

Alma Mater Studiorum Università di Bologna
Archivio istituzionale della ricerca

Reconstruction of proximal humeral fractures with a reduced number of screws and a reinforced bone substitute

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

Published Version:

Cristofolini L., Morellato K., Cavallo M., Guerra E. (2020). Reconstruction of proximal humeral fractures with a reduced number of screws and a reinforced bone substitute. *MEDICAL ENGINEERING & PHYSICS*, 82, 97-103 [10.1016/j.medengphy.2020.06.002].

Availability:

This version is available at: <https://hdl.handle.net/11585/808817> since: 2021-02-27

Published:

DOI: <http://doi.org/10.1016/j.medengphy.2020.06.002>

Terms of use:

Some rights reserved. The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

This item was downloaded from IRIS Università di Bologna (<https://cris.unibo.it/>).
When citing, please refer to the published version.

(Article begins on next page)

This is the final peer-reviewed accepted manuscript of:

Med Eng Phys. 2020 Aug;82:97-103. Epub 2020 Jul 8.

Reconstruction of proximal humeral fractures with a reduced number of screws and a reinforced bone substitute

Luca Cristofolini, Kavin Morellato, Marco Cavallo, Enrico Guerra

PMID: 32709270 DOI: 10.1016/j.medengphy.2020.06.002

The final published version is available online at:

<https://doi.org/10.1016/j.medengphy.2020.06.002>

Rights / License:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

Reconstruction of proximal humeral fractures with a reduced number of screws and a reinforced bone substitute

Luca Cristofolini, PhD (1), Kavin Morellato, MEng (1),
Marco Cavallo, MD (2), Enrico Guerra, MD (2)

¹ Department of Industrial Engineering, School of Engineering and Architecture, Alma
Mater Studiorum – Università di Bologna, Bologna, Italy

² Shoulder and Elbow Surgery, Istituto Ortopedico Rizzoli, Bologna, Italy

Running title: Humeral fracture repair using fewer screws

Submitted to: Medical Engineering & Physics

Statistics:

Word count (manuscript): 3560

Word count (abstract): 250

Figures: 6

Tables: 1

References: 46

Corresponding author:

Luca Cristofolini

Department of Industrial Engineering

School of Engineering and Architecture

Alma Mater Studiorum – Università di Bologna

Viale Risorgimento, 2

40136 Bologna, Italy

1 **ABSTRACT**

2 Multi-fragmented fractures of the proximal humerus are difficult to treat, especially in
3 the case of osteoporotic bone. Intra-operative risks include cartilage damage when
4 inserting multiple screws. A common post-operative complication is distal-varus
5 collapse of the head. The aim of this study was to investigate if an *Innovative* technique
6 (reduced number of screws and injection of a beta-TCP additivated partially resorbable
7 cement) provides the same or better stability of the reconstructed head compared to the
8 *Standard* technique (using more screws). A four-fragment fracture was simulated in six
9 pairs of humeri, with partial removal of the cancellous bone to simulate osteoporotic
10 “eggshell” defect. One humerus of each pair was repaired with a *Standard* (locking
11 plate, 2 cortical and 6 locking screws), and the other with the *Innovative* technique (same
12 plate, 2 cortical and only 3 locking screws, plus cement injection). The reconstructed
13 specimens were subjected to a biomechanical test where a cyclic force of increasing
14 amplitude was applied axially until failure. The *Innovative* reconstructions withstood a
15 force 3.49 times larger than the contralateral *Standard* reconstructions before failure
16 started. The maximum force before final collapse for the *Innovative* reconstructions was
17 4.24 times larger than the contralateral *Standard* reconstructions. These differences
18 were statistically significant. The *Innovative* reconstructions, based on fewer screws
19 and beta-TCP additivated acrylic cement, showed positive results, demonstrating better
20 biomechanical properties compared to the *Standard* reconstructions. These laboratory
21 findings, along with the advantages of a reduced number of screws, may help perform a
22 surgically safer, and more effective procedure in osteoporotic patients.

23 **Keywords:** Proximal humeral fracture; osteoporotic multi-fragment fracture; locking
24 plate; augmentation; number of screws.

25

26 **1. INTRODUCTION**

27 Proximal humeral fractures account for about 10% of all fractures in the elderly [1, 2]
28 and affect approximately 66 out of 10,000 persons per year [3]. The incidence of these
29 fractures increases with age, leading to a crucial burden on the society, with a worrying,
30 increasing trend expected for the next 30 years [4, 5]. Locking plate fixation is generally
31 considered the optimal treatment for these fractures [6, 7]. In particular, thanks to their
32 specific surgical principle, second generation locking plates provided stronger fixation
33 of the fracture fragments in the last decade [6].

34 Locking plate fixation is associated with several intra-operative and post-operative
35 complications [8], with increasing incidence according to patient's age, number of
36 fragments, and fracture pattern [9-13]. The main intra-operative risk is articular
37 cartilage damage while drilling or inserting the screws (incidence: 17-25% [14, 15]).
38 This risk is higher as the surgeon needs to use multiple screws to stabilize the different
39 fragments [14]. This risk is also higher in osteoporotic settings, as the screws must be
40 long enough to achieve fixation in the subchondral bone [14]. In fact, the cancellous
41 bone in the proximal metaphysis soon disappears in osteoporotic subjects, while the only
42 strong bone remaining is found in the subarticular cortical region [16]. The most
43 common post-operative failure mechanism of proximal humeral fractures is secondary
44 loss of reduction, with consequent varus malalignment [11, 17]. Low bone mineral
45 density (BMD) is the primary cause of this complication, along with medial
46 comminution of the humeral neck [7, 18]. BMD is a key factor for stability of fixation,
47 as osteoporosis reduces the screw pull-out strength, and the mechanical competence of
48 the bone-implant construct [19-21]. The screws therefore gradually cut into the
49 osteoporotic cancellous bone, allowing varus sliding of the head [22-24].

50 In elderly patients it is important to obtain immediate post-operative fixation strength,
51 to mobilize the shoulder soon after the operation and prevent post-operative stiffness.
52 In poor quality bone, a higher number of screws can improve the construct stability [25],
53 but multiple screws hinder the possibility for bone healing and increase the risk of head
54 perforations. To reduce the incidence of mechanical failure, several augmentation
55 techniques have been developed. The small amount of cement required for
56 augmentation does not cause risk of thermal bone necrosis or cartilage apoptosis [26].
57 If augmentation is delivered in the most critical area, it effectively reduces the rate of
58 head migration [27] and prevents head collapse [28]. While augmentation provides
59 some improvements, it also has different specific drawbacks, mainly in relation to screw
60 extraction in cases of failure [24, 29]. Furthermore, polymethylmethacrylate (PMMA)
61 does not promote bone healing; calcium-phosphate cements are osteoconductive but fail
62 early compared to PMMA under shear loads [30], and their rapid degradation often leads
63 to excessively fast loss of strength [31]. Recently some products have been released,
64 combining the positive aspects of the different augmenting materials. In particular the
65 cement used for this study is a combination of PMMA and beta-tricalcium phosphate
66 (beta-TCP). This is meant to conjugate good initial mechanical properties, with bone
67 ingrowth with partial substitution over time [32, 33]. To the Authors' knowledge,
68 cement augmentation has never been exploited to reduce the number of screws and
69 reduce the associated risks.

70 The aim of this study was to investigate if an *Innovative*-technique to repair humeral
71 fractures, based on a reduced number of screws and injection of a beta-TCP additivated
72 acrylic cement, provides the same or better stability of the bone fragments compared to
73 the *Standard*-technique, based on a larger number of screws. The focus was the risk of
74 slippage of the reconstructed head in cases of four-fragment fractures in proximal
75 humeri with bone defects. This technique has the potential advantage of reducing the

76 number of drill-holes in osteoporotic heads, thus reducing bone damage, and the risk of
77 cartilage drill-in, in combination with the advantages of a partially resorbable and
78 osteoconductive biomaterial.

79 **2. MATERIALS AND METHODS**

80 **2.1 Bone specimens**

81 Six pairs of fresh-frozen humeri were obtained through an ethically-approved donation
82 program (Anatomy Gifts Registry, Hannover, USA), excluding donors with history of
83 upper limb fracture or metastases. To address bones with limited quality, donors older
84 than 55 were selected (Table 1). The BMD has not been measured. Both the bone
85 strength during preparation and the micro-CT scans (see below) confirmed that the
86 bones had relatively poor bone quality. No information about donor's laterality was
87 available. The bones were thawed at room temperature prior to testing. They were
88 wrapped in cloths soaked with physiological saline solution when not in use.

89 The bones were stripped of all soft tissues to expose the bone landmarks. The intact
90 humeri were prepared with a set of reference axes to allow for reproducible alignment
91 [34]. The distal portion of the humeri was resected. The diaphysis was potted in an
92 aluminium box with PMMA so that 40% of the biomechanical length (Table 1)
93 protruded out of the cement.

94 **2.2 Surgical technique**

95 One humerus of each pair was randomly assigned to one of these two reconstruction
96 techniques (Fig. 1):

97 • *Standard-technique*: one of the most commonly used pre-contoured plates (Philos,
98 DePuy Synthes, Oberdorf, Switzerland) was used in conjunction with six locking
99 screws (fixing the proximal fragments), and two cortex screws (distally).

100 • *Innovative-technique*: the same model of plate was used, with only three locking
101 screws (fixing the proximal fragments), and two cortex screws (distally). There is
102 a debate about which and how many screws are ideal for augmentation [29]. Our
103 choice was to implant the two superior screws to lock the greater tuberosity, and
104 the lower-anterior screw directed towards the lesser tuberosity. To verify the
105 biomechanical strength without other mechanical support in the most critical area,
106 the calcar screws were not used. An acrylic bone cement additivated with 26%
107 beta-TCP (Cal-CEMEX, Tecres, Sommacampagna, Italy) was injected inside the
108 fracture site. This material is already approved for clinical use.

109 To enable reproducible preparation of the screw holes for the reconstruction, they were
110 drilled before simulating the fracture. An experienced shoulder surgeon identified the
111 optimal position of the plates, preparing the humeri in pairs, aiming to minimize intra-
112 pair differences. The direction of the holes ($\varnothing 2.5$ mm) was guided by the drill sleeve
113 (Philos, Synthes):

- 114 • In all the specimens the plate was fixed distally with two cortex screws.
- 115 • In the *Standard-technique* specimens six holes were prepared for the proximal
116 locking screws.
- 117 • In the *Innovative-technique* specimens only three holes were prepared for the
118 proximal locking screws, with the addition of an extra hole for later injection of
119 the cement.

120 After drilling the holes, the plates and screws were removed to allow preparation of the
121 fractures.

122 **2.3 Simulation of fracture and bone defect**

123 A four-fragment fracture (adapted from the AO-11-C2 [35]) was simulated in all humeri.
124 To allow consistent preparation, the fractured humeri were prepared in pairs, following
125 well-defined resection planes, aligned with the previously defined reference frame,
126 using custom-built cutting jigs (Fig. 2). In addition, to simulate the most osteoporotic
127 cases, where this technique is possibly more frequent, a portion of the cancellous bone
128 was removed to mimic lack of support due to poor bone quality (“eggshell defect”) by
129 drilling the head, and the metaphysis [16]. To ensure reproducible preparation, a hole
130 was drilled in the cancellous bone under the drill press following a standardized
131 procedure for the head (ø30 mm bit, for a depth equivalent to 40% of the head diameter),
132 and the metaphysis (ø20 mm bit, for a depth of 31 mm). No cortical bone was removed.

133 **2.4 Reconstruction of the fractured humeri**

134 A total of 4 plates (regular size) and 51 screws (ø3.5 mm, 28-50 mm long as required)
135 of titanium alloy were used for all the humeri. The plates and screws were carefully
136 checked before re-use following a validated procedure to exclude critical damage of the
137 threads, or bending [36]. One humerus of each pair was reconstructed with the
138 *Standard*-technique with 2 cortex and 6 locking screws, following the technique
139 indicated by the manufacturer of the fixation system).

140 Reconstruction with the *Innovative*-technique of the contralateral humerus of each pair
141 was derived from that of the *Standard*-technique: the plate was fixed to the diaphysis

142 with the 2 cortex screws. The 3 locking screws were inserted proximally while the
143 fragments were held in place. Finally, 40 g of beta-TCP additivated acrylic cement (Cal-
144 CEMEX) pre-chilled at 4°C were injected (5 minutes after mixing started) through a
145 hole on the lateral side (Fig. 1) This amount, the same for all *Innovative-technique*
146 specimens, was chosen based on the estimated volume of the bone defect. No leakage
147 of cement was observed through the bone fractures.

148 After reconstruction (Fig. 1), the samples were inspected to exclude ones with damage
149 induced by preparation, bone defects that had become evident only during preparation,
150 and critical differences between contralateral specimens. As the direction of the screws
151 with the Philos system is guided by the plate and a dedicated sleeve, the quality of the
152 reconstructions was assessed visually, with no aid of post-operative radiographs. No
153 protrusion of the locking screws was observed. In all the specimens, gaps between
154 fragments were smaller than 1 mm, and the malpositioning between the reconstructed
155 fragments never exceeded 2 mm.

156 The specimens were seasoned for 48 hours at 37°C in physiological saline solution
157 (additivated with 0.18% methyl-4-hydroxybenzoate to avoid degradation), before
158 mechanical testing. Such seasoning reflects the earliest reasonable time when a shoulder
159 patient would load the operated limb [37].

160 **2.5 Biomechanical test**

161 In order to measure the strength of the two types of reconstructions, the repaired humeri
162 underwent a biomechanical test where a cyclic force of increasing magnitude was
163 applied. The loading direction was chosen to address the risk of distal migration of the
164 reconstructed head with respect to the humeral diaphysis. This is one of the most

165 common failure mechanisms: due to repetitive axial loading, the screws gradually cut
166 into the cancellous bone, allowing varus sliding of the head [38, 39]. To test this
167 scenario, a vertical force was applied to the humeral head while the distal end was fixed
168 to the load-cell of the testing machine (Mod.8800, Instron, Canton, USA; Fig. 3). A
169 system of low-friction bearings ensured that no horizontal force was transmitted while
170 the humeral head was free to roll against the flat loading plate. The force was therefore
171 aligned with the axis of the humerus. Considering the range of joint force directions for
172 different motor tasks (for a ball-and-socket joint, the reaction transmitted to the humeral
173 head consists of a force passing through the joint centre [40-42]), this corresponds to
174 the worst-case-scenario. Indeed, application of a force aligned with the humeral axis
175 elicits the highest risk of distal slippage of the humeral head, while an oblique force
176 would also apply a compression at the fracture site, which would stabilize the
177 reconstruction.

178 The applied force followed a haversine at 1 Hz: the baseline force was constant (80 N);
179 the amplitude started from 60 N for the first cycle and increased by 1% at each cycle
180 until specimen failure (see below). The force and displacement were measured at 2000
181 Hz with a high-performance datalogger (PXIe-6341+PXIe-8135, National-Instruments,
182 Austin, USA). The entire test lasted between 125 and 436 cycles (between 2 and 7
183 minutes). To document the mode of failure, the biomechanical test was filmed from the
184 posterior with a high-resolution camera.

185 **2.6 Identification of failure**

186 Final failure was defined when the distal migration of the head (obtained from the
187 displacement of the actuator of the testing machine) exceeded 5.0 mm with respect to

188 the beginning of the test (the tests were extended further, to 8.0 mm, for practical
189 reasons, to ensure all specimens did fail). This is consistent with the criterion indicated
190 by Neer et al, where a displacement of 5.0 mm or more was considered an indication for
191 surgical treatment for humeral head fractures [43]. The maximum force was defined as
192 the largest value recorded before or at 5.0 mm migration. This corresponds to the
193 maximal force that can be resisted by the reconstructed humerus before gross failure
194 occurs.

195 The 0-5 mm interval was further investigated to unambiguously identify the first failure
196 event, defined as a change of slope in the force-displacement curve. This would
197 correspond to an initial migration of a reconstructed humeral head in a shoulder patient.
198 To identify such a transition in an operator-independent way, the first failure was defined
199 in a manner similar to the elastic limit in material testing: the initial slope of the force-
200 displacement curve was calculated; a line with a 0.2 mm offset was then drawn; the
201 intersection of the offset line with the force-displacement plot defined the end of the
202 linear region (first failure).

203 **2.7 Radiographic analysis of the cement-bone interdigitation**

204 To document the delivery and interdigitation of the cement in the cancellous bone, the
205 *Innovative*-reconstructions were subjected to micro-computed tomography (micro-CT).
206 To avoid metal artefacts, the specimens were scanned after the biomechanical test so
207 that the plates and screws could be removed. The specimens were scanned with a cone-
208 beam micro-CT scanner (A-TOM-1Z, RAR-CompaCT, Verona, Italy) with 80 kV, 0.6
209 mA, and a voxel size of 36 micrometers. ImageJ-v1.51 (NIH, Bethesda, Maryland,
210 USA) was used to measure cement-bone interdigitation [44].

211 **2.8 Statistics**

212 The F-test was used to compare the variance of the two samples. The Wilcoxon signed-
213 rank one-tailed non-parametric test was used to compare the strength of the paired
214 samples. All statistical analyses were performed with StatPlus (AnalystSoft, Walnut,
215 USA).

216 **3. RESULTS**

217 **3.1 Failure mechanism**

218 For both types of reconstruction, our test elicited the expected type of failure: a
219 progressive varus-distal collapse of the humeral head with respect to the diaphysis. The
220 force-displacement plots had a monotonic trend until failure for all the specimens (Fig.
221 4). In most specimens (nine out of twelve) of both reconstruction types, the force
222 showed a second increase after a migration of 1.5-4.5 mm: this was associated with a
223 compaction of the fragments.

224 Each group showed a typical and consistent failure mechanism:

- 225 • The *Standard*-reconstructions (i.e. repaired with 6 locking screws) failed
226 progressively, starting at a force (first failure) that was lower than the maximum
227 peak. In most cases, the first failure was associated with a change of slope, and
228 the beginning of extensive migration. The maximum force was 1.74 times larger
229 (median of 6 specimens) than the first failure.
- 230 • For the *Innovative*-reconstructions (i.e. with 3 locking screws and injection of the
231 beta-TCP additivated acrylic cement), failure was more progressive than with the

232 *Standard*-technique, with the force still increasing after the first failure. The
233 maximum force was 2.52 times larger (median of 6 specimens) than the force at
234 first failure.

235 **3.2 Strength of the reconstructions**

236 The force at first failure of the *Innovative*-reconstructions (range: 712-1818 N) was 3.49
237 times larger (median of the ratio) than the contralateral *Standard*-reconstructions (range:
238 163-450 N). This difference was statistically significant (Wilcoxon signed-rank,
239 $p=0.016$). Similarly, the maximum force of the *Innovative*-reconstructions (range:
240 1064-3729 N) was 4.24 times larger than the contralateral *Standard*-reconstructions
241 (range: 278-801 N). This difference was statistically significant (Wilcoxon signed-rank,
242 $p=0.016$). Remarkably, all of the *Innovative*-reconstructions were at least as strong as
243 the contralateral *Standard*-reconstructions (Fig. 5).

244 The inter-specimen variability (standard deviation) was lower for the *Standard*-
245 reconstructions than for the *Innovative*-reconstructions both for the force at first failure
246 and for the maximum force (F-test, $p<0.005$). If the coefficient of variation (standard
247 deviation/mean) were compared, the two samples were more similar (coefficient of
248 variation = 30-40%).

249 **3.3 Cement-bone interdigitation**

250 The micro-CT analysis (performed after the biomechanical test) confirmed that the
251 cement in the *Innovative*-reconstructions was delivered in the space corresponding to
252 the osteoporotic “eggshell” defect. Over 90% of the cavity was filled by the cement

253 injected. A penetration of 0.2-2.8 mm of the cement in the cancellous bone was visible
254 (Fig. 6).

255 **4. DISCUSSION**

256 Treatment of proximal humerus fractures still yields dissatisfactory clinical outcomes,
257 especially with multi-fragment fractures in patients with poor bone quality [9, 17, 22].
258 In fact, elderly subjects often show fractures with multiple fragments and bone
259 impaction. Even after the anatomic reduction, bone stock to support the screws is often
260 missing at the centre of the humeral head [11, 17]. We developed an *Innovative-*
261 *technique*, where some of the locking screws used to hold the proximal fragments in
262 place were replaced with a beta-TCP additivated acrylic cement.

263 To test if this *Innovative-technique* provides the same or better stability compared to the
264 *Standard-technique* (larger number of screws), pairs of cadaveric humeri reconstructed
265 with both techniques were tested to failure. All the specimens showed a failure
266 mechanism (varus-distal slippage of the head) that is clinically relevant. Our
267 biomechanical test showed that, before failure initiated, the fractured humeri
268 reconstructed with the *Innovative-technique* withstood a significantly larger force (3.49
269 times) compared to the *Standard-reconstructions*. Similarly, the *Innovative-technique*
270 withstood a significantly larger maximal force (4.24 times) compared to the *Standard*
271 before catastrophic failure occurred. This confirms that the *Innovative-reconstructions*
272 can better prevent both early post-operative head migration and gross failure due to
273 loading.

274 A recent review showed that locking plates have better mechanical performance than
275 non-locking ones, and the Philos plate was most frequently tested [23]. Opposing results

276 have been published comparing non-locking blade plates and polyaxial locking screws
277 [28, 38]. Augmentation with cement or allografts was found to improve the mechanical
278 performance of the bone-plate [23, 24]. Nevertheless, it is still unclear if a rigid implant
279 is better than a semi-rigid one, and controversies remain about the insertion of
280 inferomedial screws for calcar region support [23, 45].

281 It is interesting to compare the failure loads measured *in vitro* with the expected patient
282 loading. One of the most critical motor tasks for a patient with a repaired humeral
283 fracture is standing up from seated using the arm support [38, 39]. This action is
284 associated with a peak force of 1.8 times the body weight [40] (this was calculated from
285 numerical models, possibly overestimating the actual load, thus providing a conservative
286 comparison). For an 80 kg patient, this corresponds to 1413 N. The strength we
287 measured compares favourably with such load magnitude: in fact, the maximum force
288 for the *Innovative*-reconstructions was on average 2255 N, whereas the *Standard*-
289 reconstructions could only resist 564 N on average. Other activities are less demanding
290 than the strength provided by the *Innovative*-reconstruction [46]. For instance,
291 abduction with straight arm causes a resultant force at the glenohumeral joint of 600 N;
292 abduction with straight arm and a weight of 1.1 kg causes a force of 2070 N; wheelchair
293 propulsion causes a force of 1900 N. Therefore, these actions would not represent a risk
294 of failure for the *Innovative*-reconstructions, but some of these would bring to failure
295 the *Standard*-reconstruction.

296 A limitation of this study relates to the fact that we mainly focused on the possible
297 slippage of the reconstructed head. For this reason, we simulated the worst loading for
298 this scenario, where the force is aligned with the humeral axis. The angle spanned by
299 the force for different activities, abduction, external rotation and internal rotation is large
300 (30°-95°) [41, 42]. It is possible that loading in different directions triggered failure

301 scenarios different from those simulated in this study. Nevertheless, the mechanism
302 investigated in the present study is the most commonly observed in elderly patients [22].
303 Furthermore, the displacement of the actuator of the testing machine was used to
304 measure the fracture stability. This measured only the vertical component of motion,
305 and with a slight overestimate (the actuator displacement depends mainly on the slippage
306 of the head, but also on the deformation of the cartilage).

307 The bone defect simulating the lack of cancellous bone resembled the condition
308 clinically observed in elderly osteoporotic subjects, where the subarticular cortex is the
309 only viable area for screw fixation [16]. To ensure consistent preparation between
310 specimens, the geometry had to be simplified to the one that can be obtained with a drill
311 press. While this simulation was only a first approximation of real patients, the fact that
312 the same defect was generated in paired humeri make comparisons possible.

313 Finally, bone fragments were repositioned accurately, with minimal gaps in order to
314 allow better pairwise comparison, enhance test repeatability, and grant high statistical
315 power. This represents an ideal condition, that might not always occur in real patients.

316 It must be emphasized that the present findings apply to osteoporotic bones (which are
317 the most difficult ones to treat) and to a specific fracture fixation kit (currently one of
318 the most commonly used). Different results could possibly be obtained under different
319 conditions.

320 The strength we measured for the *Innovative*-technique has the potential of preventing
321 failures even in cases of severe loading. This is a significant improvement compared to
322 the *Standard*-technique, which cannot withstand such loading. The potential benefits of
323 this technique are remarkable. In fact, a reduced number of screws could grant an
324 inferior rate of complications by screw protrusion on the humeral head, screws cut off

325 or secondary protrusion at follow up after a humeral head collapse (e.g. due to
326 osteonecrosis). In addition, the fact that fewer screws are inserted in the head means
327 that less bone is removed/damaged, and that cancellous vascularization is possibly better
328 preserved, thus reducing the risks of osteonecrosis. Moreover, the specific properties of
329 the beta-TCP additivated cement used in this study are also expected to promote bone
330 formation. In fact, it has been shown that the osteoconductivity due to the beta-TCP in
331 the Cal-CEMEX, and the size and morphology of the pores in the PMMA after
332 dissolution of the mineral component, promotes significant apposition of new bone [32,
333 33]. Additionally, the screws were easily removed from the bones and the cement after
334 the test, suggesting that removal of the hardware should not be difficult, if required after
335 fracture healing.

336 **5. CONCLUSIONS**

337 The *Innovative*-reconstructions, based on a reduced number of screws and augmentation
338 with an acrylic bone cement additivated with beta-TCP, showed positive results,
339 demonstrating better biomechanical properties compared to the *Standard*-
340 reconstructions in cases of osteoporosis and bone defects. These laboratory findings,
341 along with the advantages of a reduced number of screws, may help the surgeon in
342 performing a procedure that is surgically safer and more effective for elderly patients.

343 **Acknowledgments:** The Authors wish to thank rd. Renzo Soffiatti and dr. Roberta
344 Tosato for the valuable technical advice about the cement; dr. Federico Morosato for the
345 help with the preparation of the specimens; dr. Marco Palanca for the help and advice
346 about the mechanical tests; Roberto Rotini, MD, and Alessandro Marinelli, MD, for the
347 stimulating discussions; Samuele L. Gould, MEng, for language editing. Tecres SpA
348 (Sommacampagna, Verona, Italy) is gratefully acknowledged for the financial support.

349 **Competing interests:** None declared

350 **Funding:** The Department of Industrial Engineering of the School of Engineering and
351 Architecture, Alma Mater Studiorum – Università di Bologna received from Tecres SpA
352 (Sommacampagna, Verona, Italy) research funds and the test specimens for this study.

353 **Ethical approval:** This study is based on humeri from human donors, which were
354 obtained through an international ethically-approved donation program (Anatomy Gifts
355 Registry, Hannover, USA). This Study was authorized by the Bioethics Committee of
356 the University of Bologna (Prot. 68448 of 10 May 2018).

REFERENCES:

- [1] Baron JA, Karagas M, Barrett J, Kniffin W, Malenka D, Mayor M, et al. Basic epidemiology of fractures of the upper and lower limb among Americans over 65 years of age. *Epidemiology*. 1996;7:612-8.
- [2] Tsuda T. Epidemiology of fragility fractures and fall prevention in the elderly: a systematic review of the literature. *Current orthopaedic practice*. 2017;28:580-5.
- [3] Lanting B, MacDermid J, Drosdowech D, Faber KJ. Proximal humeral fractures: A systematic review of treatment modalities. *Journal of Shoulder and Elbow Surgery*. 2008;17:42-54.
- [4] Kannus P, Palvanen M, Niemi S, Parkkari J, Järvinen M, Vuori I. Osteoporotic fractures of the proximal humerus in elderly Finnish persons: Sharp increase in 1970-1998 and alarming projections for the new millennium. *Acta Orthopaedica Scandinavica*. 2000;71:465-70.
- [5] Singh A, Adams AL, Burchette R, Dell RM, Funahashi TT, Navarro RA. The effect of osteoporosis management on proximal humeral fracture. *Journal of Shoulder and Elbow Surgery*. 2015;24:191-8.
- [6] Gavaskar AS, Karthik B B, Tummala NC, Srinivasan P, Gopalan H. Second generation locked plating for complex proximal humerus fractures in very elderly patients. *Injury*. 2016;47:2534-8.
- [7] Schliemann B, Seifert R, Rosslenbroich SB, Theisen C, Wähnert D, Raschke MJ, et al. Screw augmentation reduces motion at the bone-implant interface: a biomechanical study of locking plate fixation of proximal humeral fractures. *Journal of Shoulder and Elbow Surgery*. 2015;24:1968-73.
- [8] Greiwe RM. Proximal humerus fractures: 5 Percutaneous fixation, proximal humeral nailing, and open reduction and internal fixation. *Shoulder and Elbow Trauma and its Complications Elsevier*; 2015. p. 83-112.
- [9] Brunner F, Sommer C, Bahrs C, Heuwinkel R, Hafner C, Rillmann P, et al. Open Reduction and Internal Fixation of Proximal Humerus Fractures Using a Proximal Humeral Locked Plate: A Prospective Multicenter Analysis. *Journal of Orthopaedic Trauma*. 2009;23:163-72.
- [10] Berkes MB, Little MTM, Lorich DG. Open reduction internal fixation of proximal humerus fractures. *Current Reviews in Musculoskeletal Medicine*. 2013;6:47-56.
- [11] Schliemann B, Siemoneit J, Theisen C, Kösters C, Weimann A, Raschke MJ. Complex fractures of the proximal humerus in the elderly—outcome and complications after locking plate fixation. *Musculoskeletal Surgery*. 2012;96:3-11.
- [12] Sproul RC, Iyengar JJ, Devcic Z, Feeley BT. A systematic review of locking plate fixation of proximal humerus fractures. *Injury*. 2011;42:408-13.
- [13] Thanasas C, Kontakis G, Angoules A, Limb D, Giannoudis P. Treatment of proximal humerus fractures with locking plates: a systematic review. *Journal of shoulder and elbow surgery*. 2009;18:837-44.
- [14] Charalambous CP, Siddique I, Valluripalli K, Kovacevic M, Panose P, Srinivasan M, et al. Proximal humeral internal locking system (PHILOS) for the treatment of proximal humeral fractures. *Archives of Orthopaedic and Trauma Surgery*. 2007;127:205-10.
- [15] Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J. Internal fixation versus nonoperative treatment of displaced 3-part proximal humeral fractures in elderly patients: a randomized controlled trial. *J Shoulder Elbow Surg*. 2011;20:747-55.

- [16] Kamer L, Noser H, Popp AW, Lenz M, Blauth M. Computational anatomy of the proximal humerus: An ex vivo high-resolution peripheral quantitative computed tomography study. *Journal of orthopaedic translation*. 2016;4:46-56.
- [17] Owsley KC, Gorczyca JT. Fracture displacement and screw cutout after open reduction and locked plate fixation of proximal humeral fractures [corrected]. *The Journal of bone and joint surgery American volume*. 2008;90:233-40.
- [18] Namdari S, Voleti PB, Mehta S. Evaluation of the osteoporotic proximal humeral fracture and strategies for structural augmentation during surgical treatment. *Journal of Shoulder and Elbow Surgery*. 2012;21:1787-95.
- [19] Fankhauser F, Schippinger G, Weber K, Heinz S, Quehenberger F, Boldin C, et al. Cadaveric-Biomechanical Evaluation of Bone-Implant Construct of Proximal Humerus Fractures (Neer Type 3). *The Journal of Trauma: Injury, Infection, and Critical Care*. 2003;55:345-9.
- [20] Maldonado ZM, Seebeck J, Heller MOW, Brandt D, Hepp P, Lill H, et al. Straining of the intact and fractured proximal humerus under physiological-like loading. *Journal of Biomechanics*. 2003;36:1865-73.
- [21] Seebeck J, Goldhahn J, Städele H, Messmer P, Morlock MM, Schneider E. Effect of cortical thickness and cancellous bone density on the holding strength of internal fixator screws. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*. 2004;22:1237-42.
- [22] Hertel R. Fractures of the proximal humerus in osteoporotic bone. *Osteoporosis International*. 2005;16:S65-S72.
- [23] Jabran A, Peach C, Ren L. Biomechanical analysis of plate systems for proximal humerus fractures: a systematic literature review. *Biomedical engineering online*. 2018;17:47-.
- [24] Kammerlander C, Neuerburg C, Verlaan J-J, Schmoelz W, Miclau T, Larsson S. The use of augmentation techniques in osteoporotic fracture fixation. *Injury*. 2016;47:S36-S43.
- [25] Varga P, Inzana JA, Gueorguiev B, Südkamp NP, Windolf M. Validated computational framework for efficient systematic evaluation of osteoporotic fracture fixation in the proximal humerus. *Medical Engineering & Physics*. 2018;57:29-39.
- [26] Blazejak M, Hofmann-Fliri L, Büchler L, Gueorguiev B, Windolf M. In vitro temperature evaluation during cement augmentation of proximal humerus plate screw tips. *Injury*. 2013;44:1321-6.
- [27] Kathrein S, Kralinger F, Blauth M, Schmoelz W. Biomechanical comparison of an angular stable plate with augmented and non-augmented screws in a newly developed shoulder test bench. *Clin Biomech (Bristol, Avon)*. 2013;28:273-7.
- [28] Röderer G, Scola A, Schmölz W, Gebhard F, Windolf M, Hofmann-Fliri L. Biomechanical in vitro assessment of screw augmentation in locked plating of proximal humerus fractures. *Injury*. 2013;44:1327-32.
- [29] Goetzen M, Windolf M, Schmoelz W. Augmented screws in angular stable plating of the proximal humerus: what to do when revision is needed? *Clinical biomechanics (Bristol, Avon)*. 2014;29:1023-6.
- [30] Danesi V, Faldini C, Cristofolini L. Methods for the characterization of the long-term mechanical performance of cements for vertebroplasty and kyphoplasty: Critical review and suggestions for test methods. *J Mechanics in Medicine and Biology*. 2017;17:1-33.
- [31] Urban RM, Turner TM, Hall DJ, Infanger SI, Cheema N, Lim T-H, et al. Effects of altered crystalline structure and increased initial compressive strength of calcium

- sulfate bone graft substitute pellets on new bone formation. *Orthopedics*. 2004;27:s113-8.
- [32] Dall'Oca C, Maluta T, Cavani F, Morbioli GP, Bernardi P, Sbarbati A, et al. The biocompatibility of porous vs non-porous bone cements: a new methodological approach. *European journal of histochemistry : EJH*. 2014;58:2255-.
- [33] Dall'Oca C, Maluta T, Micheloni GM, Cengarle M, Morbioli G, Bernardi P, et al. The biocompatibility of bone cements: progress in methodological approach. *European journal of histochemistry : EJH*. 2017;61:2673-.
- [34] Cristofolini L. *Anatomical Reference Frames for Long Bones: Biomechanical Applications*. New York, NY: Springer New York; 2012. p. 2971-99.
- [35] Rüedi TP, Murphy WM. *AO principles of fracture management*. Stuttgart: Georg Thieme Verlag; 2001.
- [36] Danesi V, Cristofolini L, Stea S, Traina F, Beraudi A, Tersì L, et al. Re-use of explanted osteosynthesis devices: a reliable and inexpensive reprocessing protocol. *Injury*. 2011;42:1101-6.
- [37] Doshi C, Sharma GM, Naik LG, Badgire KS, Qureshi F. Treatment of Proximal Humerus Fractures using PHILOS Plate. *Journal of clinical and diagnostic research : JCDR*. 2017;11:RC10-RC3.
- [38] Brianza S, Plecko M, Gueorguiev B, Windolf M, Schwieger K. Biomechanical evaluation of a new fixation technique for internal fixation of three-part proximal humerus fractures in a novel cadaveric model. *Clinical Biomechanics*. 2010;25:886-92.
- [39] Lescheid J, Zdero R, Shah S, Kuzyk PRT, Schemitsch EH. The Biomechanics of Locked Plating for Repairing Proximal Humerus Fractures With or Without Medial Cortical Support. *The Journal of Trauma: Injury, Infection, and Critical Care*. 2010;69:1235-42.
- [40] Anglin C, Wyss UP, Pichora DR. Glenohumeral contact forces. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*. 2000;214:637-44.
- [41] Westerhoff P, Graichen F, Bender A, Halder A, Beier A, Rohlmann A, et al. In vivo measurement of shoulder joint loads during activities of daily living. *Journal of Biomechanics*. 2009;42:1840-9.
- [42] Westerhoff P, Graichen F, Bender A, Halder A, Beier A, Rohlmann A, et al. Measurement of shoulder joint loads during wheelchair propulsion measured in vivo. *Clinical biomechanics (Bristol, Avon)*. 2011;26:982-9.
- [43] Neer CS, Watson KC, Stanton FJ. Recent experience in total shoulder replacement. *The Journal of bone and joint surgery American volume*. 1982;64:319-37.
- [44] Schneider CA, Rasband WS, Eliceiri KW. NIH Image to ImageJ: 25 years of image analysis. *Nature methods*. 2012;9:671-5.
- [45] Walsh S, Reindl R, Harvey E, Berry G, Beckman L, Steffen T. Biomechanical comparison of a unique locking plate versus a standard plate for internal fixation of proximal humerus fractures in a cadaveric model. *Clinical Biomechanics*. 2006;21:1027-31.
- [46] Bergmann G, Graichen F, Bender A, Käab M, Rohlmann A, Westerhoff P. In vivo glenohumeral contact forces—Measurements in the first patient 7 months postoperatively. *Journal of Biomechanics*. 2007;40:2139-49.

CAPTIONS TO FIGURES

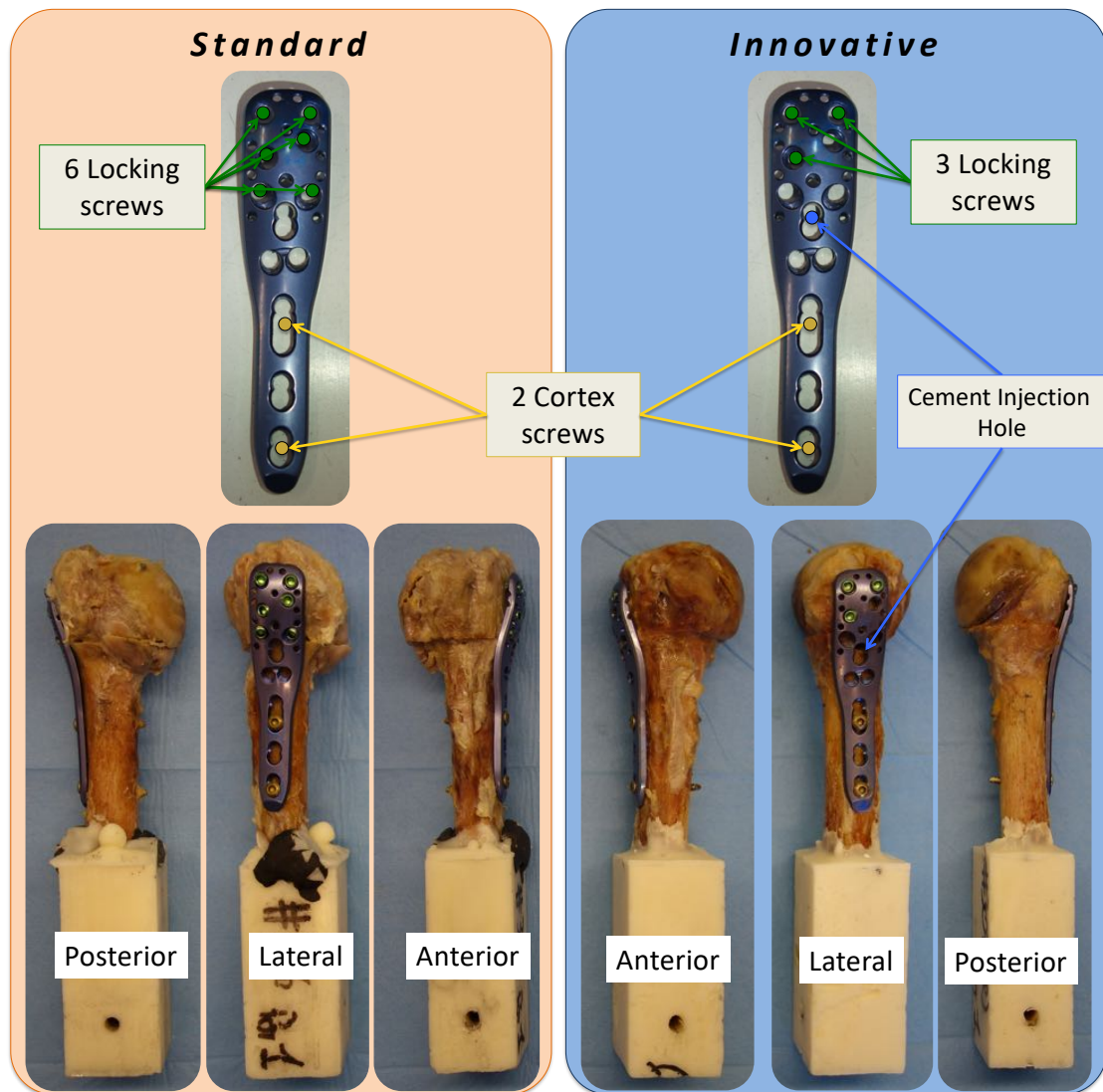


Fig. 1 – TOP: Lateral view of the plate, showing the position of the screws for the *Standard* and the *Innovative* techniques. The screws were positioned in the same holes for all the specimens of each group (regardless of if it was a right or left humerus). BOTTOM: Pair of humeri after simulation of fracture and reconstruction with the *Standard*-technique (left humerus in this pair) or with the *Innovative*-technique (right humerus): anterior, lateral and posterior views. The position of the hole for the cement injection in the *Innovative* specimens is indicated.

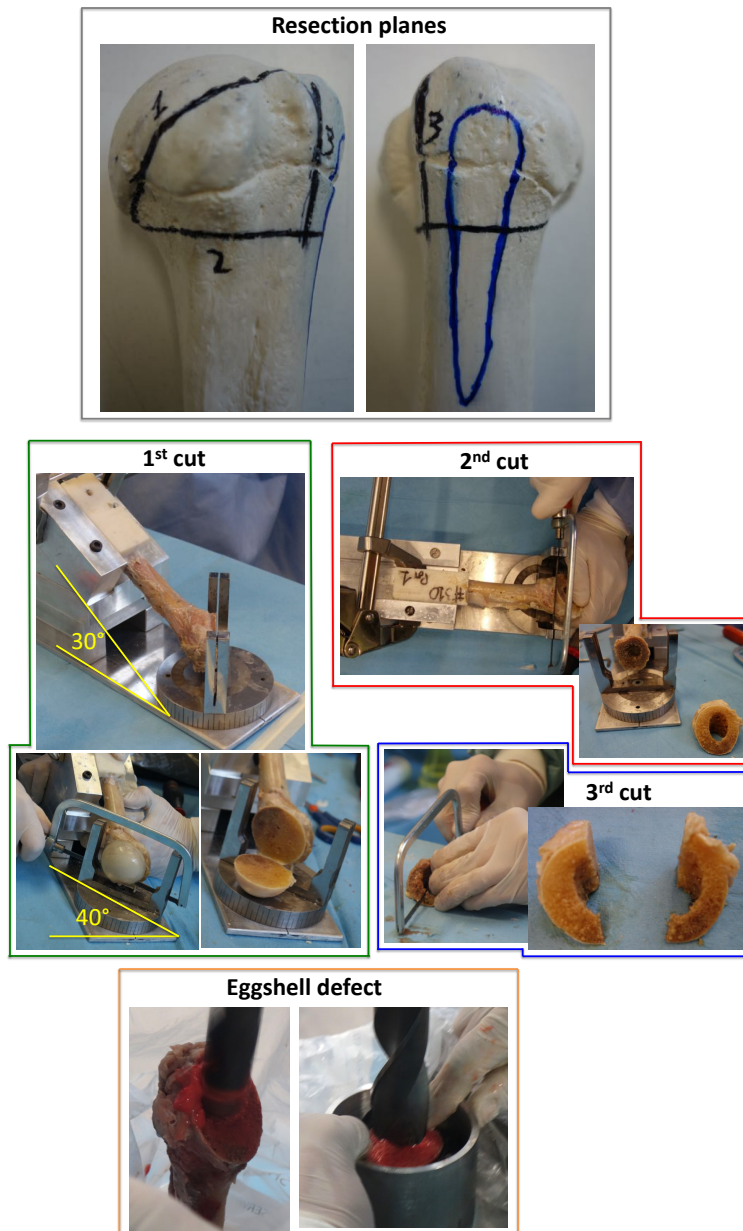


Fig. 2 – Top: Schematic of the three resection planes to simulate a four-fragment fracture (left humerus: anterior and lateral views); also visible is the planned position of the plate. Centre and bottom: procedure to simulate the bone fracture using the cutting jig for the three osteotomies. With the 1st cut, the head was resected on a plane parallel to the end of the epiphysis. The 2nd cut resected the metaphysis at the height of the end of the epiphysis. The lateral fragment was cut in a frontal plane between the greater and lesser tubercle (3rd cut). To simulate poor bone quality (“eggshell defect”), holes were drilled to remove most of the cancellous bone from the head, and the metaphysis, without affecting the cortical bone.

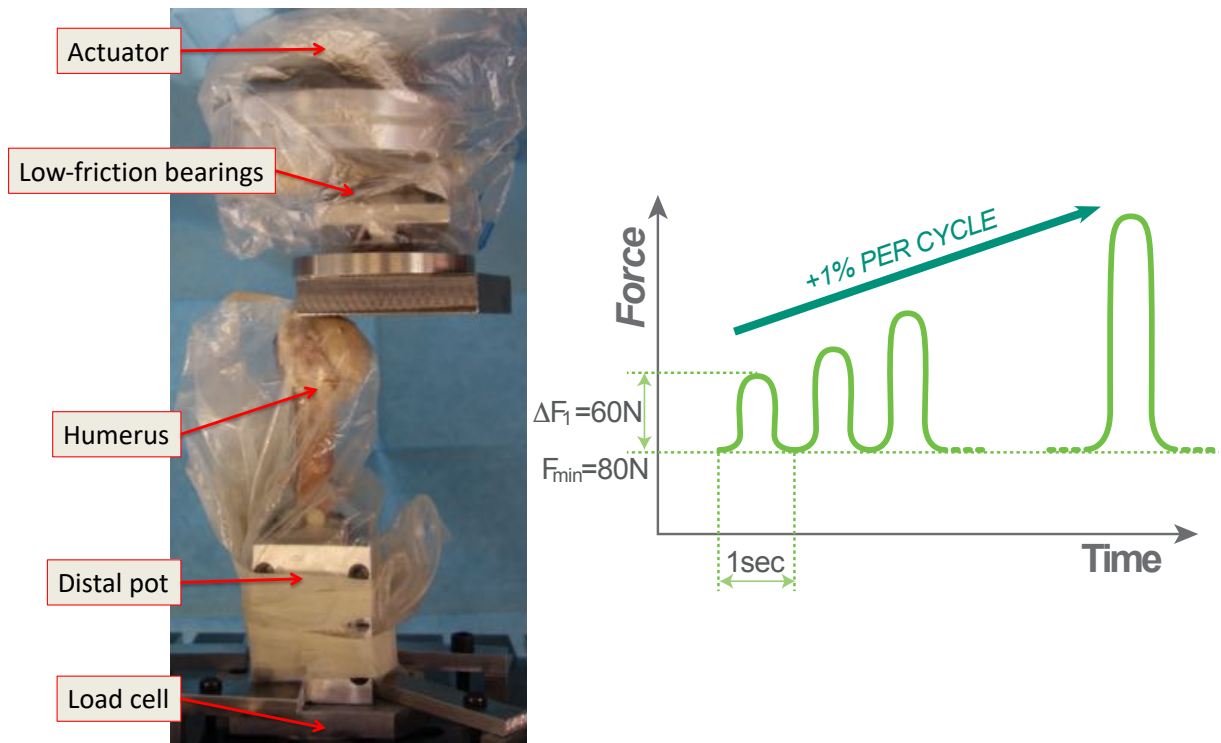


Fig. 3 – Left: Overview of the test setup, showing a fractured and reconstructed left humerus (wrapped in a plastic bag to prevent leakage of fluids), and the system for application of the force (actuator and low-friction bearings); the load cell is under the distal support system. A metal block was used to ensure that the force was applied to the humeral head (and not to the greater tuberosity). The diagram on the right explains the load profile (of increasing amplitude) applied during the mechanical cyclic test. A cyclic compressive force was applied at 1 Hz. The baseline force was constant (80 N), while the amplitude increased by 1% at every cycle, starting from an amplitude of 60 N for the first cycle.

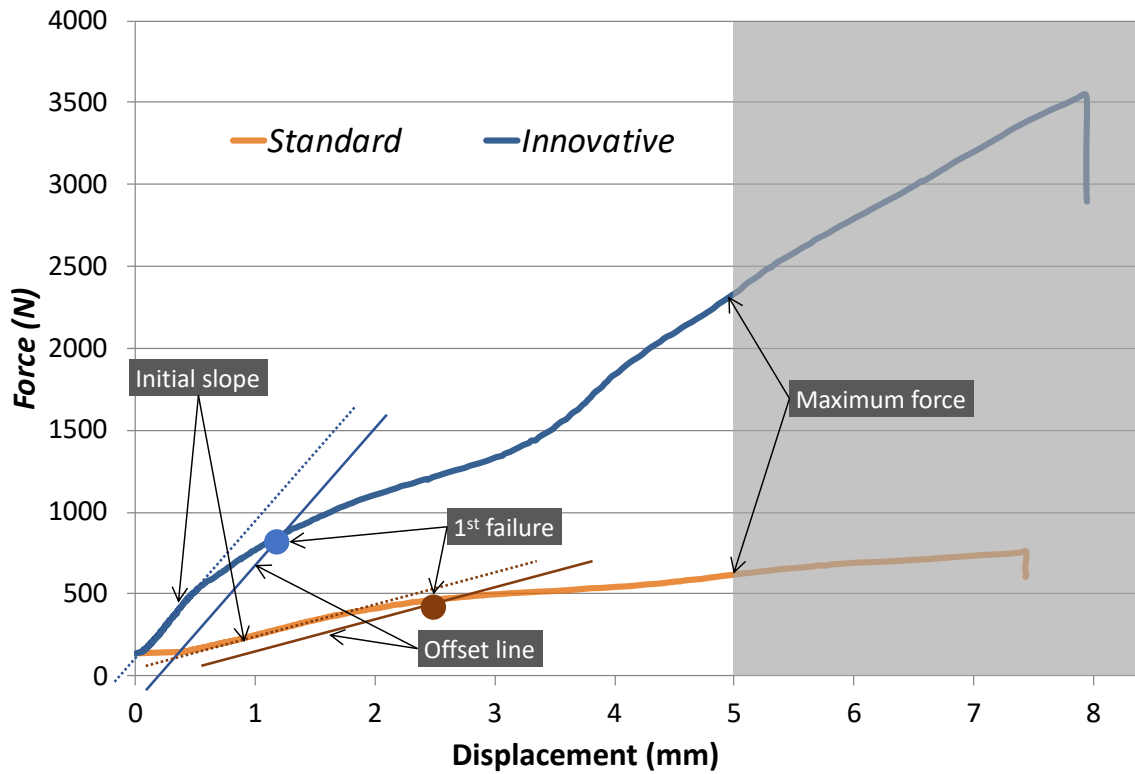


Fig. 4 – Typical force-displacement plots throughout the mechanical destructive test for the *Standard* and for the *Innovative*-reconstruction techniques. The envelope of the load peaks is shown. The procedure for identifying the first failure event (based on an offset line) and the maximum force are indicated. While the criterion for failure was a migration of 5.0 mm, the test was extended as far as 8.0 mm to ensure that failure became clear in all specimens.

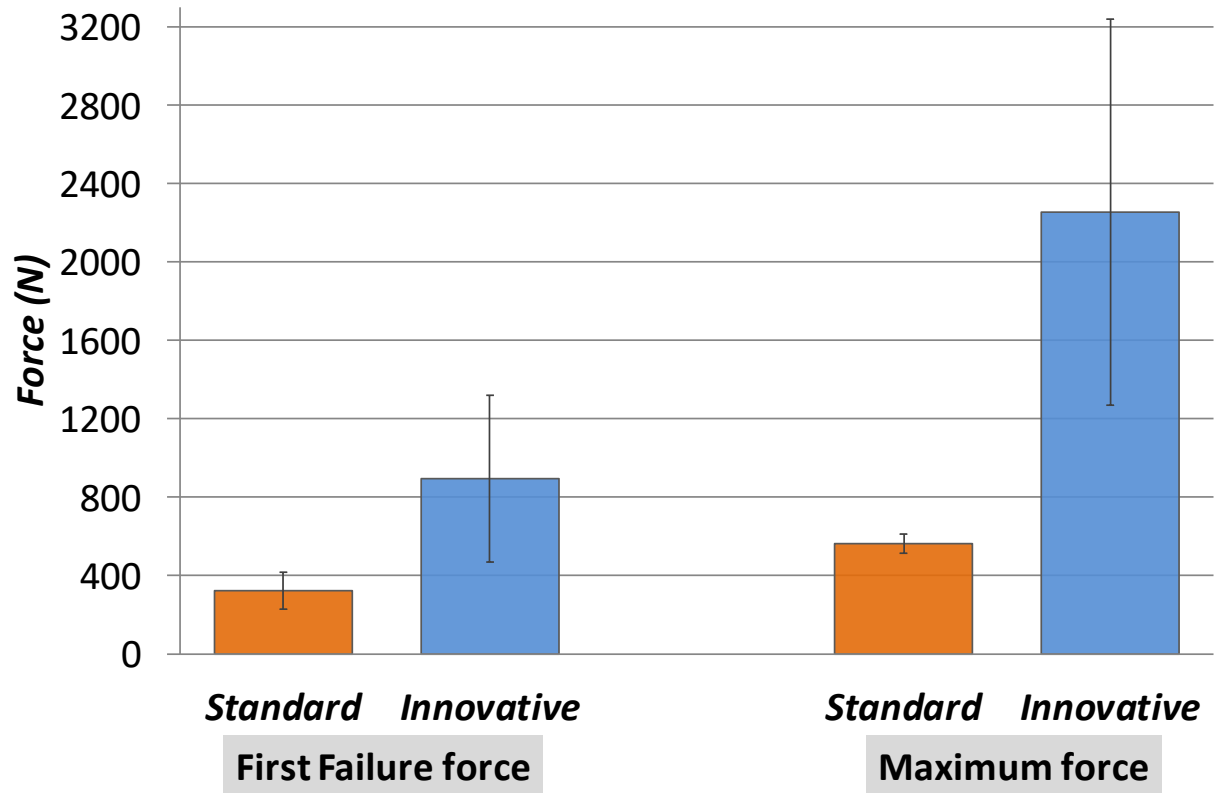


Fig. 5 – Strength of the *Standard* and of the *Innovative* techniques: the force to reach the first failure event and the maximum force are compared (median and standard deviation over 6 specimens of each type).

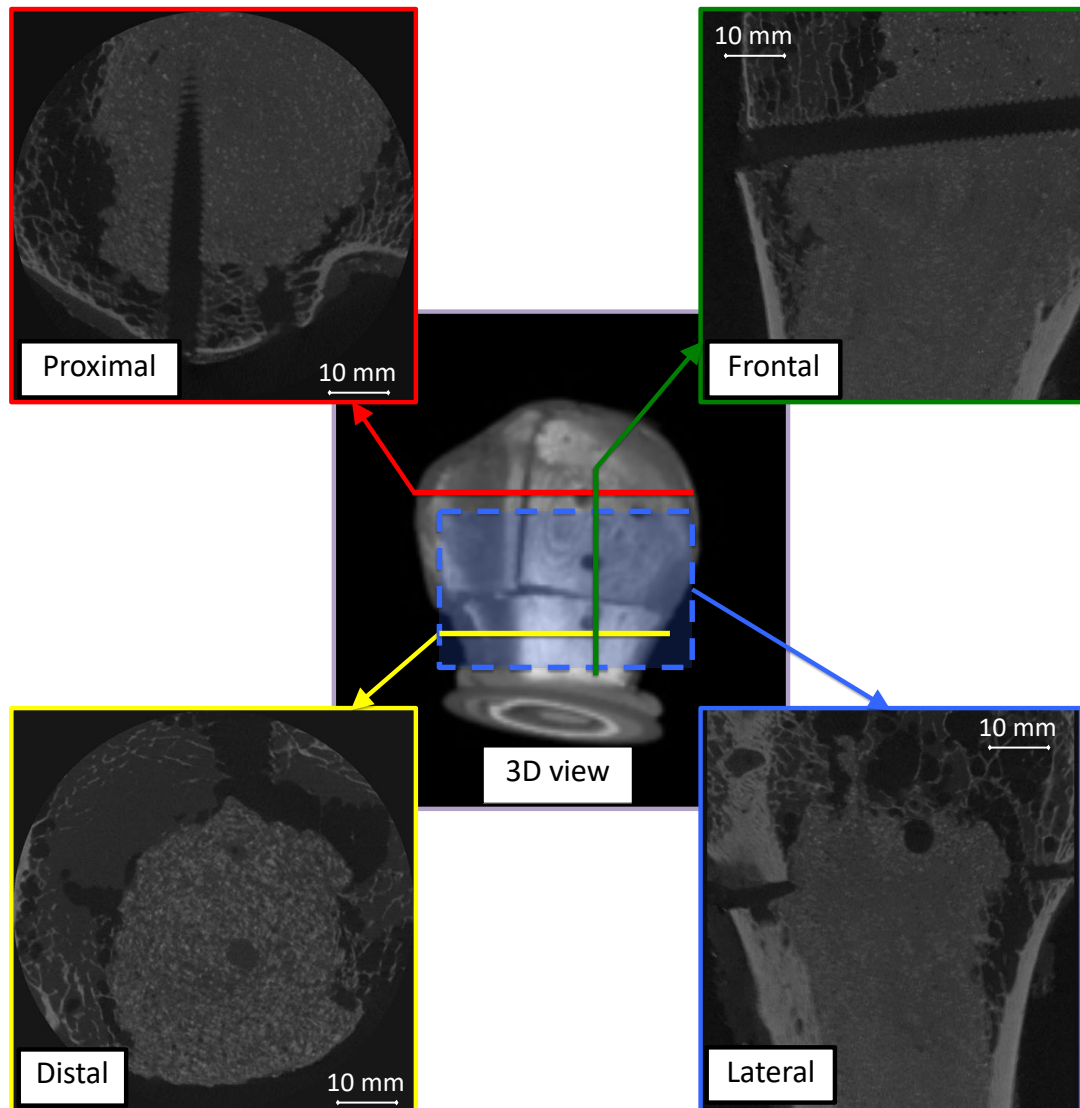


Fig. 6 – Representative micro-CT images of the *Innovative*-reconstructions. A three-dimensional view is reported (centre) together with selected slices (transversal proximal and distal, frontal and lateral planes). The specimens were scanned after removal of the metal components: the threaded holes were visible. The cement properly filled the space corresponding to the osteoporotic “eggshell” defect. The interdigitation of the cement in the cancellous bone was clearly visible. A similar filling was observed in all the *Innovative*-reconstructions.

TABLES

Table 1 – List of the humeri used in this study, including the donors’ details and the biomechanical length of each bone specimen (defined as the distance between the most proximal point of the humeral head, and the most distal point of the trochlea [34]). Two types of fracture fixations were prepared (*Standard* reconstruction with only screws, and *Innovative* reconstruction with fewer screws and cement).

Donor	Cause of death	Sex	Age (years)	Height (cm)	Body weight (kg)	BMI (kg/m ²)	Side	Biomechanical length (mm)	Type of Reconstruction
#1	End stage diabetes	Female	56	149	141	64	L	300	<i>Standard</i>
							R	315	<i>Innovative</i>
#2	Renal failure	Female	62	166	168	61	L	332	<i>Standard</i>
							R	335	<i>Innovative</i>
#3	Atherosclerotic cardiovascular disease	Male	67	170	79	27	L	340	<i>Innovative</i>
							R	340	<i>Standard</i>
#4	Sepsis	Female	69	158	95	38	L	295	<i>Standard</i>
							R	300	<i>Innovative</i>
#5	Atherosclerotic cardiovascular disease	Female	68	161	138	53	L	340	<i>Innovative</i>
							R	340	<i>Standard</i>
#6	Cirrhosis of liver	Female	56	154	126	53	L	310	<i>Standard</i>
							R	305	<i>Innovative</i>
Median			64.5	159.6	131.8	53.3	6 pairs	323	6 vs. 6
SD			5.4	7.2	29.5	12.8		18	