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Injectable calcium phosphate cement for augmentation around cancellous bone screws. In vivo biomechanical studies

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ABSTRACT

In lower cancellous apparent bone density, it can be difficult to achieve adequate screw fixation and hence stable fracture fixation. Different strategies have been proposed, one of them is through augmentation using calcium phosphate cement in the region at or close to the screw thread itself. To support the hypothesis of an improved screw fixation technique by augmentation of the bone surrounding the implanted screw, in vivo biomechanical and densitometric studies are performed on rabbit specimen where normal and simulated weak bone quality are considered. In particular, the evolution of screw stability till 12 weeks following the implantation is quantified. A statistical significance in the pull out force for augmented versus non-augmented screws was found for the shorter time periods tested of ≤ 5 days whilst the pull out force was found to increase with time for both augmented and non-augmented screws during the 12 week course of the study. The results of the study demonstrate that the use of an injectable calcium phosphate cement which sets in vivo can significantly improve screw pull out strength at and after implantation for normal and simulated weak bone quality.

1. Introduction

Different kinds of screws are commonly used either alone or in combination with other implants for internal fixation of fractures. In most cases the stability provided by the screw threads is enough to ensure a stable anchorage of the screw during the course of healing. This is especially true when used in healthy bone with high apparent density as in younger patients. When dealing with the increasing number of elderly patients with lower apparent bone density, or even more so when established osteoporosis is present, conventional screws do less well. In order to reduce the number of complications, new implant designs have been developed (Chapman et al., 1996; Goldhahn et al., 2005). Nevertheless, bone screws keep failing in compromised bone with failure rates in the range 10–25% (Cornell, 2003). Another concept

would therefore be to improve the strength in the bone around the screw threads through an augmentation technique.

Augmenting bone in fracture fixation with polymethylmethacrylate (PMMA) was indeed already proposed in 1962 (Mueller, 1962). However, PMMA has drawbacks such as poor biocompatibility, exothermic polymerization, and non-resorbability (Enis et al., 1974; Leeson and Lippitt, 1993). Osteoconductive cements, such as calcium-phosphate cement (CPC), are becoming more popular in orthopedics and traumatology (Kawagoe et al., 2000) and are progressively replacing PMMA (Larsson, 2006; Yi et al., 2008). Nevertheless, the mechanical properties of CPC are inferior to PMMA justifying then a biomechanical evaluation of the possibility to use them for bone augmentation as performed in this study.

The use of CPC to fill fracture voids is widely reported (Larsson and Bauer, 2002). However, the use of CPC in low-quality cancellous bone to enhance screw purchase is less well described although the technique has proven to significantly reduce the frequency of complications such as loosening and migration (Mermelstein et al., 1996; Andreassen et al., 2004). In hip fractures, small amounts of CPC have been shown to enhance conventional hip fracture screw purchase and to increase the fracture construct stiffness and minimize hip fracture screw

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displacement (Stankewich et al., 1996; Elder et al., 2000; von der Linden et al., 2006).

In a previous paper we established the in vitro efficacy of screw augmentation using CPC in sawbones (Stadelmann et al., 2010). The aim of the present study was to quantify the pull out strength of bone screws with and with out CPC augmentation in an in vivo animal model for normal bone and following over drilling to simulate inadequate screw purchase. We hypothesize that the CPC augmentation results in improved initial mechanical stability of bone screws compared to non-augmented controls.

2. Material and methods

2.1. Experimental design

This study was performed using cancellous bone screws that were implanted in a rabbit in vivo model to examine the influence of the following factors on screw stability under pull out loading: augmentation vs. non-augmentation at various time points and bone quality. As even osteopenic animal bone provides higher bone densities compared to osteoporotic human bone, the authors decided to extend a recent over drilling model, intended to simulate weak bone quality in vivo (Hoshikawa et al., 2003). Rabbit bone has been shown to demonstrate an apparent bone density that is only slightly higher than human bone and was therefore deemed suitable for use in this in vivo approach (Bouchgua et al., 2009).

2.2. In vivo model

Sixty-nine New Zealand White rabbits were used for the study. The in vivo evaluation was performed using titanium cancellous bone screws (ø4 mm × 14 mm, Ref: SYK-604014, Stryker Osteosynthesis) that were implanted in the medial femoral condyle in both legs of the rabbits (Fig. 1). On one side augmentation with a CPC (HydroSet®, Stryker Osteosynthesis) was used around the screw while the contra lateral control was non-augmented. Implantation site (left or right leg) for screw augmentation was randomized within each group.

The rabbits were premedicated with a subcutaneous injection of a mixture containing glycopyrrolate (Robinul V®, Vetoquinol, France), acepromazine (Vetranquil®, Ceva Santé animale, France), and butorphanol (Torbugesic, Fort Dodge Animal Science, UK). The anesthesia was performed by intramuscular injection of xylazine (Rompun® 2%, Bayer, France) and ketamine (Imalgene® 1000, Merial, France). Pre-operative subcutaneous injections of antibiotic (sulfadoxime-trimethoprime, Borgal®, Intervet, France) and of anti-inflammatory drug (Carprofen, Rimadyl® injectable, Pfizer, France) were administered. The femur was clipped free of fur from above the hip to below the knee joint. A skin incision was made on the medial side of the distal femur. The muscles were separated using blunt dissection to access the femur. The entry point for drilling was localized using the insertion point of the medial collateral ligament as a landmark. The entry point for drilling was set at 5 mm proximal to the ligament with the direction of drilling being perpendicular to the bone surface. Cannulated drills were used to ensure appropriate allocation of the drill hole. Drilling was initiated by introducing a 2.0 mm diameter guide wire, customized with a 1.4 mm tip. To avoid perforation of the second cortex, the guide wire was labeled by a laser marker at 10 mm insertion depth. The thermal impact of drilling was limited by flushing the area with saline solution during drilling.

After the screw insertion, the incision was closed by suturing the subcutaneous layers and the skin layer with absorbable thread (Vicryl® 2–0, Ethicon). The
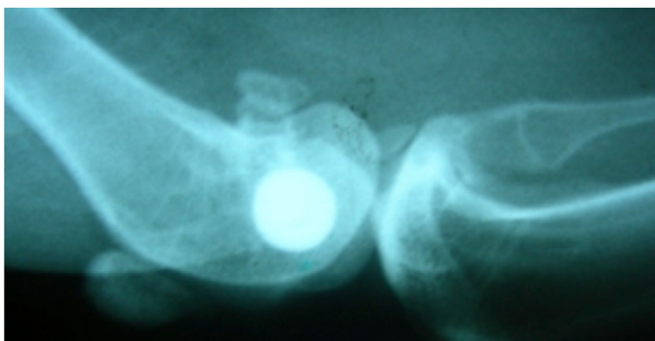
animals received an analgesic treatment of butorphanol-benzalkonium chloride (Turbogesic, Wyeth, UK, 0.5 mg/kg) the day after the surgery. Each day, rabbits were observed to detect morbidity or any other abnormal clinical event. At the end of the study, the rabbits were anesthetized by intramuscular injection of tiletamine–zolazepam (Zoletil®, Virbac, France) and terminated by an intravenous injection of Dolethal® (pentobarbital, Vetoquinol, France).

2.3. Normal and simulated weak bone quality

To compare the screw stability for different bone qualities, two test series were performed using different drill sizes. In study 1, a drill diameter of 3 mm was used (normal bone quality) and samples harvested at 24 h, 6, 12 and 26 weeks (Table 1). In study 2, the drill diameter was enhanced to 3.5 mm to simulate less good bone (weak bone quality) with the samples being harvested at 24 h, 5, 10 and 12 day (Table 2) in order to provide more detailed information on the effect of augmentation during the early course after fixation. Drilling with an increased diameter, the so-called "over drilling technique", enabled simulation of reduced screw stability and ensured a reasonable volume of cement between the implant and bone to create a zone of interlocking interface between bone and implant.

2.4. Screw insertion and augmentation

After removing drill and guide wire, the drill hole was hand-driven tapped by a screw tap. The tap was removed and the drill hole was extensively rinsed with saline, followed by hand-driven insertion of the 4.0 mm diameter screw. A customized spacer was used to create a standardized distance (3 mm) between the head of the screw and the bone surface to facilitate the handling of the screw for the pull out test. For the augmented specimens, prior to screw insertion, the drill hole was injected with CPC (HydroSet®, Stryker Osteosynthesis) at 2 min from start of mixing of the cement using a 10 gage cannula. The drill hole was completely filled, and any cement above the surface of the bone was removed prior to screw application.

2.5. µCT scanning & image reconstruction

After sacrifice, femurs were dissected to remove all soft tissues (Fig. 2a). Each specimen was wrapped in plastic conservation paper (Freshstar, Migros, Switzerland). The screw head was clamped in a specially designed screw holding sleeve to ensure the alignment of the screw with the scanning axis (Fig. 2b). The holding sleeve was then placed in the polystyrene support of the in vivo µCT 1076 (SkyScan, Belgium). Each sample was scanned at 100 kV/100 mA source voltage/current, with a 1 mm aluminum filter. The pixel size (resolution) was 18 µm, rotation step was 0.6° over 360°, exposure time was 400 ms, and each image was averaged three times. The total scanning time was about 25 min. After scanning, specimens were placed in the wet gauze and respective Falcon tube at 4 °C until further testing.

At the beginning of each scanning session and after every four specimens, a flat-field correction was performed for the selected scanning parameters to reduce the signal to noise ratio, and ensure a constant exposure of the images, as the X-ray source may fluctuate slightly over time. The dataset was reconstructed with NRecon software (SkyScan, Belgium).

Fig. 1. Mediolateral X-Ray of implantation site. The implanted screw head is clearly visible in the rabbit femoral condyle.

Table 1
Number of specimens (control/augmented) per time point for the study 1 (normal bone quality).

Time point			
24 h	6 weeks	12 weeks	26 weeks
8/8	8/8	8/8	8/8

Table 2
Number of specimens (control/augmented) per time point for the study 2 (simulated weak bone quality).

Time point			
24 h	5 days	10 days	12 days
11/11	14/14	9/9	3/3

2.6. Bone mineral apparent density (BMD) measures

The calibration and the accuracy of the measurements done by the scanner were first checked with two reference phantoms of 0.25 g/mm^3 and 0.75 g/mm^3 before each measurement. The reconstruction and the analysis of the scanning were achieved from the end of the cortical shell through to a depth of 15 mm in the direction of the bone core. The volume of interest for the BMD was a hollow cylinder of outer diameter 12 mm and inner diameter 5 mm, to ensure the exclusion of the cement effect in the BMD measurements as it was verified on each specimen that the cement penetration was smaller than 5 mm radially to the screw surface.

2.7. Biomechanical testing

All specimens were prepared by being embedded in Beracryl cement that were brought to 37 °C in a PBS warm bath until the beginning of the pull out test. They
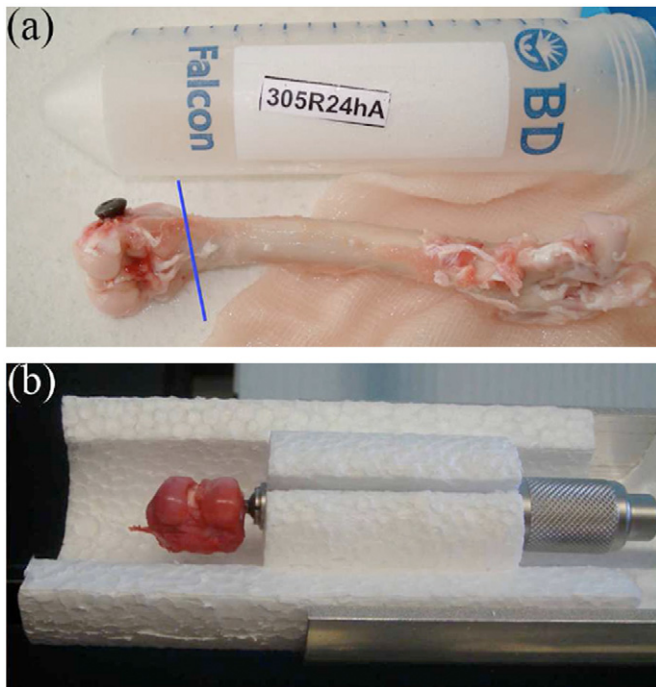

Fig. 2. Preparation of the specimens for scanning. (a) The specimens were dissected 1 cm superior to the screw axis (blue line). (b) Screw head is clamped in screw holding sleeve and place in the polystyrene support for scanning (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

were then placed in the special Beracryl cementing mold and fixture box as previously described (Stadelmann et al., 2010). A 1 mm thick metal plate drilled with a ⌀ 10 mm hole was put over the screw to enhance the support of the condyle during the pull out process. The head of the screw to be tested was held in a fixture mounted on the test machine jack (Instron Microtester 5848, Instron, USA). An axial displacement was applied with a speed of 5 mm/min on the screw, while the special fixture box containing the specimen was fixed. The load and the displacement were recorded during the screw pull out. The test was stopped after complete separation of the screw from the bone and maximum load for failure recorded. Biomechanical testing was performed at least on eight augmented samples and eight non-augmented samples for each time point, except for study 2 at 12 day where three animals were used. The biomechanical tests were performed in a blinded manner for the augmented versus non-augmented specimens.

2.8. Statistical analysis

All statistical procedures were performed with Mathematica (Wolfram, USA) Statistics Package. Group comparisons were performed with ANOVA followed by Tukey and Bonferroni posthoc-tests. Pair wise comparisons were performed with Student paired t-test, and randomization tests. Values were expressed as means ± standard deviation (SD). Differences were considered statistically significant if $p < 0.05$.

3. Results

3.1. BMD measures

The average BMD around the screw increased over time for the augmented and for the non-augmented specimens, although this change was not statistically significant. The strongest trend was seen for augmented specimens between 24 h and 6 weeks (Fig. 3; $p < 0.07$).

3.2. Biomechanical tests of study 1 (normal bone quality)

For the 24 h group, average pull out forces for the augmented specimens were significantly higher when compared with the non-augmented controls ($p < 0.05$, paired comparison), while there were no statistically significant differences at 6 and 12 weeks between the augmented and non-augmented groups (Fig. 4). Pull out forces were significantly higher at both 6 and 12 weeks when compared with the 24 h group for both the augmented and non-augmented specimens, while there were no differences between the 6 and 12 weeks groups.
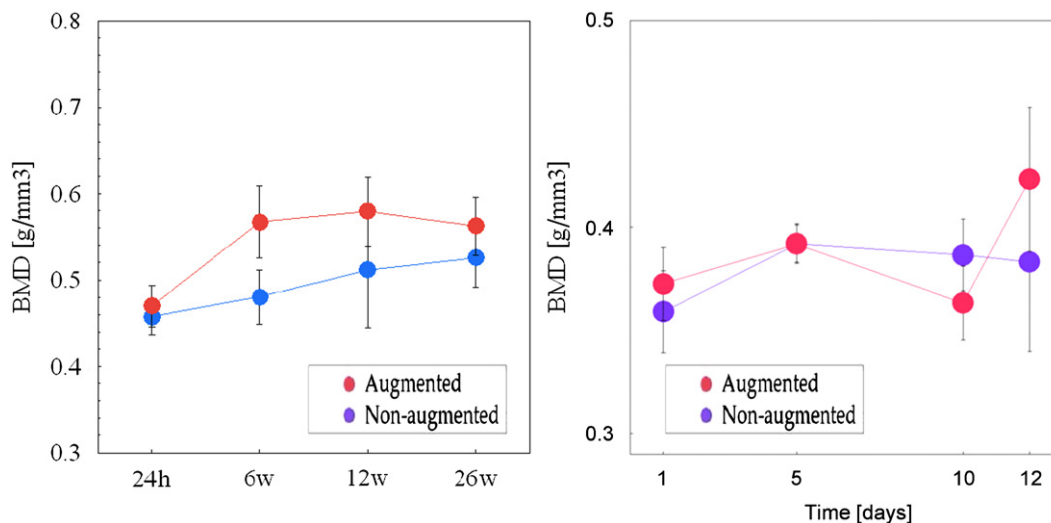

Fig. 3. Bone apparent mineral density in the femoral condyle of rabbits at 5–12 mm around implanted screws for Study 1 (left) and study 2 (right) (mean ± SD).
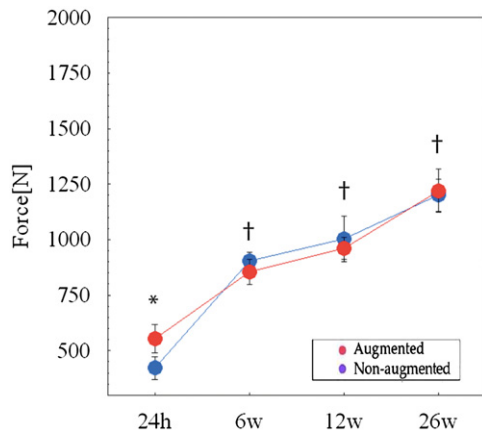
Fig. 4. Average pull out force at different time points for augmented and non-augmented specimens for the normal bone quality (Mean $\pm$ SD). † indicates significant difference compared to 24 h groups with one way ANOVA test for both augmented and non-augmented specimens ($p < 0.01$, one-way ANOVA). * indicates significant difference between groups at 24 h ($p < 0.05$, paired Student t test).
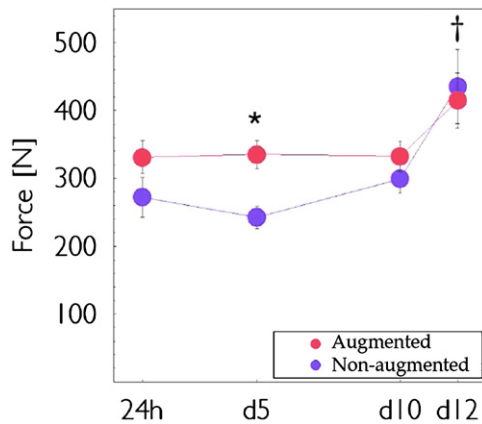

Fig. 5. Average pull out force at different time points for augmented and non-augmented specimens for the simulated weak bone quality (Mean $\pm$ SD). † indicates significant difference between the 12 day group and the previous time groups for both augmented and non-augmented specimens ($p < 0.01$, one-way ANOVA). * indicates significant difference between groups at 5 day ($p < 0.05$, paired Student t test).

3.3. Biomechanical tests of study 2 (simulated weak bone quality)

At day 5 the average pull out forces for the augmented specimens were significantly higher when compared with the non-augmented specimens ($p < 0.05$, paired comparison, Fig. 5). At 24 h and 10 day there were also differences although not statistically significant ($p < 0.08$, paired comparison). Pull out forces were fairly constant over time in the augmented and non-augmented groups, respectively, during the time periods from 24 h to 10th day, while a significant increase in the pull out force was noted at 12th day compared to the previous time points.

4. Discussion

The principal finding in this study was the verification of the hypothesis that the pull out strength increases for bone screws with CPC augmentation in weak rabbit bone quality for the early time points (< 5 days). After 10 days and later, no significant difference was observed in the pull out force between augmented

and non-augmented groups. However a significant increase in the pull out force was present for all times points after 10 days compared to the early time points for both augmented and non augmented specimens.

The main purpose of using CPC for augmentation is to fill the cavities within the cancellous bone and thereby producing enhanced stiffness and strength of the bone surrounding the inserted screw. In a preliminary in vitro evaluation using rabbit cadaver bone and corresponding then to time-point zero, a significantly higher pull out force was also found for the augmented versus non-augmented situation (data not shown). The lack of differences in pull out resistance at time points later than 10 days was a surprising but consistent finding in the rabbit model used. No clear explanation to this finding could be found, but theoretically it could have been an effect of the non-augmented side catching up with the augmented side, due to formation of mechanically competent bone around the screw making the early advantage with augmentation disappear. Indeed, the bone formation around implants in rabbits is much faster than in humans. According to Slaets et. al., (Slaets et al., 2007), the length of the bone remodeling cycle is 6 weeks in the rabbit compared with about 4 months in humans. Another explanation might have been alterations in the CPC mechanical properties over time. However, this seems unlikely as we observed that cement integrity was preserved during the time period of the study (data not shown).

The presented study has some limitations including the use of rabbit bones. Rabbit bones have a higher apparent density than the compromised human bone where augmentation primarily might be indicated. The high apparent density means that screws will gain a good purchase even without augmentation but in addition it means that augmentation will be less efficient as penetration of CPC into the dense cancellous bone will be restricted compared with penetration seen in low apparent bone density presenting a high porosity. Finally, the bone augmentation with CPC was performed in a moderate load-bearing situation. The obtained results are then relevant only for these particular situations.

In conclusion, a statistical significance in the pull out force for augmented versus non-augmented screw was found for the shorter time periods tested of ≤ 5 days whilst the pull out force was found to increase with timze for both augmented and non-augmented screws during the 12 week course of the study. This increase can be correlated to increasing apparent bone density surrounding the implanted region.

The results of the study demonstrate that the use of an injectable calcium phosphate cement which sets in vivo can significantly improve screw pull out strength at and after implantation for normal and simulated weak bone quality.

Conflict of interest statement

Acknowledgments

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