 months in the IBR

260   group, which could be critical to the productivity of the working aged patient experiencing a small

261   full-thickness tear. While not the purpose of this study, the absence of a sutured repair allowed

262   "progression as tolerated" through rehabilitation, resulting in a shorter sling time, fewer physical

263   therapy visits and a shorter time to return to work for patients in the IBR group, all without

264   detriment to tendon healing. The days spent in a sling in the IBR group (median = 12.5) aligns

265   more with the published partial-thickness rehabilitation program following IBR[25] and is more

266   aggressive than "accelerated" rehabilitation programs previously described following a sutured

267   repair for full thickness tears <3cm, citing 21 to 41 days in a sling.[18, 20, 22] The ability to adapt the

268   rehabilitation progression to the patient could contribute to improved patient satisfaction and cost

269   effectiveness, however, further analysis is warranted to evaluate this relationship.

12

270     It should be noted that no retears occurred within the first 24 postoperative months, even

271     in the absence of a sutured repair in the IBR group. The healing response provided by the BCI was

272     further captured in the direct comparison of tendon histology results between the groups at 6

273     months after the intervention. In support of each tendon being classified as healed on MRI,

274     histology results from patients in the IBR group consisted of highly organized, mature collagen

275     without evidence of necrosis or inflammation, which is consistent with previous histology

276     evaluations.[3, 11, 37] The presence of healthy tendon tissue, visualized by biopsy, in the three patients

277     having less than full gap fill-in at 6 months likely created an environment conducive of continued

278     tendon healing, which was demonstrated by their complete healing at 12 months. Additionally, no

279     implant material was present in any IBR patient in the current study, which is consistent with

280     previous literature in which no implant material was present on MRI[11] or biopsy[3, 11, 37] at 6 months.

281     In comparison, the control group tendons were also classified as healed on MRI but featured

282     minimal-to-mild inflammation and fibrosis, as well as poorly organized collagen.

283     The superior tendon integrity and healing reported in the current study are applicable to

284     stable rotator cuff tears, as seen in partial-thickness tears and smaller full-thickness tears, as well

285     as to larger full-thickness tears when the BCI is used to augment a sutured repair. Similar to

286     previous research on partial-thickness tears,[5, 6, 9, 12, 13, 25, 34] this Level I evidence demonstrates

287     through biopsy and MRI data that tendon healing and superior tendon integrity is possible with an

288     IBR for smaller, stable full-thickness tears, while avoiding lengthy sling and rehabilitation

289     timelines. In larger full-thickness tears, this study provides comparative biopsy and MRI data that

290     demonstrates the superior tendon integrity and may provide greater clarity for recent clinical

291     benefits reported in scientific literature. In combination with superior tendon integrity, a recent

292     RCT reported a three-times lower retear rate (25.8% vs 8.3%) for medium to large full-thickness

293    repairs when augmented with the BCI. [31] In large/massive retracted tears (mean:15cm$^2$) augmented

294    with the BCI, patients sustaining a postoperative retear were reported to have smaller retears than

295    a non-augmented group.[38] It is important to note that an IBR in both of these cohort would not

296    have been appropriate, given the lack of tendon stability and the non-loadbearing structure of the

297    BCI. Nevertheless, the histology results of the current study suggest the BCI provides considerable

298    biological support to tendon healing in a variety of rotator cuff tear sizes.

299          The strengths of this study include the randomized, double blinded design and the inclusion

300    of comparative MRI, biopsy, and clinical outcomes. However, these results should be viewed with

301    respect to its' limitations as well. First, a formal sample size calculation was not performed, nor

302    was an interim analysis conducted to assess the appropriateness of the sample size. Despite this

303    limitation, between-group difference reached statistical significance ($P < 0.0001$) for most

304    outcomes, indicating that the number of the patients enrolled was sufficient to test the study

305    hypothesis. Second, a 24-month follow-up may be considered a limitation. Although longer

306    follow-up is certainly of clinical interest, all patients in the IBR group displayed histological

307    outcomes consistent with healing at 6 months and 100% gap fill-in at 12 months, indicating that

308    healing was complete before the 24-month follow-up. Hence, any retears that may occur in the

309    longer term, after the end of the 24-month follow-up period, are unlikely to be associated with the

310    performed repair. Third, the control group was found to be significantly older and have a lower

311    CMS score at baseline. Despite being statistically different, the numerical difference was rather

312    low (2 years and 2 points on CMS) and likely not clinically relevant. Fourth, ultrasound-guided

313    biopsy may be associated with extraction-site variability, which could potentially limit the

314    findings. To ensure extraction consistency, lateral anchors were used in the control group and bone

315    anchors in the IBR group to define the extraction location. The latter allowed for greater precision

14

316 of extraction and less variability compared with the conventional repair group. Finally, this was

317 an independent study conducted by the senior surgeon with industry funding required to support

318 only statistical analysis and publication preparation following study completion. However, the

319 senior surgeon oversaw all acquisition, analysis, and interpretation, therefore, reducing the

320 potential for bias.

321

322 **Conclusion**

323 The results of this double blinded, RCT support IBR of small to medium-sized full-thickness tears

324 with intact rotator cable, which resulted in complete tendon healing, significantly greater tendon

325 thickness, and superior tendon quality compared with conventional sutured repair. Patient benefits

326 offered by an IBR included fewer days in a sling, fewer physical therapy visits, superior PROMs,

327 and a faster return to work. This study suggests that an IBR of rotator cuff tears with remaining

328 structural integrity resulted in a robust, biologic healing response.

329

330 **Legends for Figures and Tables**

331 Figure 1. Study flowchart.

332 Figure 2. Postoperative satisfaction with the outcomes of the rotator cuff repair. IBR,
333 isolated bioinductive repair. Statistical significance was set at $P < 0.002$

334 Table 1. Baseline characteristics of study participants.

335 Table 2. Tear and surgical characteristics.

336 Table 3. Postoperative assessment of tendon quality on biopsy.

337 Table 4. Pre- and postoperative tendon thickness on MRI.

15

338    Table 5. Pre- and postoperative patient-reported outcome measures.

339    Table 6. Postoperative employment status, return to work, and rehabilitation
340    characteristics.

341    **References**

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480

| | IBR (n = 30) | Conventional sutured repair (n = 30) | P value |
|---|---|---|---|
| Mean age, years (SD) | 54.2 (2.4) | 56.4 (8.9) | <0.01 |
| Sex, n (%) | | | |
| Male | 14 (46.7%) | 16 (53.3%) | <0.01 |
| Female | 16 (53.3%) | 14 (46.7%) | |
| Employment status, n (%) | | | |
| Full-time | 26 (86.7%) | 25 (83.3%) | 1.00 |
| Part-time | 4 (13.3%) | 4 (13.3%) | |
| Not reported | 0 (0.0%) | 1 (3.3%) | |
| Type of employment, n (%) | | | |
| Heavy work | 19 (63.3%) | 19 (63.3%) | 1.00 |
| Light/Medium work | 7 (23.3%) | 7 (23.3%) | |
| Sedentary | 3 (10.0%) | 3 (10.0%) | |
| Not reported | 1 (3.3%) | 1 (3.3%) | |
| Side of operation, n (%) | | | |
| Dominant | 17 (56.7%) | 20 (66.7%) | 0.60 |
| Non-dominant | 13 (43.3%) | 10 (33.3%) | |
| Nicotine use status, n (%) | | | |
| Current | 5 (16.7%) | 5 (16.7%) | 1.00 |
| Previous | 1 (3.3%) | 1 (3.3%) | |
| Never | 24 (80.0%) | 24 (80.0%) | |
| Diabetes, n (%) | | | |
| Yes | 1 (3.3%) | 1 (3.3%) | 1.00 |
| No | 29 (96.7%) | 29 (96.7%) | |

Abbreviations: IBR, isolated bioinductive repair; SD, standard deviation.

| | IBR (n = 30) | Conventional sutured repair (n = 30) | *P* value |
|---|---|---|---|
| Bateman grade, n (%)[a] | | | |
| Grade I | 18 (60.0%) | 17 (56.7%) | 1.00 |
| Grade II | 12 (40.0%) | 13 (43.3%) | |
| Goutallier class, n (%)[b] | | | |
| Class I | 17 (56.7%) | 19 (63.3%) | 0.79 |
| Class II | 13 (43.3%) | 11 (36.7%) | |
| Class III | 0 (0.0%) | 0 (0.0%) | |
| Biceps Treatment, n (%) | | | |
| Tenotomy | 28 (93.3%) | 27 (90.0%) | 1.00 |
| Tenodesis | 2 (6.7%) | 3 (10.0%) | |
| Acromioplasty, n (%) | 3 (10.0%) | 4 (13.3%) | 1.00 |
| Subacromial decompression, n (%) | 5 (16.7%) | 4 (13.3%) | 1.00 |

Abbreviations: IBR, isolated bioinductive repair.

[a] Bateman grades are defined as follows[4]:

Grade I: tear <1 cm after debridement

Grade II: tear 1-3 cm after debridement

[b] Goutallier classes are defined as follows[14]:

Class I - Some fatty streaks

Class II - Less than 50% fatty muscle atrophy

Class III - 50% fatty muscle atrophy

|  | IBR (n = 30) | Conventional sutured repair (n = 30) | *P* value |
|---|---|---|---|
| Necrosis |  |  |  |
| No | 30 (100.0%) | 28 (93.3%) | 0.492 |
| Minimal | 0 (0.0%) | 2 (6.7%) |  |
| Mild | 0 (0.0%) | 0 (0.0%) |  |
| Moderate | 0 (0.0%) | 0 (0.0%) |  |
| Severe | 0 (0.0%) | 0 (0.0%) |  |
| Inflammation |  |  |  |
| No | 30 (100.0%) | 0 (0.0%) | <0.0001 |
| Minimal | 0 (0.0%) | 13 (43.3) |  |
| Mild | 0 (0.0%) | 15 (50.0) |  |
| Moderate | 0 (0.0%) | 2 (6.7) |  |
| Severe | 0 (0.0%) | 0 (0.0%) |  |
| Fibrosis |  |  |  |
| No | 30 (100.0%) | 0 (0.0%) | <0.0001 |
| Minimal | 0 (0.0%) | 12 (40.0%) |  |
| Mild | 0 (0.0%) | 13 (43.3%) |  |
| Moderate | 0 (0.0%) | 5 (16.7%) |  |
| Severe | 0 (0.0%) | 0 (0.0%) |  |
| Collagen quality |  |  |  |
| Grade 0 | 0 (0.0%) | 3 (10.0%) | <0.0001 |
| Grade 1 | 0 (0.0%) | 24 (80.0%) |  |
| Grade 2 | 0 (0.0%) | 3 (10.0%) |  |
| Grade 3 | 0 (0.0%) | 0 (0.0%) |  |
| Grade 4 | 30 (100.0%) | 0 (0.0%) |  |

Abbreviations: IBR, isolated bioinductive repair.

All data are presented as n (%). Statistical significance was set at *P* < 0.002

|  | Baseline | 6 months |  | 12 months |  | 24 months |  |
|---|---|---|---|---|---|---|---|
|  | Tendon thickness, mm | Tendon thickness, mm | Change from baseline, mm | Tendon thickness, mm | Change from baseline, mm | Tendon thickness, mm | Change from baseline, mm |
| IBR (n=30) | 4.2 (0.0) | 6.2 (0.3) | 2.0 (0.3) | 6.3 (0.3) | 2.1 (0.3) | 6.3 (0.3) | 2.1 (0.2) |
| Conventional sutured repair (n=30) | 4.2 (0.0) | 5.0 (0.2) | 0.8 (0.0) | 5.0 (0.1) | 0.9 (0.1) | 5.0 (0.2) | 0.9 (0.1) |
| *P* value[a] | 0.028 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Abbreviations: IBR, isolated bioinductive repair.

All data are presented as median (interquartile range).

[a] *P* values correspond to the differences between the treatment groups; Statistical significance was set at *P* < 0.002

|  |  | IBR<br>(n = 30) | Conventional sutured repair<br>(n = 30) | *P* value |
|---|---|---|---|---|
| ASES score |  |  |  |  |
| Baseline | Score, median (IQR) | 49 (4) | 48 (2) | 0.064 |
| 6 months | Score, median (IQR) | 82 (5) | 68 (5) | <0.0001 |
|  | MCID, n (%)[a] | 30 (100.0%) | 29 (96.7%) |  |
| 12 months | Score, median (IQR) | 87 (5) | 75 (2) | <0.0001 |
|  | MCID, n (%) | 30 (100.0%) | 30 (100.0%) |  |
| 24 months | Score, median (IQR) | 88 (5) | 80 (5) | <0.0001 |
|  | MCID, n (%) | 30 (100.0%) | 30 (100.0%) |  |
| CMS score |  |  |  |  |
| Baseline | Score, median (IQR) | 59 (2) | 57 (4) | 0.001 |
| 6 months | Score, median (IQR) | 76 (4) | 63 (5) | <0.0001 |
|  | MCID, n (%)[b] | 30 (100.0%) | 5 (16.7%) |  |
| 12 months | Score, median (IQR) | 86 (5) | 72 (4) | <0.0001 |
|  | MCID, n (%) | 30 (100.0%) | 30 (100.0%) |  |
| 24 months | Score, median (IQR) | 88 (2) | 78 (3) | <0.0001 |
|  | MCID, n (%) | 30 (100.0%) | 30 (100.0%) |  |
| VAS-Pain |  |  |  |  |
| Baseline | Score, median (IQR) | 7 (1) | 6.5 (1) | 0.270 |
| 6 months | Score, median (IQR) | 0 (0) | 1 (1) | <0.0001 |
| 12 months | Score, median (IQR) | 0 (0) | 0 (1) | <0.0001 |
| 24 months | Score, median (IQR) | 0 (0) | 0 (1) | 0.135 |

Abbreviations: ASES, American Shoulder and Elbow Society; IBR, isolated bioinductive repair; CMS, Constant-Murley Shoulder; IQR, interquartile range; VAS, visual analog scale; MCID, minimal clinically important difference. Statistical significance was set at *P* < 0.002.

MCID is defined as follows[17]:

[a]The number of patients who met a minimal clinically important difference for ASES (change from baseline of ≥15.5).

[b]The number of patients who met a minimal clinically important difference for CMS (change from baseline ≥10.4).

| | IBR (n = 30) | Conventional sutured repair (n = 30) | *P* value |
|---|---|---|---|
| Employment status at 12 months, n (%) | | | |
| Full-time | 26 (86.7%) | 24 (80.0%) | 0.731 |
| Part-time | 4 (13.3%) | 6 (20.0%) | |
| Employment status change at 12 months, n (%)[a] | | | |
| No change in status | 27 (90.0%) | 24 (80.0%) | 0.706 |
| Decreased status | 2 (6.7%) | 5 (16.7%) | |
| Increased status | 1 (3.3%) | 1 (3.3%) | |
| Time to RTW, days, median (IQR) | 90 (25) | 163.5 (24) | <0.0001 |
| Sling time, days, median (IQR) | 12.5 (3) | 27 (3) | <0.0001 |
| Physical therapy visits, median (IQR) | 6 (1) | 10 (1) | <0.0001 |

Abbreviations: IBR, isolated bioinductive repair; IQR, interquartile range; RTW, return to work.

[a]Change in employment status is a comparison of baseline work status with post-operative works status.

Statistical significance was set at *P* < 0.002

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┌─────────────────────────────┐
│ 74 Assessed for eligibility │
└─────────────────────────────┘
              │
              │            ┌──────────────────────┐
              ├───────────▶│ 14 Did not meet      │
              │            │ inclusion criteria   │
              ▼            └──────────────────────┘
┌─────────────────────────────┐
│ 60 Randomized               │
└─────────────────────────────┘
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| 30 Randomized to isolated bioinductive repair | 30 Randomized to conventional sutured repair |
|---|---|
| 30 6-month follow-up | 30 6-month follow-up |
| 30 12-month follow-up | 30 12-month follow-up |
| 30 24-month follow-up | 30 24-month follow-up |
| 30 Analyzed | 30 Analyzed |