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

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ABSTRACT

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

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

1. INTRODUCTION

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

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

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

The aim of this study was to investigate if an *Innovative*-technique to repair humeral fractures, based on a reduced number of screws and injection of a beta-TCP additivated acrylic cement, provides the same or better stability of the bone fragments compared to the *Standard*-technique, based on a larger number of screws. The focus was the risk of slippage of the reconstructed head in cases of four-fragment fractures in proximal humeri with bone defects. This technique has the potential advantage of reducing the number of drill-holes in osteoporotic heads, thus reducing bone damage, and the risk of cartilage drill-in, in combination with the advantages of a partially resorbable and osteoconductive biomaterial.

2. MATERIALS AND METHODS

2.1 Bone specimens

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

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

2.2 Surgical technique

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

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

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

To enable reproducible preparation of the screw holes for the reconstruction, they were drilled before simulating the fracture. An experienced shoulder surgeon identified the optimal position of the plates, preparing the humeri in pairs, aiming to minimize intra-pair differences. The direction of the holes (ø2.5 mm) was guided by the drill sleeve (Philos, Synthes):

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

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

2.3 Simulation of fracture and bone defect

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

2.4 Reconstruction of the fractured humeri

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

Reconstruction with the *Innovative*-technique of the contralateral humerus of each pair was derived from that of the *Standard*-technique: the plate was fixed to the diaphysis with the 2 cortex screws. The 3 locking screws were inserted proximally while the fragments were held in place. Finally, 40 g of beta-TCP additivated acrylic cement (Cal-CEMEX) pre-chilled at 4°C were injected (5 minutes after mixing started) through a hole on the lateral side (Fig. 1) This amount, the same for all *Innovative*-technique specimens, was chosen based on the estimated volume of the bone defect. No leakage of cement was observed through the bone fractures.

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

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

2.5 Biomechanical test

In order to measure the strength of the two types of reconstructions, the repaired humeri underwent a biomechanical test where a cyclic force of increasing magnitude was applied. The loading direction was chosen to address the risk of distal migration of the reconstructed head with respect to the humeral diaphysis. This is one of the most common failure mechanisms: due to repetitive axial loading, the screws gradually cut into the cancellous bone, allowing varus sliding of the head [38, 39]. To test this scenario, a vertical force was applied to the humeral head while the distal end was fixed to the load-cell of the testing machine (Mod.8800, Instron, Canton, USA; Fig. 3). A system of low-friction bearings ensured that no horizontal force was transmitted while the humeral head was free to roll against the flat loading plate. The force was therefore aligned with the axis of the humerus. Considering the range of joint force directions for different motor tasks (for a ball-and-socket joint, the reaction transmitted to the humeral head consists of a force passing through the joint centre [40-42]), this corresponds to the worst-case-scenario. Indeed, application of a force aligned with the humeral axis elicits the highest risk of distal slippage of the humeral head, while an oblique force would also apply a compression at the fracture site, which would stabilize the reconstruction.

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

2.6 Identification of failure

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

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

2.7 Radiographic analysis of the cement-bone interdigitation

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

2.8 Statistics

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

3. RESULTS

3.1 Failure mechanism

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

Each group showed a typical and consistent failure mechanism:

- The *Standard*-reconstructions (i.e. repaired with 6 locking screws) failed progressively, starting at a force (first failure) that was lower than the maximum peak. In most cases, the first failure was associated with a change of slope, and the beginning of extensive migration. The maximum force was 1.74 times larger (median of 6 specimens) than the first failure.

- For the *Innovative*-reconstructions (i.e. with 3 locking screws and injection of the beta-TCP additivated acrylic cement), failure was more progressive than with the

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

3.2 Strength of the reconstructions

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

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

3.3 Cement-bone interdigitation

The micro-CT analysis (performed after the biomechanical test) confirmed that the cement in the *Innovative*-reconstructions was delivered in the space corresponding to the osteoporotic “eggshell” defect. Over 90% of the cavity was filled by the cement injected. A penetration of 0.2-2.8 mm of the cement in the cancellous bone was visible (Fig. 6).

4. DISCUSSION

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

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

A recent review showed that locking plates have better mechanical performance than non-locking ones, and the Philos plate was most frequently tested [23]. Opposing results have been published comparing non-locking blade plates and polyaxial locking screws [28, 38]. Augmentation with cement or allografts was found to improve the mechanical performance of the bone-plate [23, 24]. Nevertheless, it is still unclear if a rigid implant is better than a semi-rigid one, and controversies remain about the insertion of inferomedial screws for calcar region support [23, 45].

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

A limitation of this study relates to the fact that we mainly focused on the possible slippage of the reconstructed head. For this reason, we simulated the worst loading for this scenario, where the force is aligned with the humeral axis. The angle spanned by the force for different activities, abduction, external rotation and internal rotation is large (30°-95°) [41, 42]. It is possible that loading in different directions triggered failure scenarios different from those simulated in this study. Nevertheless, the mechanism investigated in the present study is the most commonly observed in elderly patients [22]. Furthermore, the displacement of the actuator of the testing machine was used to measure the fracture stability. This measured only the vertical component of motion, and with a slight overestimate (the actuator displacement depends mainly on the slippage of the head, but also on the deformation of the cartilage).

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

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

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

The strength we measured for the *Innovative*-technique has the potential of preventing failures even in cases of severe loading. This is a significant improvement compared to the *Standard*-technique, which cannot withstand such loading. The potential benefits of this technique are remarkable. In fact, a reduced number of screws could grant an inferior rate of complications by screw protrusion on the humeral head, screws cut off or secondary protrusion at follow up after a humeral head collapse (e.g. due to osteonecrosis). In addition, the fact that fewer screws are inserted in the head means that less bone is removed/damaged, and that cancellous vascularization is possibly better preserved, thus reducing the risks of osteonecrosis. Moreover, the specific properties of the beta-TCP additivated cement used in this study are also expected to promote bone formation. In fact, it has been shown that the osteoconductivity due to the beta-TCP in the Cal-CEMEX, and the size and morphology of the pores in the PMMA after dissolution of the mineral component, promotes significant apposition of new bone [32, 33]. Additionally, the screws were easily removed from the bones and the cement after the test, suggesting that removal of the hardware should not be difficult, if required after fracture healing.

5. CONCLUSIONS

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

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Ethical approval: This study is based on humeri from human donors, which were obtained through an international ethically-approved donation program (Anatomy Gifts Registry, Hannover, USA). This Study was authorized by the Bioethics Committee of 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, Tersi 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, Kääb 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

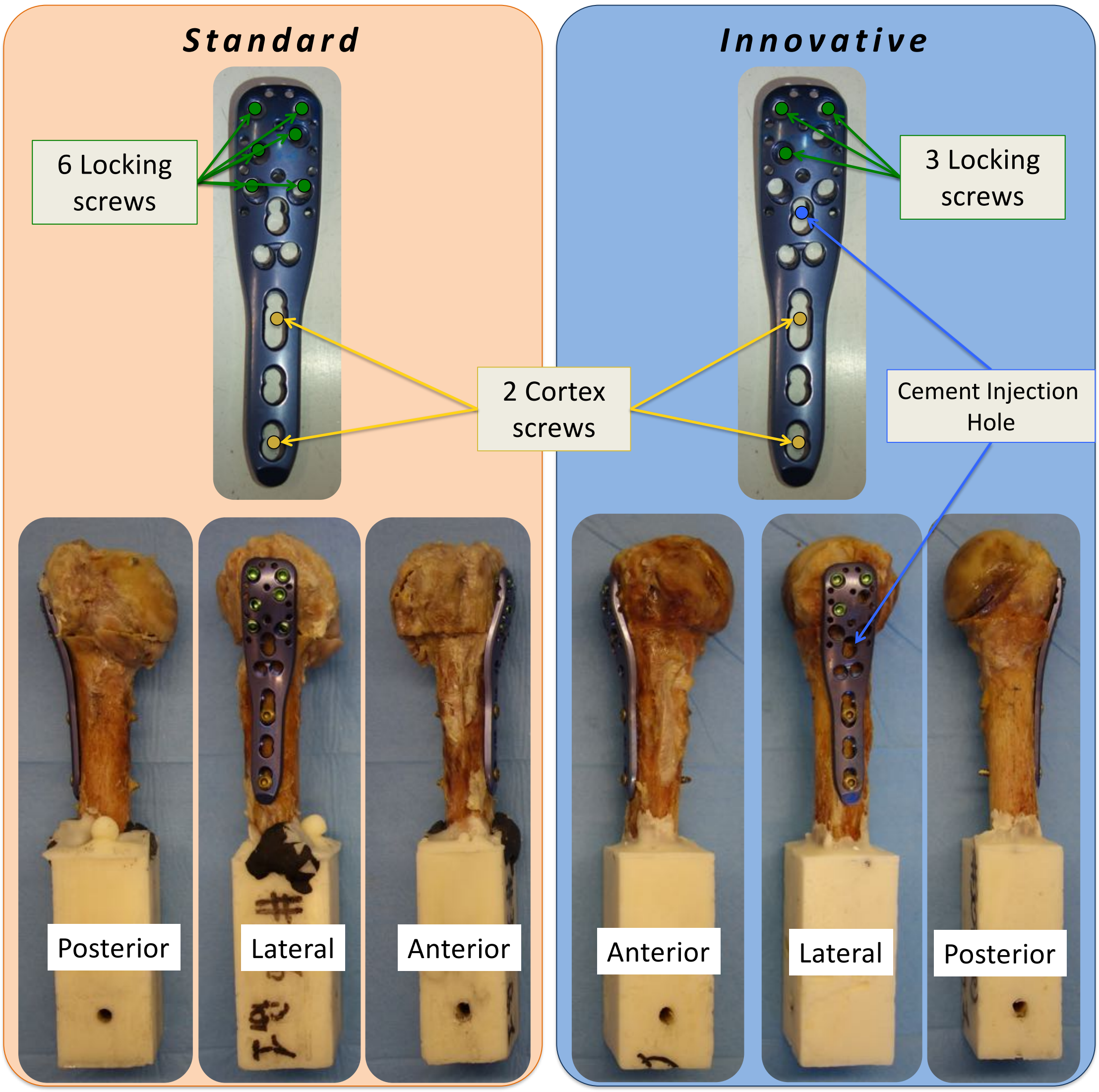

Fig. 1 – TOP: Lateral view of the plate, showing the position of the screws for the *Standard* and the *Innovative* techniques. The screws were positioned in the same holes for all the specimens of each group (regardless of if it was a right or left humerus). BOTTOM: Pair of humeri after simulation of 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.

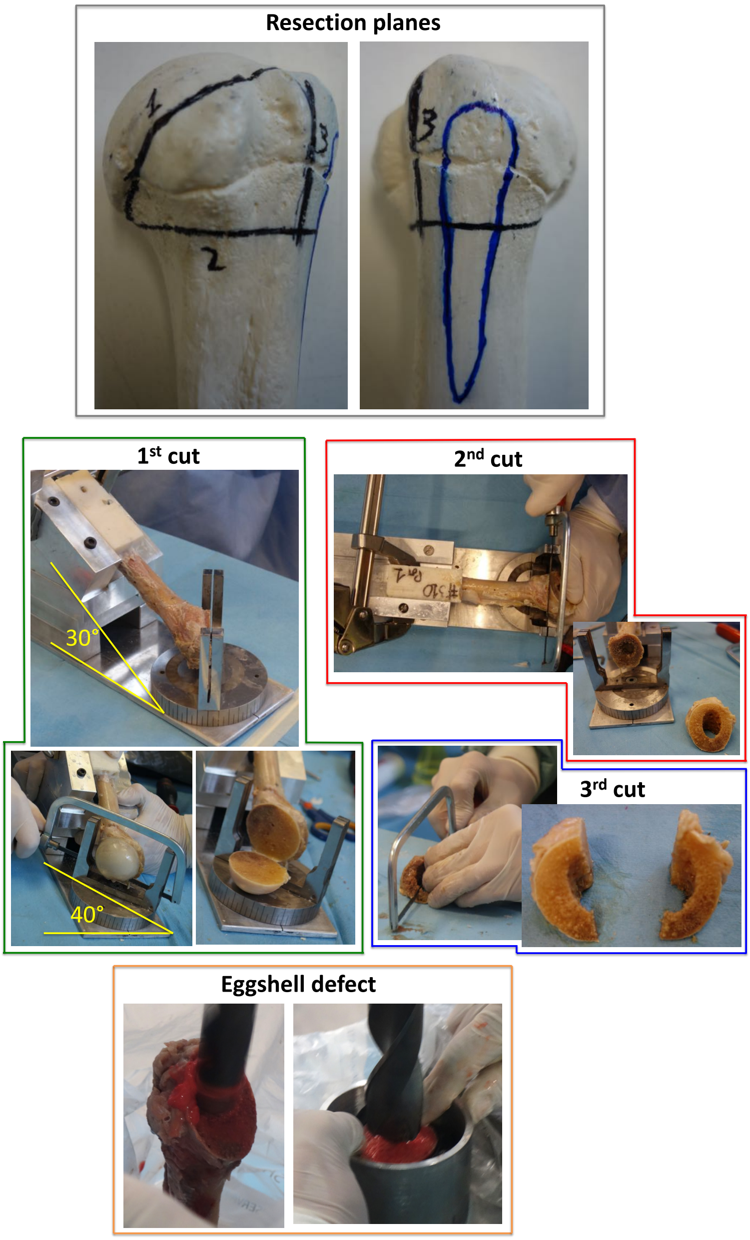

Fig. 2 – Top: Schematic of the three resection planes to simulate a four-fragment fracture (left humerus: anterior and lateral views); also visible is the planned position of the plate. Centre and bottom: procedure to simulate the bone fracture using the cutting jig for the three osteotomies. With the 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.

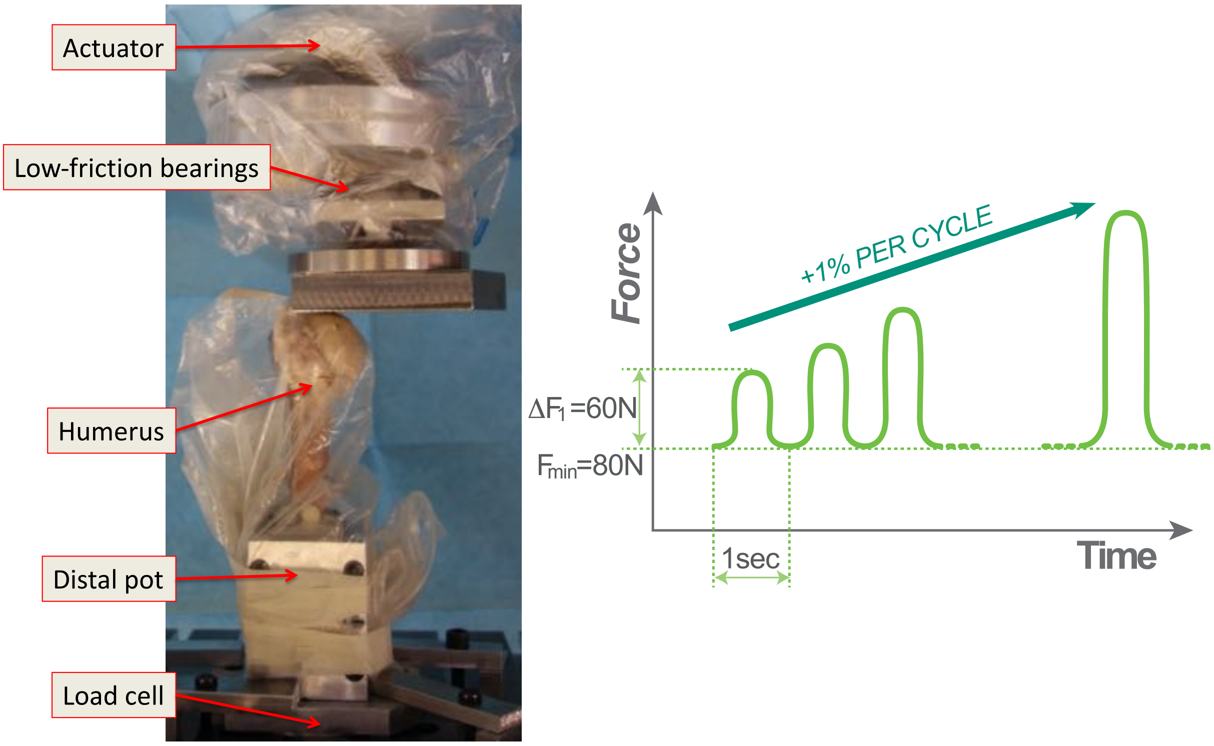

Fig. 3 – Left: Overview of the test setup, showing a fractured and reconstructed left humerus (wrapped in a plastic bag to prevent leakage of fluids), and the system for application of the force (actuator and low-friction bearings); the load cell is under the distal support system. A metal block was 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.

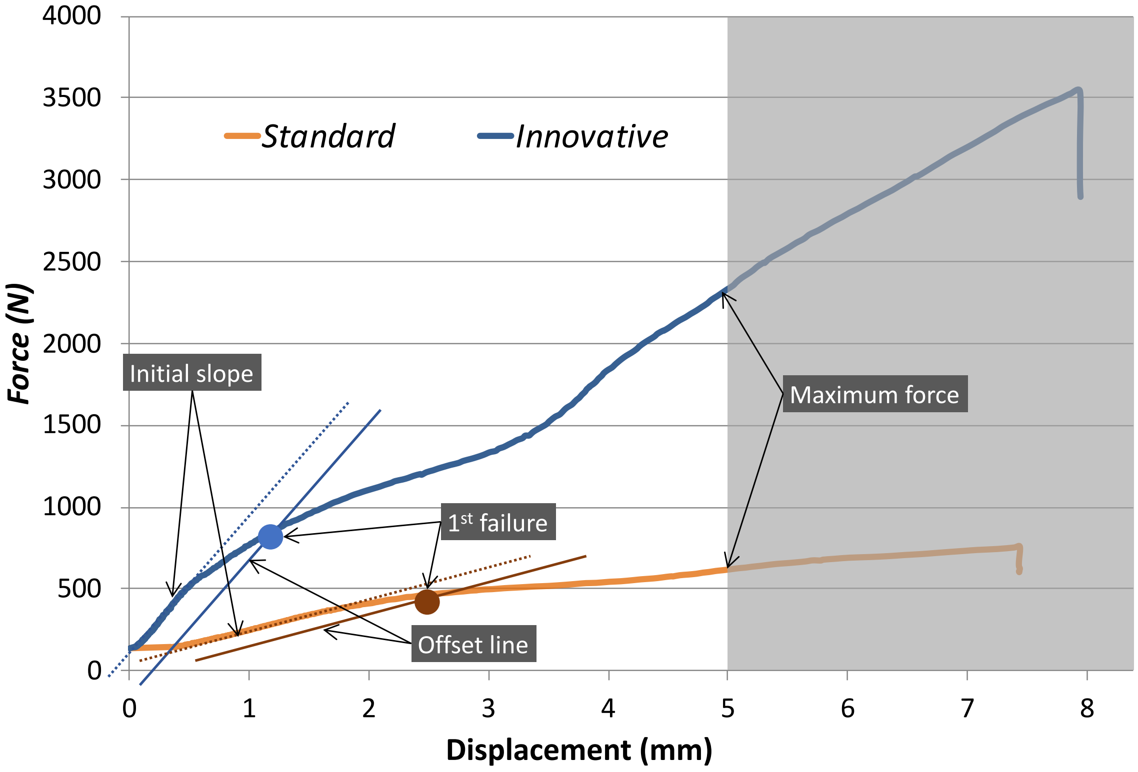

Fig. 4 – Typical force-displacement plots throughout the mechanical destructive test for the *Standard* and for the *Innovative*-reconstruction techniques. The envelope of the load peaks is shown. The procedure for identifying the first failure event (based on an offset line) and the maximum force are 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.

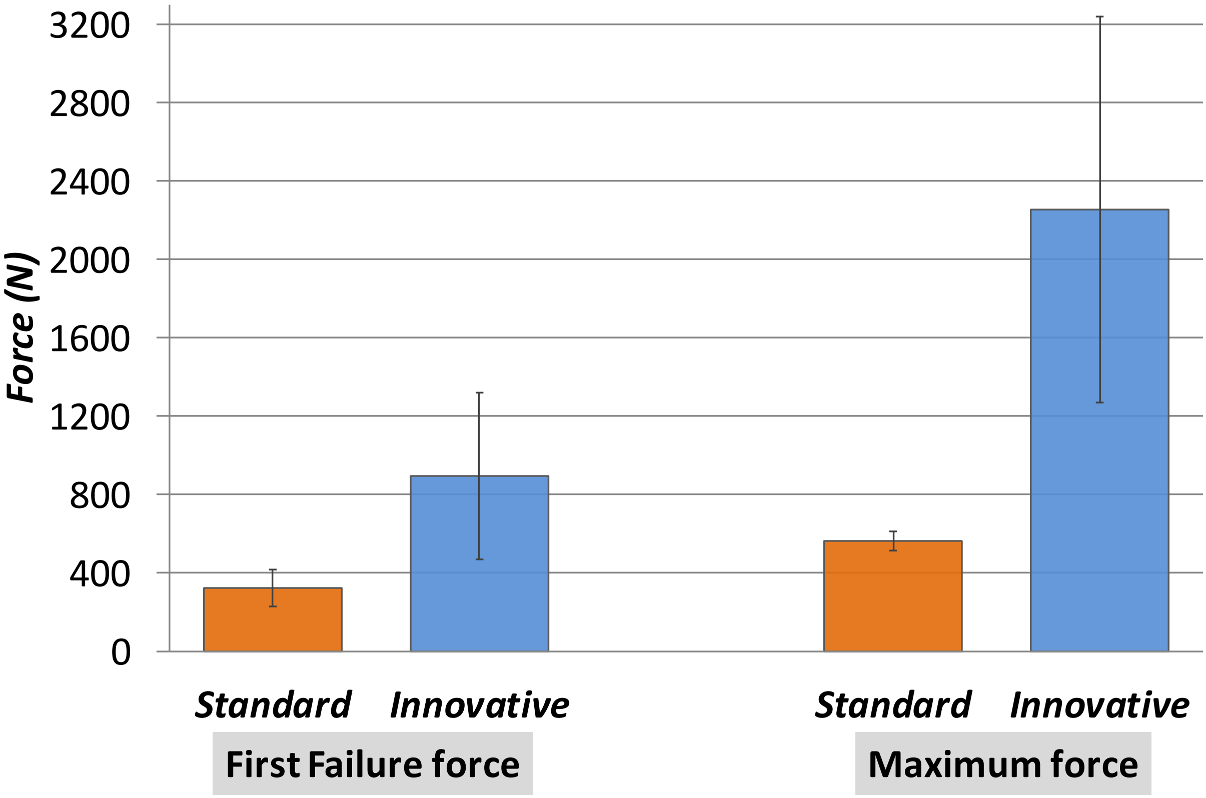

Fig. 5 – Strength of the *Standard* and of the *Innovative* techniques: the force to reach the first failure event and the maximum force are compared (median and standard deviation over 6 specimens of each type).

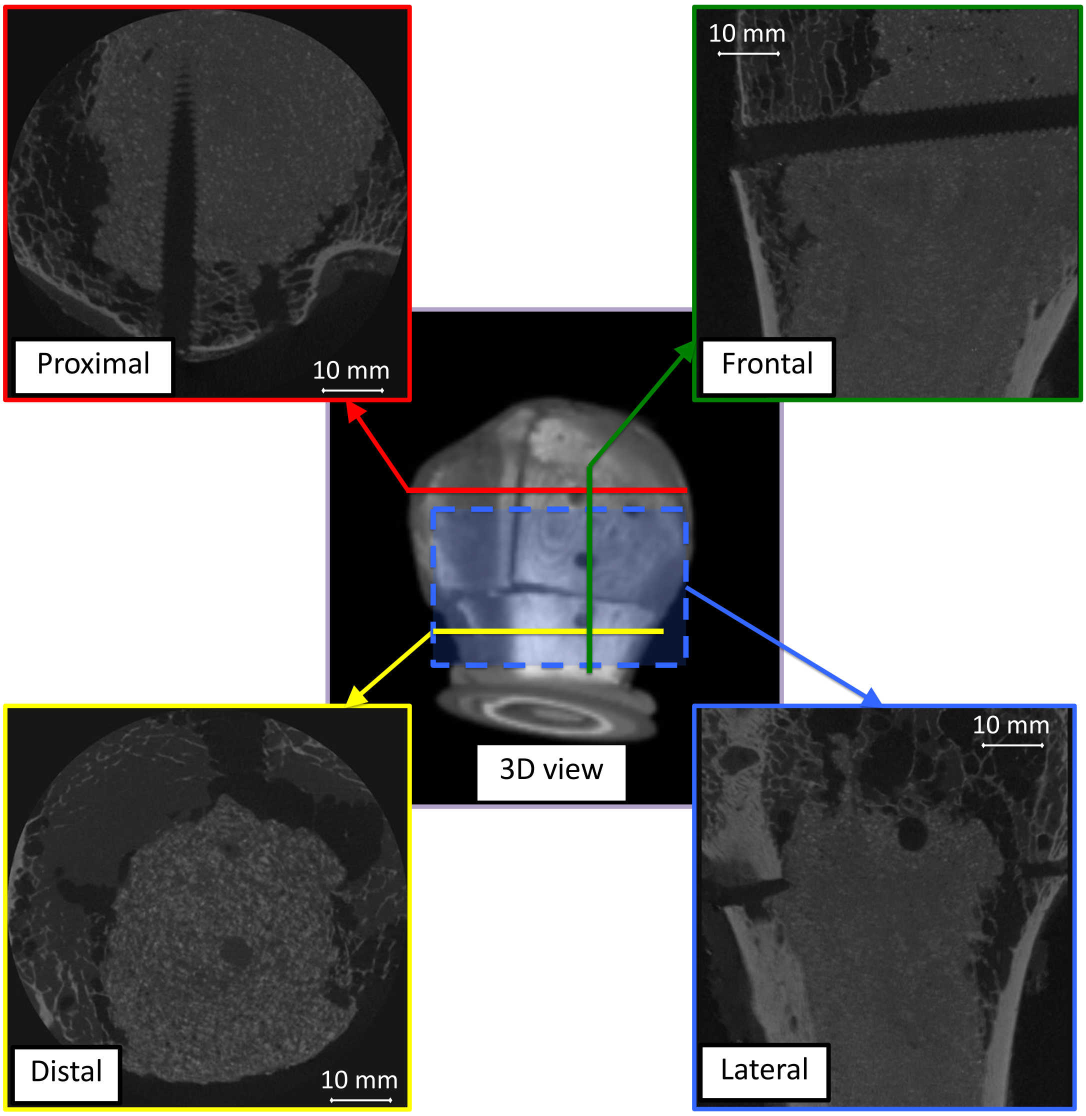

Fig. 6 – Representative micro-CT images of the *Innovative*-reconstructions. A three-dimensional view is reported (centre) together with selected slices (transversal proximal and distal, frontal and lateral planes). The specimens were scanned after removal of the metal components: the threaded holes 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	*Standard*
							R	315	*Innovative*
#2	Renal failure	Female	62	166	168	61	L	332	*Standard*
							R	335	*Innovative*
#3	Atherosclerotic cardiovascular disease	Male	67	170	79	27	L	340	*Innovative*
							R	340	*Standard*
#4	Sepsis	Female	69	158	95	38	L	295	*Standard*
							R	300	*Innovative*
#5	Atherosclerotic cardiovascular disease	Female	68	161	138	53	L	340	*Innovative*
							R	340	*Standard*
#6	Cirrhosis of liver	Female	56	154	126	53	L	310	*Standard*
							R	305	*Innovative*
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**	