

Hydroxyapatite particle shape affects screw attachment in cancellous bone when augmented with hydroxyapatite-containing hydrogels

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ABSTRACT

Screw-bone construct failures are a true challenge in orthopaedic implant fixation, particularly in poor quality bone. Whilst augmentation with bone cement can improve the primary stability of screws, there are cements, e.g. PMMA, that may impede blood flow and nutrients and hamper bone remodelling. In this study, soft, non-setting biomaterials based on Hyalactin gels and hydroxyapatite (HA) particles with different morphological parameters were evaluated as potential augmentation materials, using a lapine *ex vivo* bone model. The pull-out force, stiffness, and work to fracture were considered in evaluating screw attachment. The pull-out force of constructs reinforced with Hyalactin containing irregularly shaped nano-HA and spherically shaped micro-HA particles were found to be significantly higher than the control group (no augmentation material). The pull-out stiffness increased for the micro-HA particles and the work to fracture increased for the irregular nano-HA particles. However, there were no significant augmentation effect found for the spherical shaped nano-HA particles. In conclusion, injectable Hyalactin gel loaded with hydroxyapatite particles was found to have a potentially positive effect on the primary stability of screws in trabecular bone, depending on the HA particle shape and size.

1. Introduction

Screws are widely used in orthopaedic surgery, e.g. to fixate femoral neck fractures and to attach rods and plates in fracture fixation (Chen et al., 2021; Lu et al., 2022; Xia et al., 2021; Li et al., 2020). However, particularly in poor quality bone, the screw loosening rate can be as high as 28% (Bokov et al., 2019), leading to a risk of fixation failure and damage to surrounding tissues (Konstantinidis et al., 2016). Failure of a fixation usually requires a reoperation, which would cause unnecessary pain and pose additional risks, especially in elderly patients (Kruke et al., 2016).

To improve the attachment of the screw in bone, the use of a self-setting bone cement around the screw has been reported in several previous studies (Wu et al., 2020a; Pujari-Palmer et al., 2018a). Here, a poly methyl methacrylate (PMMA) or calcium phosphate (CaP) cement is injected into the bone before or after insertion of the screw, in the latter case using cannulated and fenestrated screws (Ehresman et al., 2021). In this way, the holding power can be significantly increased, in particular through the use of PMMA, as shown in several *in vitro* and *in vivo* studies (Sermon et al., 2012; Robo et al., 2018). However, the PMMA bone cement blocks the flow of marrow and blood, which can

cause bone cement implantation syndrome (BCIS), potentially resulting in hypoxia and/or hypotension (Donaldson et al., 2009).

To overcome these disadvantages of current bone cements, different alternative strategies have been proposed. To enhance the fixation of screws in trabecular bone, HA coatings have been suggested by several previous studies (Rappoport et al., 2021; Filip et al., 2019), potentially leading to a significant increase in local bone density over time (Pesce et al., 2014a). However, this approach does not ensure primary stability of the construct. As an alternative approach another study substituted the bone cement with a non-setting, injectable biomaterial, which could allow for local flow of nutrients through the material (Muñoz et al., 2018). This material consisted in a hydrogel containing hydroxyapatite (HA) particles, which was found to be able to improve the holding power of screws by about 30 % in primary stability compared with the control group, without blocking the fluidity of marrow (Muñoz et al., 2018). This material might also be used to deliver bone growth stimulating drugs (Abtahi et al., 2012; Greiner et al., 2008; Kettenberger et al., 2017). Considering the potential long-term positive effects of HA on the trabecular bone remodelling (Pesce et al., 2014b), further evaluation and achieving an increased understanding of the mechanisms involved in the positive augmentation effect of this material combination is of

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high interest.

Indeed, while the positive augmentation result in the previous study was explained with the spaces between trabecular struts being filled with loose bone debris (Steeves et al., 2005), the results from this earlier study have been challenging to repeat, and the mechanism of augmentation is not entirely clear. In light of previous observations around the potential effects of bone debris in terms of enhancing screw attachment (Muñoz et al., 2018; Steeves et al., 2005), we hypothesized that different HA particle shapes and sizes could influence the augmentation, and thereby the primary stability of screws. Therefore, in this study, the pull-out force, stiffness, and work to fracture were compared between different groups of screws inserted into rabbit trabecular bone, with and without hydrogel augmentation, and with hydrogels containing different types of HA particles.

2. Materials and methods

2.1. Bone sample preparation

60 bone samples were acquired from rabbit (4–6 months old) distal femurs, using a hand saw after removing soft tissues. The femurs were stored in the freezer at -20°C until use. Rabbit bone was chosen as it has a relatively high porosity compared with e.g. bovine bone, approaching that of human bone, and has been extensively used in screw attachment studies (Muñoz et al., 2018; Eby et al., 2021).

2.2. Micro-computed tomography

The bone samples were scanned with a micro-CT (Skyscan 1172 and 1275, Bruker, Kontich, Belgium) to acquire data on the ratio between bone volume and total volume (BV/TV). For the samples scanned by the Skyscan 1172, the following parameters were utilized: filter aluminium plus copper, voxel size $12\text{ }\mu\text{m}$, voltage 100 kV , current $100\text{ }\mu\text{A}$, exposure time 2100 ms rotation step 0.4° , 360° rotation. For the samples scanned by the Skyscan 1275, the following parameters were utilized: filter aluminium, voxel size $15\text{ }\mu\text{m}$, voltage 60 kV , current $100\text{ }\mu\text{A}$, exposure time 135 ms , rotation step 0.4° , 360° rotation. After scanning, the images were reconstructed using NRecon (Bruker, Kontich, Belgium) and analysed using CTAn (Bruker, Kontich, Belgium). The region of interest was selected with the largest cuboid possible ($\sim 4\text{ mm}$ edge length) around the screw insertion position without intersecting the cortical bone. The BV/TV was used for sample division into groups and analysis of the influence of bone density on pull-out strength.

2.3. Sample division

The samples were divided into five groups to assess the influence of HA particles, i.e. control (non-augmented screws), Hyalectin-augmented (500–700 kDa, Fidia Farmaceutici S.p.A., Abano Terme (PD), Italy) screws, Hyalectin with nano-sized irregular HA particles (irregular nHA) (04238, Merck KGaA, Darmstadt, Germany), Hyalectin with nano-sized spherical HA particles (spherical nHA) (677418 ($<200\text{ nm}$ particle size (BET)), Merck KGaA, Darmstadt, Germany), and Hyalectin with micro-sized spherical HA particles (spherical mHA) (900203 (D10 = $9.94\text{ }\mu\text{m}$), Merck KGaA, Darmstadt, Germany). There were 12 samples in each group (Table 1).

2.4. HA powder characterization

Three kinds of HA powders were used as mentioned above, namely irregular nHA, spherical nHA, and spherical mHA. The particle size and particle size distribution of nHA particles were also measured with a dynamic light scattering (DLS) instrument (Zetasizer nano, Malvern Panalytical, Worcestershire, United Kingdom). The particles were dissolved in pure ethanol and pre-processed with an ultrasonic device to disperse the agglomerated powders. The particle size and distribution of

Table 1

The five tested groups specifying the composition of the augmentation material. N = 12 for each group.

Group	Hyalectin [wt/vol%]	nHA (irregular) [wt/vol%]	nHA (spherical) [wt/vol%]	mHA (spherical) [wt/vol%]
Control	–	–	–	–
Hyalectin	3.5	–	–	–
Irregular nHA	3.5	40	–	–
Spherical nHA	3.5	–	40	–
Spherical mHA	3.5	–	–	40

mHA particles were measured with another DLS instrument (MasterSizer, Malvern Panalytical, Worcestershire, United Kingdom). The particles were dissolved in pure ethanol and pre-processed with an ultrasonic device to disperse the agglomerated powders.

2.5. Gel preparation

The Hyalectin gel was prepared by dissolving 3.5 wt/vol% pure Hyalectin powder in pH 7.4 phosphate-buffered saline (PBS) solution (Thermo Fisher Scientific Inc., Waltham, Massachusetts, U.S.) under continuous stirring with a magnetic stirrer. The gel was stored in a fridge (4°C) for further use. In the irregular nHA group, 40 wt/vol% of irregular nHA was mixed with the prepared Hyalectin gel under stirring. It was stirred until the gel was homogenous and no bubbles were present. In the spherical nHA and mHA groups, the same amount of spherical nHA and mHA particles was mixed. After preparation of the particle-containing gels, they were stored in a fridge at 4°C .

2.6. Particle distribution characterization in hydrogel

The particle shape, size, and distribution in Hyalectin hydrogel were verified by scanning electron microscopy (SEM) (Crossbeam550, Carl Zeiss AG, Oberkochen, Germany), at a working distance of 4.9 mm , with acceleration voltage of $1\text{--}5\text{ kV}$. The gel was spread on carbon tape, air dried, and no coating was applied.

2.7. Rheology measurements

Viscosity measurements were performed on a Discovery Hybrid Rheometer 2 (TA Instruments, Solentuna, Sweden) using a 40 mm parallel plate stainless steel geometry. Flow sweep measurements were performed under shear rate control on all samples to obtain the viscosity as a function of shear rate. The samples were placed on the rheometer stage using a plastic spatula, after which the geometry was lowered to $1000\text{ }\mu\text{m}$, and the excess sample was trimmed off to form a uniform sample-disc between the plates. All measurements were performed at a constant gap and in triplicates. The shear rate was varied between 0.001 and 100 s^{-1} .

2.8. Mechanical testing

Screw attachment was evaluated using pull-out tests (Fig. 1a), according to the ASTM F543-07 standard (ASTM, 2010). Commercially available titanium orthopaedic screws (Jiangsu Trauhui Medical Instrument Co., China) (Pujari-Palmer et al., 2018b; Wu et al., 2020b; Joffe et al., 2017) with the following characteristics were used: 4 mm outer diameter, 1.9 mm inner diameter, 1.75 mm pitch. For each sample, a 10 mm deep pilot hole was pre-drilled with a pillar drill machine (PB40, Robert Bosch GmbH, Gerlingen, Germany) and a 2.5 mm drill bit. The position of the pilot hole was selected to avoid the intersection with cortical bone by the intercondylar fossa (Fig. 1b). The augmentation

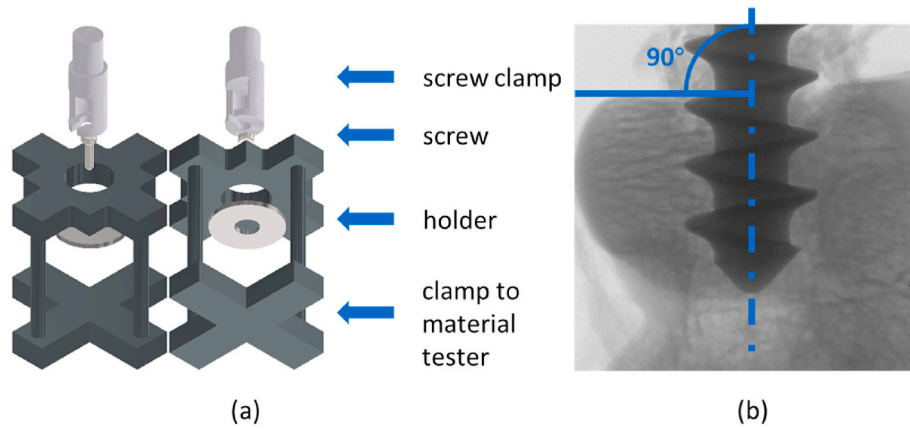


Fig. 1. Schematic illustration of the pull-out device (a), and a cross section view of the screw and bone with micro-CT (b), also indicating the placement of the screw in relation to the cortical bone.

material was then injected into the pilot hole of each sample until overfilling to ensure an even and complete distribution of the injected material. In the next step, a screw was inserted in the pilot hole with a hex key. The insertion depth of the screw was calculated using the length of the uninserted part, which was measured with a calliper. The target insertion depth was 8 mm which ensured that at least three threads engaged in the trabecular bone structure. The target insertion angle between the screw and cortical bone was 90° to ensure a vertical pull-out direction.

After the insertion step, the samples were scanned again with the micro-CT to verify the insertion position and angle. Pull-out tests were then conducted using a universal testing machine (AGS-X, Shimadzu, Kyoto, Japan). The capacity of the load cell was 5 kN and the pull-out rate was 1 mm/min. The screw was mounted with a custom-made clamp as shown in Fig. 1a. A typical screw insertion position is shown in Fig. 1b.

The pull-out force was taken as the maximum force of the force-displacement curve (ASTM, 2010). The stiffness was measured on the linear part of the force-displacement curve. The pull-out work to fracture was obtained by integrating the area between the force-displacement curve with the x-axis ($y = 0$).

2.9. Statistical analysis

A one-way analysis of variance (ANOVA) was used to assess any differences between groups in terms of pull-out force, stiffness, and work to fracture. The pull-out force F , stiffness K , and work to fracture W were normalized by the BV/TV before the statistical analysis (Muñoz et al., 2018), i.e., $F_{norm} = F/(BV/TV)$, $K_{norm} = K/(BV/TV)$, and $W_{norm} = W/(BV/TV)$, where F_{norm} is the normalized force, K_{norm} is the normalized stiffness, and W_{norm} is the normalized work to fracture. If the p-value was equal to or smaller than 0.05, the difference was considered significant. Each group was compared against the control group by a post-hoc test (Dunnett test). All post-processing and analysis of the data were implemented in MATLAB (MathWorks, Natick, United States).

3. Results

3.1. Bone density

The average BV/TV, as measured by micro-CT, for the five groups is shown in Table 2.

3.2. Particle size and morphology

The particle size distribution of irregular nHA, spherical nHA, and spherical mHA, as measured by DLS, can be found in Fig. 2. The average

Table 2
The BV/TV of the bone samples in the four tested groups.

Group	Control	Hyalactin	nHA (irregular)	nHA (spherical)	mHA (spherical)
BV/TV	$40.20 \pm$	$40.29 \pm$	$40.31 \pm$	$40.28 \pm$	$30.44 \pm$
[%]	3.76	5.88	5.32	5.55	2.41

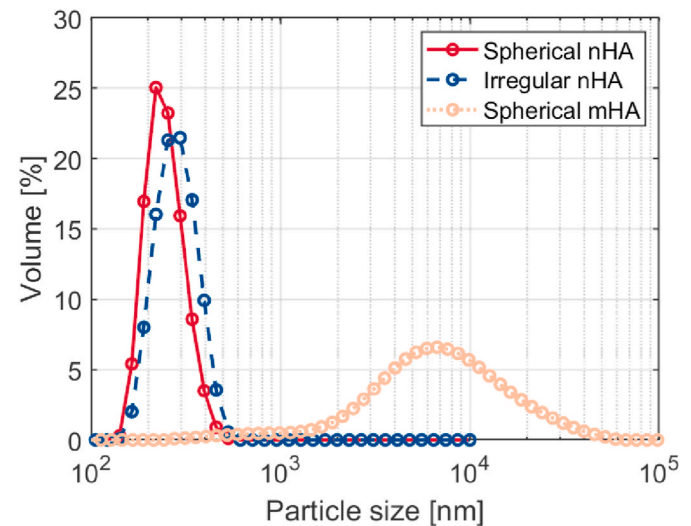


Fig. 2. Particle size distribution of spherical nHA, irregular nHA, and spherical mHA.

particle size of irregular nHA was 289 ± 71 nm. The average particle size of spherical nHA was 251 ± 60 nm. The average particle size of spherical mHA was 9 ± 8 μ m. There was no statistically significant difference between the two nHA groups ($p = 0.68$).

The difference in size of the mHA and the nHA particles were confirmed by the SEM images (Fig. 3). Furthermore, the SEM images confirmed the differences in particle shape, showing spherical (a and c) and irregular (b) shapes of the respective particles.

3.3. Rheology results

The viscosity-shear rate curves from the rheology measurement are shown in Fig. 4. As a quasi-static pull-out test was implemented, the viscosities with low shear rate (0.01 s^{-1}) between different gels were compared. The viscosity measured for the irregular nHA group was

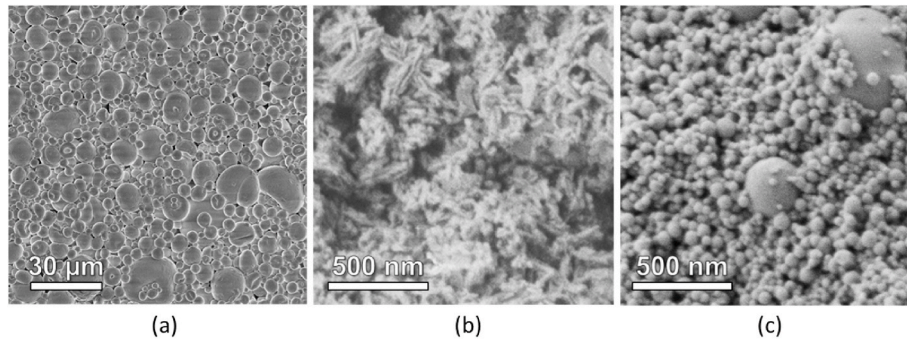


Fig. 3. SEM images of (a) spherical mHA, (b) irregular nHA, and (c) spherical nHA inside the Hyalactin gel.

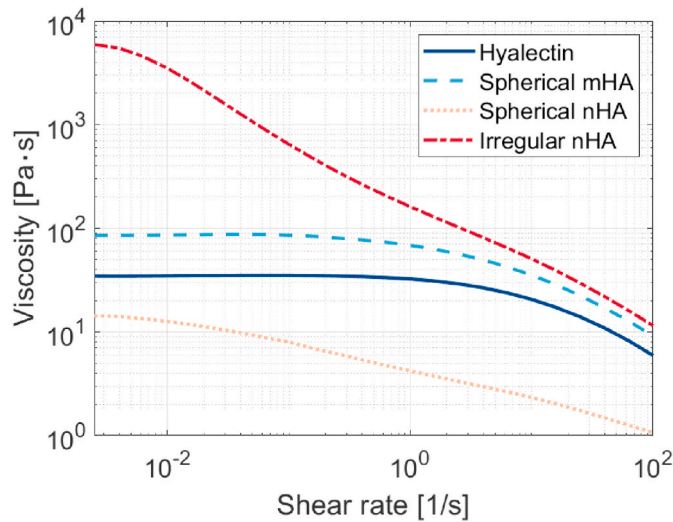


Fig. 4. Average viscosity as a function of shear rate for the different materials, i.e. Hyalactin gel only, Hyalactin-spherical mHA, Hyalactin-spherical nHA, and Hyalactin-irregular nHA. $N = 3$ for each group.

3493.96 ± 261.97 Pa·s, i.e. significantly higher than the Hyalactin group (34.68 ± 1.64 Pa·s), the spherical nHA group (12.58 ± 0.95 Pa·s), as well as the spherical mHA group (86.10 ± 4.70 Pa·s).

3.4. Pull-out tests

Force-displacement curves from the screw pull-out tests before normalization are shown in Fig. 5. One typical curve is shown for each group (Fig. 5a). A clear force augmentation effect could be observed for the irregular nHA group and spherical mHA group. However, no stiffness augmentation could be observed for the irregular nHA group. Similar results could be found in average and standard deviation curves (Fig. 5b).

The average pull-out force, stiffness, and work to fracture, normalized for BV/TV, are shown in Fig. 6. The average pull-out force of the group containing irregular nHA and spherical mHA particles were significantly higher compared to the control ($p = 0.04$, $p = 0.02$). The stiffness of the mHA spherical group was significantly higher than the control group ($p < 0.001$). The work to fracture was only augmented by the irregular nHA particles ($p = 0.03$). There were no other statistically significant differences found.

4. Discussion

As reported in a previous study (Muñoz et al., 2018), the primary stability of cancellous bone screws can be improved by augmentation with a non-setting soft material, namely Hyalactin loaded with a specific amount of hydroxyapatite particles. The main reason provided for the augmentation effect was the compaction of HA particles between the trabeculae (Muñoz et al., 2018). In this study, we hypothesized that different morphological parameters of HA particles, i.e. the particle shape and size, could influence the augmentation effect. Therefore, the effect of a screw augmentation of Hyalactin gels loaded with HA particles of different shapes and sizes was tested with pull-out tests in rabbit

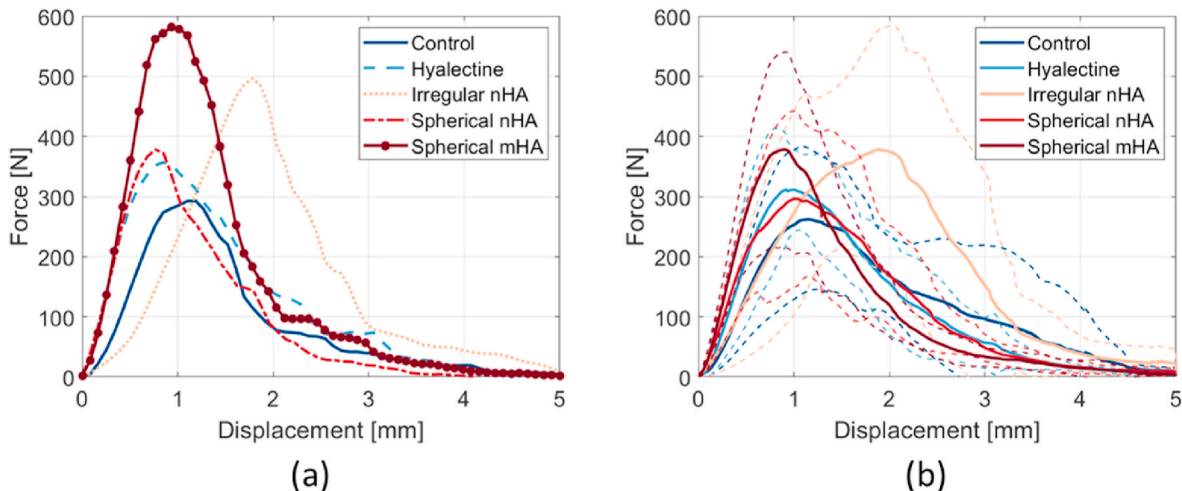


Fig. 5. The typical force-displacement curves for all five groups (a); average and standard deviation curves of each group (b). Non-normalized data.

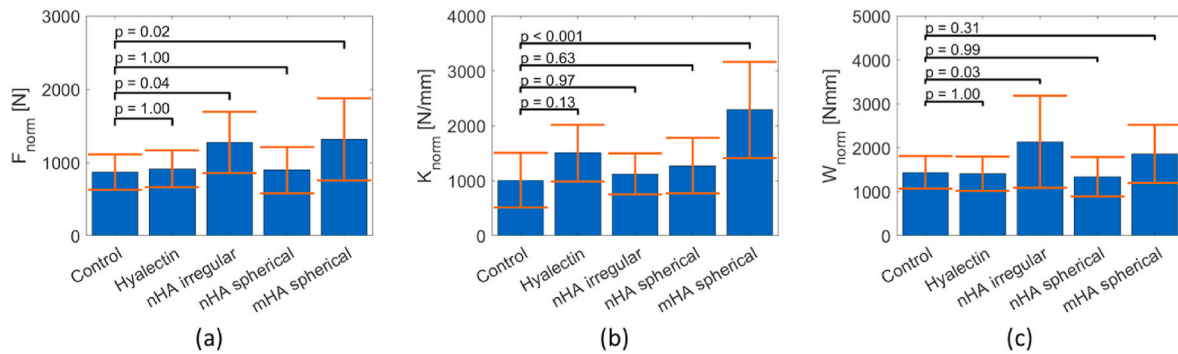


Fig. 6. Average \pm standard deviations of (a) pull-out strength, (b) stiffness, and (c) work to fracture for the tested groups, as normalized to BV/TV. $N = 12$ for each group.

femoral bone, using the same amounts as in the previous study. The results of these materials were compared to those of a control group with screws without any augmentation material. The pull-out force, stiffness, and work to fracture were evaluated to assess the screw stability for the different groups.

In the previous study (Muñoz et al., 2018), the enhancement of the pull-out force by using HA in Hyalectin was explained by making an analogue between the HA particles and loose bone debris, which can fill the space between trabeculae (Steeves et al., 2005). The interaction between the particles and the trabecular structure, and the interaction among the particles themselves could provide resistance to the pull-out process. However, in this study, we found an effect only for irregular nHA and spherical mHA particles, which gave a significantly higher pull-out force. No reinforcement effect was found for spherical nHA particles of similar amounts, hence validating our hypothesis that particle shape and size would have an effect. The non-setting hydrogel without any hydroxyapatite did not provide any improvement of screw attachment either, as expected. The results are discussed below in order to explain these findings.

BV/TV has previously been found to be the main predictor of screw pull-out force (Procter et al., 2015; Ovesy et al., 2020). While most groups had a similar approximate mean value for BV/TV of 40% (Table 2), one group (mHA spherical), had an average BV/TV of approximately 30%. Therefore, the ensuing comparative analysis was premised on normalized mechanical responses, following the methodology delineated in section 2.9.

One of the reasons for the higher pull-out force of the irregular nHA group (as shown in Fig. 6) may be the interactions between irregular nHA particles and surrounding structures, i.e. the screw and trabecular bone. The irregular particle shape (Fig. 3) can create more interactions between nHA particles and surrounding structures than the spherical nHA particles. The irregular nHA particles can provide a better improvement of the local interactions as debris packing in between trabeculae, where the irregularity of the particles would also increase the friction in between themselves and other structures and hence provide better stress transfer and distribution during the pull-out process. The shape and size of the particles was verified herein using SEM, as shown in Fig. 3. The SEM images showed clear differences between the two particle groups, where the irregular particles appeared to consist in irregular agglomerates of smaller particles, and the spherical particles were indeed spherical. The relative size of the particles was submicron, as measured by DLS (Fig. 2), and not statistically different. Another indication of the enhanced augmentation effect of the irregular nHA hydrogel is the higher viscosity measured for this material combination, as illustrated in Fig. 4. While the same hydrogel was used as in the previous study, a viscosity change was found when adding the particles. When there were no HA particles present, a viscosity of 34.68 ± 1.64 Pa·s (at 0.01s^{-1}) was observed in the Hyalectin only group. When the irregular nHA particles were mixed with the Hyalectin gel, the viscosity

was found to be much higher at low shear rates (3493.96 ± 261.97 Pa·s at 0.01s^{-1}), and when the spherical mHA particles were used, the viscosity was found to be slightly higher (86.10 ± 4.70 Pa·s) than the Hyalectin group. When the spherical nHA particles were added, the viscosity was lower than the Hyalectin only, consistently over the shear rate range evaluated (12.58 ± 0.95 Pa·s at 0.01s^{-1}). The HA particles can indeed influence the flow of Hyalectin, and therefore, the viscosity of the hydrogel. Several parameters can influence the viscosity of a Hyalectin-HA composite material, namely the solid fraction, particle size, particle size distribution, and particle shape (Pabst et al., 2006; Procter et al., 2015). The spherical nHA particles would provide lower interaction forces among the particles, as the irregular nHA particles can deflect the flow lines around the particles (Procter et al., 2015) as well as result in higher friction forces between the particles. The noted differences in the pull-out force may hence also result from the higher resistance to flow of the irregular nHA particles.

As depicted in Fig. 6, the spherical mHA particles also provided a statistically significant augmentation effect. Although the mHA particles are mostly sphere-like (Fig. 3), the larger particle size can provide a more stable load transfer between particles compared to nano-sized particles, as plenty of micro-motions between nano-sized particles can be avoided when the particle size increases. Furthermore, the particle size ($\sim 10\text{ }\mu\text{m}$) is more suitable for the voids between trabeculae (on the order of hundreds of μm (van der Meulen et al., 2009)). If the particle size is too small, e.g. as for the spherical nano-HA particles, the load is hard to transfer between the particles, as the friction dominates the interaction rather than deformation. However, if the particle size is too large, it could be hard for the HA particles to move within the bone's porous structure, i.e. the particles can only distribute around the pilot hole and screw.

Indeed, while the spherical nHA particles did not have any effect on the average pull-out force, the introduction of irregular nHA particles or spherical mHA particles in the Hyalectin gave a larger variation in the results (Fig. 6), suggesting that the stochastic distribution of Hyalectin gel and HA particles can influence the augmentation effect.

There were only statistically significant differences in stiffness between the control and the spherical mHA group (Fig. 6). The non-setting property of the Hyalectin hydrogel could be one of the reasons. The interfaces between the screw and trabecular bone structure did not improve significantly by the Hyalectin hydrogel compared with the control group. Furthermore, the small particle sizes of nHA cannot influence the trabeculae deformation mechanism, i.e. bending- or compression-dominated, however, the mHA with around 50 times larger particles can influence the same, leading to a higher pull-out stiffness, as demonstrated in Fig. 6. The work to fracture of the irregular nHA group was higher than other groups on average, as both the pull-out force and the displacement until fracture were higher for this group, i.e. relatively low stiffness but higher pull-out strength were found in this group.

Similar augmentation effects were found in the previous study using

Hyalactin hydrogel and HA particles (Muñoz et al., 2018). The augmentation effect of the non-setting, HA-containing hydrogel is lower compared with PMMA bone cement (Pujari-Palmer et al., 2018b; Erhart et al., 2011). Although the PMMA bone cement generally enhances the pull-out strength with an augmentation effect of approximately 100% (Liu et al., 2011; Renner et al., 2004; Sarzier et al., 2002), PMMA is not biodegradable, which can limit the osseointegration (Elder et al., 2015). Ceramic bone cement has been reported to have potential for bone remodelling (Wu et al., 2020b). However, the ceramic bone cement may not even enhance the pull-out strength (Wu et al., 2020b; Procter et al., 2015) compared to samples without augmentation, which can be explained by the material injection volume as well as the distribution, and the higher importance of the underlying bone conditions (Procter et al., 2015; Steiner et al., 2017). However, a degradable ceramic adhesive has shown promise in strength improvement (approximately 50%) (Wu et al., 2020b). Nevertheless, considering the advantage of Hyalactin hydrogel of not blocking the fluidity of blood and nutrients from day one, it could consist in a future alternative in specific cases, with better long-term bone viability around the screw. Furthermore, it was also reported in a previous study that calcium phosphate particles can serve as nucleation sites within hydrogel matrices, fostering HA precipitation, which can result in a rapid *in vivo* mineralization of the hydrogel (Kettenberger et al., 2017). Incorporating HA particles within a hydrogel could potentially yield a distinctive set of properties: i) injectable nature, ii) augmented primary mechanical fixation, and iii) enhanced secondary biological fixation. Therefore, there lies an enticing prospect to delve into these properties using appropriate animal models in future investigations.

There are some limitations to the present study. First, the cortical bone was not removed before the pull-out experiment due to size limitations of the small rabbit femur, restricting the possible insertion depth. Removing the cortical bone would entail a reduction also of part of the trabecular bone structure. To ensure that more than three threads were inserted in the trabecular bone structure, the cortical bone was hence conserved. The cortical bone influences the pull-out process and affects the load transfer in the trabecular structure (Ruffoni et al., 2012). However, the behaviour of cortical bone should not be influenced by the HA particles. The existence of cortical bone also leads to difficulties in measuring the insertion depth and angle, which could have induced some additional variation between samples. Another limitation is the anisotropy and complexity of the trabecular bone, which can be one of the main reasons that caused the higher standard deviation between samples in each group (Fig. 6). The pull-out force may vary substantially depending on the insertion position and the surrounding trabecular structure. Twelve samples per group still gave a considerable variability. Another potential source of the observed variability might stem from the heterogeneity in the bone conditions of the rabbits. Specifically, the samples were procured from rabbits of varying ages and genders, which could result in differential developmental stages of the bone. In order to mitigate the effect of bone quality, we normalized the mechanical responses by adjusting for BV/TV. However, the model we employed postulates a linear relationship between pull-out stability and BV/TV, an assumption that might not be all-encompassing. Hence, the potential for bone variation effects to influence the outcomes may still persist to some extent.

In summary, as discussed above, the particle shape and size will influence the pull-out stability. Future studies may focus on the optimization of relevant morphological parameters of HA particles, such as particle shape and size, in order to provide moderate hydrogel viscosity to enable flow as well as the desired mechanical properties, which may result in a better augmentation effect to improve the stability of screws in different sites of the human body as well as a function of health condition.

5. Conclusions

In this paper, different non-setting hydrogel-based materials containing hydroxyapatite particles were evaluated for augmentation of trabecular bone, as assessed by screw pull-out tests. The hydroxyapatite particle shape and size were found to be important factors that have an effect on the early stability of a screw in terms of the pull-out force, stiffness, and work to fracture. The combination of Hyalactin with either irregularly shaped nano-sized hydroxyapatite particles, or spherically shaped micro-sized hydroxyapatite particles, has the potential to increase primary screw implant stability and may overcome the known biological limitations of current augmentation materials, which typically have limited local nutrition and bone remodelling rates.

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CRediT authorship contribution statement

Yijun Zhou: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation. **Lisa Höglund:** Writing – review & editing, Validation, Methodology, Investigation. **Ayan Samanta:** Writing – review & editing, Methodology, Investigation, Data curation. **Philip Procter:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Cecilia Persson:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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