

1 Title

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3 Supraspinatus Detachment Causes Musculotendinous Degeneration and a Reduction
4 in Bone Mineral Density at the Enthesis in a Rat Model of Chronic Rotator Cuff
5 Degeneration.

6

7 Short title

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9 Development of a Chronic Rotator Cuff Tear Model.

10

11 Keywords

12

13 Animal model; rotator cuff; tendon-bone healing; tendon degeneration

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15

16 **Abstract**

17

18 **Background**

19

20 In order to evaluate biological strategies that enhance tendon-bone healing in humans,
21 it is imperative that suitable animal models accurately reproduce the pathological
22 changes observed in the clinical setting following a tear. The purpose of this study
23 was to investigate rotator cuff degeneration in a rat, and assess the development of
24 osteopenia at the enthesis following tendon detachment.

25

26 **Materials and Methods**

27

28 Eighteen female Wistar rats underwent unilateral detachment of the supraspinatus
29 tendon. Specimens were retrieved at three (n = 6), six (n = 6), and nine weeks (n = 6)
30 postoperatively for histological analysis and peripheral quantitative computer
31 tomography.

32

33 **Results**

34

35 Three weeks following tendon detachment there was a significant increase in the
36 modified Movin score characterized by a loss of muscle mass, fatty infiltration, an
37 increase in musculotendinous cellularity, loss of normal collagen fiber
38 structure/arrangement, rounded tenocyte nuclei, and an increase in the number of
39 vascular bundles. This was accompanied by a reduction in bone mineral density at the
40 tendon insertion site. After three weeks though, these changes were less prominent.

41 **Conclusion**

42

43 The rotator cuff tendon-muscle-bone unit in a rat model three weeks after detachment
44 of supraspinatus represents a valid model to investigate rotator cuff degeneration.

45

46 **Introduction**

47

48 Rotator cuff tendon degeneration is common and can result in the development of
49 tears in susceptible tendons, associated with degenerative changes in the relevant
50 rotator cuff muscles and in the humeral enthesis.¹ Macroscopic structural changes
51 include rotator cuff tendon thinning and retraction, muscle atrophy and fatty
52 infiltration, and compensatory hypertrophic of the intra-articular biceps tendon. Ultra-
53 structural changes include alteration of tendon cellularity, degradation of tendon
54 matrix quality, diminution of perfusion, microcalcification, amyloid deposition, and
55 synovial proliferation.^{1;2}

56

57 Degeneration can be initiated by a number of factors that are either intrinsic or
58 extrinsic to the cuff itself. Accumulation of degenerative microtrauma has been
59 proposed as the most important intrinsic factor and encompasses age-related
60 degeneration compounded by repetitive microtrauma, eventually resulting in the
61 development of partial, and subsequently full-thickness tears.¹ Extrinsic causes
62 comprise environmental and anatomical influences. The former includes increasing
63 age, shoulder overuse, smoking, and any medical condition such as diabetes mellitus
64 that disturbs healing by microvascular impairment.¹ Abnormal acromial morphology
65 has been postulated as the principal anatomical variant initiating the degenerative
66 process.¹ Progressive change in the topography and shape of the undersurface of the
67 acromion and 'spur' formation at its antero-inferior border with thickening of the
68 coracoacromial ligament (the coraco-acromial arch) lead to stenosis of the
69 subacromial space and supraspinatus 'outlet' deforming the supraspinatus muscle and
70 tendon passing under the coracoacromial arch causing inflammation, physical damage

71 to the muscle and musculotendinous junction, and the clinical presentation of the
72 ‘impingement syndrome.’
73
74 Poor healing and recurrent tears frequently occur following repair of a degenerative
75 rotator cuff and are associated with a poor functional outcome.³ In order to select
76 appropriate tendon graft materials and to determine the effect of biological
77 augmentation on healing, it is useful to examine such strategies in a degenerative
78 tendon model which replicates what is observed in the clinical setting. Several animal
79 models of tendon degeneration have been developed: the rat shoulder is the most
80 popular.^{4:5} Advantages of using the rat model as a surrogate for investigation of
81 human rotator cuff function include the presence of an arch-like structure that
82 encloses supraspinatus (similar to the coracoacromial arch) and the high functional
83 loads generated in the tendon. Primate models have greater anatomical similarities to
84 humans but due to expense and restricted use they are an impractical alternative.⁶
85 Supraspinatus detachment has been shown, using a rat model, to lead to degenerative
86 changes comparable to those seen in the clinical setting: tendon degeneration,
87 inflammation, and muscle atrophy combined with a persisting defect. These were
88 most apparent after an interval of three weeks, with longer time points associated with
89 complete closure of the defect.⁵
90
91 The purpose of this study was to investigate rotator cuff degeneration and assess the
92 development of osteopenia at the bony insertion of supraspinatus following tendon
93 detachment. Osteopenia of the humeral head occurs following a rotator cuff tear in
94 humans and compromises fixation techniques where tendon is reattached to bone.⁷ It
95 is therefore important to describe the osteopenia that develops in models of tendon

96 degeneration following a chronic tear. The hypothesis was that detachment of
97 supraspinatus from the humerus would result in tendon degeneration and osteopenia
98 of the greater tuberosity in a rat model.
99
100
101

102 **Materials and Methods**

103

104 *Study Design*

105

106 All animal work was conducted in accordance with the UK Home Office Animals
107 (Scientific Procedures) Act 1986. Eighteen randomly allocated (using simple
108 randomization) female Wistar rats, who had not previously been subject to any
109 experimentation, underwent unilateral detachment of the supraspinatus tendon. All
110 procedures were carried out by one surgeon over several days. Using a power
111 calculation and previously published data, an n of 6 has been shown to provide a
112 power of 0.8, which provides significance at $p = 0.05$.¹ Animals were allowed to
113 freely mobilise immediately post-operatively (with cage mates and a constant supply
114 of food and water) and specimens were retrieved after euthanasia at three (n = 6), six
115 (n = 6), and nine weeks (n = 6) postoperatively for histological analysis and
116 peripheral quantitative computer tomography (pQCT).

117

118 *Surgical Technique*

119

120 A chronic, degenerative full thickness rotator cuff tear model was developed from one
121 that has been previously used to examine tendon degenerative changes.² Anaesthesia
122 was induced and maintained using 2% Isoflurane mixed with pure oxygen via a
123 facemask: this was undertaken by a veterinary anesthetist experienced with the
124 technique. Continuous monitoring of vital signs (heart rate, respiratory rate, and
125 temperature) was undertaken throughout surgery, which was performed in a dedicated
126 operating theatre throughout the day. The right shoulder was used for tendon

127 detachment in all cases and the contralateral left shoulder served as a control. A 1.5
128 cm skin incision was made directly over the anterolateral border of the acromion. The
129 deltoid was detached from the anterior, lateral, and posterior margins of the acromion
130 and split caudally for 0.5 cm. The acromio-clavicular joint was divided and a traction
131 suture was placed around the clavicle to facilitate visualization of supraspinatus
132 (Figure 1A). The bony end of the supraspinatus tendon was marked at its
133 musculotendinous junction with a 5'0 prolene suture to assess retraction during tissue
134 harvest. Under tension of the suture, the tendon was detached using sharp dissection
135 from the greater tuberosity of the humeral head and allowed to retract medially
136 (Figures 1B and 1C). The deltoid muscle and fascia were closed with absorbable 5'0
137 Vicryl suture (Ethicon, Johnson & Johnson Medical Ltd., Berkshire, UK). Skin
138 closure was achieved using absorbable 5'0 Monocryl suture (Ethicon, Johnson &
139 Johnson Medical Ltd., Berkshire, UK) and the animals were permitted unrestricted
140 cage activity (Figure 1D). Postoperative pain was assessed daily and analgesia (Intra-
141 muscular buprenorphine 0.6 mg) was given every 12 hours for three days.

142

143 *Macroscopic Assessment*

144

145 Animals were euthanized at three (n = 6), six (n = 6), and nine weeks (n = 6).

146 Supraspinatus tendon-bone defects were visually assessed and classified as:

147 persistent, partial, and completely closed.

148

149 *pQCT*

150

151 After sacrifice pQCT scanning was performed to measure bone mineral density at the
152 humeral head. Using an XCT 2000 Bone Scanner (Stratec Medizintechnik GmbH,
153 Germany) with Software version 6.20, 1 mm CT slices were taken through the
154 humeral head and supraspinatus musculotendinous unit.

155

156 *Histological Assessment*

157

158 At euthanasia, the right shoulder was dissected and a specimen comprising the
159 humerus with its attached supraspinatus musculotendinous unit was removed. The
160 contralateral left shoulder served as a control (n = 6). Each sample was fixed in 10%
161 formal saline and underwent decalcification in Ethylenediaminetetraacetic acid
162 (EDTA). Decalcification was checked by radiography at weekly intervals. Following
163 decalcification the specimens were dehydrated in ascending graded alcohol
164 dehydration followed by defatting in chloroform, and embedding in paraffin wax.
165 Multiple 4 micrometre sections were cut in the coronal plane through the humerus,
166 enthesis, supraspinatus musculotendinous unit, and any scar tissue that filled the gap
167 between tendon and bone. Sections were stained with hematoxylin and eosin (H&E).

168

169 A double blind evaluation of all sections was performed using an Olympus BH-2 light
170 microscope (Olympus, Glasgow, UK). Using a semi-quantitative scoring system (0 =
171 none, 1 = mild, and 2 = severe), four high-powered fields were examined in each
172 muscle to determine the extent of fatty infiltration, cellularity, and inflammation.⁵

173 Tendon degeneration was assessed according to a modified Movin scale ¹⁰ and
174 included the following variables: (1) fiber structure, (2) fiber arrangement, (3)
175 rounding of the nuclei, (4) regional variations in cellularity, (5) increased vascularity,
176 and (6) hyalinization. A four-point scoring system was used: 0 = normal appearance,
177 1 = slightly abnormal appearance, 2 = a moderately abnormal appearance, and 3 = a
178 markedly abnormal appearance. ¹¹ Based on this, the total score for any given slide
179 could range from 0 (normal tendon) to 18 (the greatest level of degeneration).

180

181 *Statistical Analysis*

182

183 Nonparametric statistical methods were used for all analyses because of the non-
184 normality of the data in the groups being compared. Numerical data were inputted
185 into SPSS software package, version 23 (SPSS Inc, an IBM Company, Chicago,
186 Illinois). The data are presented as median values (with 95% confidence intervals)
187 unless otherwise stated. Mann Whitney U tests were used to compare between data
188 sets for each group. Results were considered significant at the $p < 0.05$ level.

189 **Results**

190

191 All animals survived the duration of the study and none had post-operative infection.

192 **Limping was noted for all animals for the first three to five postoperative days**
193 **but a normal gait pattern returned afterwards.**

194

195 *Macroscopic Findings*

196

197 Scar tissue was noted in all animals. Based on the position of the suture marker, the
198 supraspinatus tendon had retracted approximately 5 mm in all cases. The muscle belly
199 of supraspinatus was atrophic and was pale in appearance (Figure 2). Some degree of
200 tendon-bone defect closure occurred in all animals at all time points. At three weeks,
201 partial defect closure was evident in all cases. At six weeks, two animals had partial
202 closure of the defect and four animals had complete closure. All animals in the nine-
203 week group had complete closure of the tendon-bone defect (Figure 2).

204

205 *pQCT Scans*

206

207 The contralateral shoulder in which the supraspinatus had not been detached
208 represented control specimens. Median total bone mineral density significantly
209 decreased three (p = 0.006), six (p = 0.004), and nine weeks (p = 0.025) following
210 tendon detachment (**Table 1**) (Figure 3). No significant change in bone mineral
211 density occurred between three, six, and nine weeks (Table 2).

212 *Histological Findings*

213

214 Muscle Evaluation

215

216 A loss of muscle mass was observed at all time points, and was accompanied by
217 degenerative changes (characterized by increased amounts of fibrotic tissue) that were
218 most prominent three weeks after detachment and less evident by nine weeks. No
219 inflammatory changes were present in any of the animals. All groups demonstrated a
220 degree of fatty infiltration, which peaked at three weeks (**Table 3**) (Figure 4).

221 Compared to controls (where there was no fatty infiltration present) fatty infiltration
222 significantly increased ($p = 0.002$) at three weeks but reduced at six- ($p = 0.140$) and
223 nine weeks ($p = 0.138$).

224

225 Cellularity significantly increased at three weeks ($p = 0.001$), at six weeks ($p =$
226 0.002), and at nine weeks ($p = 0.002$), compared to controls (**Table 3**). Furthermore,
227 cellularity was significantly greater in the three-week group than in the six- and nine-
228 week groups ($p = 0.006$ and 0.007 respectively).

229

230 Tendon Evaluation

231

232 Modified Movin Score

233

234 The modified Movin score was significantly higher (indicating degeneration) in the

235 three experimental groups compared to the controls ($p = 0.003$: three, six, and nine
236 weeks after supraspinatus tendon detachment) (**Table 3**) (Figure 5). There were no
237 significant inter-group differences (Table 4).

238

239 Fiber Structure

240

241 In control specimens, collagen fibers were close together and arranged in parallel.
242 Abnormal specimens lost this uniform structure (increased waviness and distance
243 between fibers) to differing degrees (Figure 6) (**Table 3**). Fiber structure was
244 significantly more abnormal in the nine-week group compared to the three- ($p =$
245 0.003) and six-week groups ($p = 0.007$).

246

247 Fiber Arrangement

248

249 In control specimens, the fibers were arranged in parallel. Abnormal specimens lost
250 this arrangement to differing degrees (Figure 6) (**Table 3**). Fiber arrangement was
251 significantly more abnormal in the three-week group compared to the controls ($p =$
252 0.002), the six-week group ($p = 0.001$), and the nine-week group ($p = 0.002$).

253

254 Tenocyte Nuclei

255

256 Tenocyte nuclei were flattened and spindle-shaped in control specimens, but
257 following tendon detachment became more rounded (Figure 7) (**Table 3**). Tenocyte

258 nuclei were significantly more abnormal than controls following tendon detachment
259 ($p = 0.002$ at three-, $p = 0.003$ at six-, and $p = 0.002$ at nine weeks), with the three-
260 week group demonstrating more abnormal rounded nuclei than the six- and nine-week
261 groups.

262

263 Cellularity

264

265 Specimens were evaluated for an increase in cellularity. There was a significant
266 increase in cellularity following tendon detachment ($p = 0.003$ at three, $p = 0.003$ at
267 six, and $p = 0.002$ at nine-weeks), however there were no significant differences
268 between experimental groups (**Tables 3** and 5).

269

270 Vascularity

271

272 Vascular bundles ran with collagen fibers and increased in number with tendon
273 degeneration.¹¹ The number of vascular bundles significantly increased at three- ($p =$
274 0.002), six- ($p = 0.002$), and nine-weeks ($p = 0.006$) following supraspinatus
275 detachment (**Table 3**). A significant reduction in vascularity was noted between three-
276 and nine-weeks ($p = 0.030$).

277

278 Hyalinisation

279

280 Hyalinisation was not observed in any of the specimens.

281 **Discussion**

282

283 This study presents a rat model for the investigation of chronic rotator cuff tears.
284 Following detachment of supraspinatus there was a significant rise in the modified
285 Movin score characterized by a loss of muscle mass, fatty infiltration, an increase in
286 musculotendinous cellularity, loss of normal collagen fiber structure/arrangement,
287 rounded tenocyte nuclei, and an increase in the number of vascular bundles. These
288 results, in conjunction with those from the pQCT evaluation, support our hypothesis
289 that tendon detachment induces supraspinatus musculotendinous degeneration and a
290 reduction in bone mineral density at the enthesis. These changes occurred acutely,
291 after three weeks duration. However after this time defect closure occurs with
292 complete closure of the defect seen at nine weeks, and there appears to be no further
293 degradation of the tendon or muscle. Contrary to previous reports, fatty infiltration
294 was present in muscle specimens at three-weeks but were no longer evident during the
295 latter stages of the study.^{3,4} These transient changes in fatty infiltration suggest that
296 with time, there is gradual reconstitution of the tendon-bone interface with fibrous
297 tissue that permits the transfer of load and subsequent remodeling of this neo-enthesis
298 into a tendon-like structure.^{4,5}

299

300 Chronic rotator cuff tears are characterized by retraction, muscle atrophy,
301 reduced/increased cellularity, reduced/increased vascularity, fatty infiltration,
302 calcification, and degeneration of the muscle.^{6,7} In humans fatty infiltration into the
303 rotator cuff is irreversible and represents an important predisposing factor to repair
304 failure and poor functional outcomes.⁸ Current rodent models have been unable to
305 establish a significant amount of fat accumulation following tendon detachment,

306 making it difficult to specifically examine hypotheses related to it.^{3,4} In this study,
307 there was a significant amount of fatty accumulation into the muscle belly of
308 supraspinatus compared with controls, peaking at three-weeks following tendon
309 detachment and subsiding thereafter. This novel finding may be associated with
310 fundamental inter-species differences between the Wistar rats used in this study and
311 the Sprague-Dawley rats used in others.^{3,4} Lipoprotein lipase catalyses the hydrolysis
312 of triglycerides and is highly expressed in skeletal tissues. It is regulated differently
313 between Wistar and Sprague-Dawley rats and may account for the lack of fat
314 accumulation in otherwise degenerative muscle tissue in some studies.⁹

315

316 Rotator cuff tears can cause osteopenia at the enthesis due to a loss of physical
317 stimuli.^{10,11} During surgery, suture anchors are inserted into the greater tuberosity
318 and therefore any reduction in bone mineral density may cause loosening or pullout
319 before adequate tendon-bone healing can occur.¹² Accordingly, this has been
320 recognised as an independent risk factor predictive of healing, with a higher bone
321 mineral density resulting in better outcomes.^{13,14} The majority of studies ascribe this
322 alteration in bone mineral density to attritional changes secondary to tendon damage,
323 but it is plausible that they may precede the tear and be causative in nature.¹⁵ In order
324 to examine biological strategies that specifically address bone quality, relevant animal
325 models are required. While the anatomical similarities between the rat and human
326 rotator cuff have been extensively described, to date, there are no studies evaluating
327 the onset of osteopenia in the rat. In this study, supraspinatus detachment caused a
328 reduction in bone mineral density at three-, six-, and nine-weeks with no significant
329 change between successive time-points. During a chronic rotator cuff tear the forces
330 borne by the greater tuberosity reduce and therefore cause an imbalance in bone

331 turnover, favoring bone resorption over bone formation: a principle governed by
332 Wolff's law.¹³

333

334 Limitations of this study include those associated with using the contralateral shoulder
335 as a control given that its mechanical and histological properties may have altered
336 during the few days that the animals were limping and therefore placing more weight
337 through the non-operated limb. Additional time points (two and 12 weeks) would
338 have been beneficial to evaluate the progression and further resolution of degenerative
339 musculotendinous changes and alterations in bone mineral density.

340

341 In conclusion, this study has shown that three weeks following detachment, the
342 supraspinatus musculotendinous unit in a rat undergoes degeneration, and the greater
343 tuberosity exhibits a reduction in bone mineral density. These changes are similar to
344 those that occur in the clinical setting following a chronic rotator cuff tear, with the
345 difference that scar tissue bridges the defect in a rat whereas in a human the tendon-
346 bone gap is largely maintained. These findings suggest that the detached rat
347 supraspinatus tendon, after three weeks, could represent a suitable model for
348 investigating biological strategies targeted towards improving tendon-bone healing in
349 chronic rotator cuff tears.

350 **Acknowledgements**

351

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest.

Table 1: Median total bone mineral density at the supraspinatus tendon-bone insertion three, six, and nine weeks following tendon detachment.

	Control (non-operated shoulder) group (n = 6)	3 week group (n = 6)	6 week group (n = 6)	9 week group (n = 6)
Median total bone mineral density (mg/ccm)	793.25 (95% CI 754.24 to 844.70)	684.70 (95% CI 639.21 to 739.82)	642.85 (CI 610.74 to 711.33)	665.20 (CI 594.01 to 763.62)

Table 2: Statistical significance (p-values) between total bone mineral density at the supraspinatus tendon-bone insertion three, six, and nine weeks following tendon detachment.

	Control (non-operated shoulder) group (n = 6)	3 week group (n = 6)	6 week group (n = 6)	9 week group (n = 6)
Control (non-operated shoulder) group (n = 6)	-	0.006	0.004	0.025
3 week group (n = 6)	0.006	-	0.200	0.749
6 week group (n = 6)	0.004	0.200	-	0.631
9 week group (n = 6)	0.025	0.749	0.631	-

Table 3: Muscle and tendon histological outcome scores three, six, and nine weeks following tendon detachment.

	Control (non-operated shoulder) group (n = 6)	3 week group (n = 6)	6 week group (n = 6)	9 week group (n = 6)
Muscle: fatty infiltration	0 (95% CI 0 to 0)	0.5 (95% CI 0.40 to 0.94)	0 (95% CI - 0.19 to 0.69)	0 (95% CI - 0.10 to 0.44)
Muscle: cellularity	0 (95% CI 0 to 0)	2 (95% CI 2 to 2)	1 (95% CI 0.91 to 1.69)	1.5 (95% CI 1.02 to 1.81)
Modified Movin score	0 (95% CI -0.27 to 0.60)	8.75 (95% CI 7.08 to 11.26)	7.75 (95% CI 6.45 to 9.38)	8 (95% CI 7.53 to 9.87)
Tendon: Fiber structure	0 (95% CI 0 to 0)	2 (95% CI 1.56 to 2.10)	1.75 (95% CI 1.40 to 2.26)	2.5 (95% CI 2.40 to 2.94)
Tendon: Fiber arrangement	0 (95% CI 0 to 0)	2 (95% CI 1.52 to 2.31)	1.5 (95% CI 1.20 to 1.63)	1.5 (95% CI 1.02 to 1.81)
Tendon: Tenocyte nuclei	0 (95% CI - 0.13 to 0.30)	2.50 (95% CI 2.06 to 2.60)	1.75 (95% CI 1.40 to 2.26)	2 (95% CI 1.56 to 2.10)
Tendon: Cellularity	0 (95% CI -0.13 to 0.30)	1.25 (95% CI 0.84 to 2.16)	1.75 (95% CI 1.40 to 2.26)	1.75 (95% CI 1.46 to 2.03)
Tendon: Vascularity	0 (95% CI 0 to 0)	1.5 (95% CI 0.68 to 2.49)	1 (95% CI 0.53 to 1.47)	0.5 (95% CI 0.67 to 1.10)

Table 4: Statistical significance (p-values) between modified Movin scores three, six, and nine weeks following tendon detachment.

	Control (non-operated shoulder) group (n = 6)	3 week group (n = 6)	6 week group (n = 6)	9 week group (n = 6)
Control (non-operated shoulder) group (n = 6)	-	0.003	0.003	0.003
3 week group (n = 6)	0.003	-	0.256	0.326
6 week group (n = 6)	0.003	0.256	-	0.513
9 week group (n = 6)	0.003	0.326	0.513	-

Table 5: Statistical significance (p-values) between cellularity three, six, and nine weeks following tendon detachment.

	Control (non-operated shoulder) group (n = 6)	3 week group (n = 6)	6 week group (n = 6)	9 week group (n = 6)
Control (non-operated shoulder) group (n = 6)	-	0.003	0.003	0.002
3 week group (n = 6)	0.003	-	0.246	0.315
6 week group (n = 6)	0.003	0.246	-	0.789
9 week group (n = 6)	0.002	0.315	0.789	-

1 **References**

2

- 3 1. Sundar S, Pendegrass CJ and Blunn GW. Tendon bone healing can be
4 enhanced by demineralized bone matrix: a functional and histological study. *Journal*
5 *of biomedical materials research Part B, Applied biomaterials*. 2009; 88: 115-22.
- 6 2. Gulotta LV, Kovacevic D, Ehteshami JR, Dagher E, Packer JD and Rodeo SA.
7 Application of bone marrow-derived mesenchymal stem cells in a rotator cuff repair
8 model. *The American journal of sports medicine*. 2009; 37: 2126-33.
- 9 3. Buchmann S, Walz L, Sandmann GH, et al. Rotator cuff changes in a full
10 thickness tear rat model: verification of the optimal time interval until reconstruction
11 for comparison to the healing process of chronic lesions in humans. *Archives of*
12 *orthopaedic and trauma surgery*. 2011; 131: 429-35.
- 13 4. Barton ER, Gimbel JA, Williams GR and Soslowky LJ. Rat supraspinatus
14 muscle atrophy after tendon detachment. *Journal of orthopaedic research : official*
15 *publication of the Orthopaedic Research Society*. 2005; 23: 259-65.
- 16 5. Gimbel JA, Van Kleunen JP, Mehta S, Perry SM, Williams GR and
17 Soslowky LJ. Supraspinatus tendon organizational and mechanical properties in a
18 chronic rotator cuff tear animal model. *Journal of biomechanics*. 2004; 37: 739-49.
- 19 6. Loew M, Magosch P, Lichtenberg S, Habermeyer P and Porschke F. How to
20 discriminate between acute traumatic and chronic degenerative rotator cuff lesions: an
21 analysis of specific criteria on radiography and magnetic resonance imaging. *Journal*
22 *of shoulder and elbow surgery / American Shoulder and Elbow Surgeons [et al]*.
23 2015; 24: 1685-93.

- 24 7. Nho SJ, Yadav H, Shindle MK and Macgillivray JD. Rotator cuff
25 degeneration: etiology and pathogenesis. *The American journal of sports medicine*.
26 2008; 36: 987-93.
- 27 8. Deniz G, Kose O, Tugay A, Guler F and Turan A. Fatty degeneration and
28 atrophy of the rotator cuff muscles after arthroscopic repair: does it improve, halt or
29 deteriorate? *Archives of orthopaedic and trauma surgery*. 2014; 134: 985-90.
- 30 9. Galan X, Llobera M and Ramirez I. Lipoprotein lipase in developing rat
31 tissues: differences between Wistar and Sprague-Dawley rats. *Biology of the neonate*.
32 1993; 64: 295-303.
- 33 10. Oh JH, Song BW, Kim SH, et al. The measurement of bone mineral density of
34 bilateral proximal humeri using DXA in patients with unilateral rotator cuff tear.
35 *Osteoporosis international : a journal established as result of cooperation between*
36 *the European Foundation for Osteoporosis and the National Osteoporosis*
37 *Foundation of the USA*. 2014; 25: 2639-48.
- 38 11. Meyer DC, Fucentese SF, Koller B and Gerber C. Association of osteopenia
39 of the humeral head with full-thickness rotator cuff tears. *Journal of shoulder and*
40 *elbow surgery / American Shoulder and Elbow Surgeons [et al]*. 2004; 13: 333-7.
- 41 12. Tingart MJ, Apreleva M, Zurakowski D and Warner JJ. Pullout strength of
42 suture anchors used in rotator cuff repair. *The Journal of bone and joint surgery*
43 *American volume*. 2003; 85-a: 2190-8.
- 44 13. Cadet ER, Hsu JW, Levine WN, Bigliani LU and Ahmad CS. The relationship
45 between greater tuberosity osteopenia and the chronicity of rotator cuff tears. *Journal*
46 *of shoulder and elbow surgery / American Shoulder and Elbow Surgeons [et al]*.
47 2008; 17: 73-7.

- 48 14. Chung SW, Oh JH, Gong HS, Kim JY and Kim SH. Factors affecting rotator
49 cuff healing after arthroscopic repair: osteoporosis as one of the independent risk
50 factors. *The American journal of sports medicine*. 2011; 39: 2099-107.
- 51 15. Chen X, Giambini H, Ben-Abraham E, An KN, Nassr A and Zhao C. Effect of
52 Bone Mineral Density on Rotator Cuff Tear: An Osteoporotic Rabbit Model. *PloS*
53 *one*. 2015; 10: e0139384.
- 54