Journal of Biomechanics 49 (2016) 1121–1127

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Mechanical behaviour of Bioactive Glass granules and morselized cancellous bone allograft in load bearing defects

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ARTICLE INFO

Article history:
Accepted 20 February 2016

Keywords:
Bioactive Glass
Bone allograft
Mechanical behaviour
Load-bearing defects
Confined compression

ABSTRACT

Bioactive Glass (BAG) granules are osteoconductive and possess unique antibacterial properties for a synthetic biomaterial. To assess the applicability of BAG granules in load-bearing defects, the aim was to compare mechanical behaviour of graft layers consisting of BAG granules and morselized cancellous bone allograft in different volume mixtures under clinically relevant conditions.

The graft layers were mechanically tested, using two mechanical testing modalities with simulated physiological loading conditions: highly controllable confined compression tests (CCT) and more clinically realistic in situ compression tests (ISCT) in cadaveric porcine bone defects. Graft layer impaction strain, residual strain, aggregate modulus, and creep strain were determined in CCT. Graft layer porosity was determined using micro computed tomography. The ISCT was used to determine graft layer subsidence in bone environment.

ANOVA showed significant differences ($p < 0.001$) between different graft layer compositions. True strains absolutely decreased for increasing BAG content: impaction strain −0.92 (allograft) to −0.39 (BAG), residual strain −0.12 to −0.01, and creep strain −0.09 to 0.00 respectively. Aggregate modulus increased with increasing BAG content from 116 to 653 MPa. Porosity ranged from 66% (pure allograft) to 15% (pure BAG). Subsidence was highest for allograft, and remarkably low for a 1:1 BAG-allograft volume mixture.

Both BAG granules and allograft morsels as stand-alone materials exhibit suboptimal mechanical behaviour for load-bearing purpose. BAG granules are difficult to handle and less porous, whereas allograft subsides and creeps. A 1:1 volume mixture of BAG and allograft is therefore proposed as the best graft material in load-bearing defects.

1. Introduction

S53P4 Bioactive Glass (BAG) is a synthetic bone graft substitute material consisting of (wt%/mol%) 23.0/22.7 Na_2O, 20.0/21.8 CaO, 4.0/1.7 P_2O_5, 53.0/53.9 SiO_2 (Andersson et al., 1990b). When exposed to a physiological environment, physicochemical reactions create a bone-like hydroxyapatite layer on the BAG surface (Andersson et al., 1990a; Andersson and Kangasniemi, 1991). This surface makes the glass osteoconductive, with very strong bonds to bone being formed in vivo (Andersson et al., 1990a; Andersson and Kangasniemi, 1991; Andersson et al., 1992; Heikkila et al., 1993, 1995). Additionally, the physicochemical reactions lead to a series of interactions that stimulate new bone formation (Gough et al., 2004b, 2004a; Loty et al., 2001; Matsuda and Davies, 1987; Vrouwenvelder et al., 1993; Vrouwenvelder et al., 1992; Waselau et al., 2012; Xynos et al., 2001, 2000b, 2000a; Zhou et al., 2010). Because of the aforementioned advantageous properties, BAG is currently used for various clinical indications. Successful applications include craniomaxillofacial surgery, otolaryngologic surgery, spine surgery, and treatment of benign bone tumours (Aitasalo et al., 2000, 2001; Peltola et al., 2006, 2008, 1998; Sarin et al., 2012; Silvola, 2012; Stoor et al., 2010; Turunen et al., 2004; Lindfors et al., 2009, 2010b; Frantzen et al., 2011; Rantakokko et al., 2012).

In the past decade, BAG has drawn attention for research on its unique antibacterial effects. In vitro studies showed that S53P4 BAG has an antibacterial effect on a large panel of clinically important pathogens (Lepparanta et al., 2008; Munukka et al., 2008; Zhang et al., 2010; Coraca-Huber et al., 2014; Drago et al.,

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http://dx.doi.org/10.1016/j.jbiomech.2016.02.047
0021-9290/

2014; Gergely et al., 2014). These findings not only mean that a BAG graft layer is unlikely to become infected, they also indicate that the material might be an adjunct to treat bacterial infections in vivo. Recent clinical studies indeed show increasing evidence that BAG granules are effective in one-step surgical treatment of chronic osteomyelitis (Lindfors et al., 2010a; McAndrew et al., 2013; Drago et al., 2013; Romano et al., 2014). Osteomyelitis is a severe infection of bone and/or bone marrow, which can arise from many different mechanisms. Appropriate treatment of the infection is necessary because osteomyelitis is associated with delayed fracture union, non-union, or failure of prosthetics. While the aforementioned studies focus on BAG granules in diaphyseal osteomyelitis, infections are also found in load-bearing defects that require more mechanical support by the bone graft substitute material.

Glass granules inherently have a high stiffness relative to bone, which could make them suitable to use in (suspected septic) load-bearing defects. Experience with BAG in such applications however remains limited. The mechanical behaviour of BAG graft layers are presently unclear, and it is unknown if these are suitable for load-bearing defects.

The purpose of the present study therefore was to compare mechanical behaviour of graft layers consisting of BAG granules and morselized cancellous bone allograft in different volume mixtures under clinically relevant conditions. For this purpose, a highly controllable confined compression test (CCT) for precise measurement of the material parameters was carried out. A second purpose was to compare subsidence of the materials in a more realistic bone environment, for which an in situ compression test (ISCT) was used.

2. Materials and methods

2.1. Graft materials

Tested graft layers consisted of allograft morsels and non-porous S53P4 BAG granules (BonAlive®, BonAlive Biomaterials Ltd., Turku, Finland) of clinically used size (2.00–3.15 mm) (Van Gestel et al., 2015). Seven human femoral heads from patients undergoing total hip arthroplasty (THA) were collected to serve as allograft source. Donor bone collection was approved by the institute's medical-ethical review committee (Maastricht University Medical Centre, Maastricht, Netherlands). Sawn femoral head fragments were milled with a surgical bone mill (Noviomagus Bone Mill, Spierings Orthopaedics BV, Nijmegen, Netherlands) using an extra fine milling drum, resulting in morsels with a size of 3–5 mm. Care was taken to avoid milling of soft tissue, femoral neck, or cortex of the femoral head. Allograft morsels were defatted using a surgical pulse lavage set with a bone-cleaning tip (InterPulse®, Stryker Orthopaedics, Limerick, Ireland), as is customary in our hospital (Maastricht University Medical Centre, Maastricht, Netherlands). All collected allograft was pooled to minimize sample variability and stored in a freezer (−80 °C). Twenty-four hours prior to use in mechanical testing, allograft material was defrosted and stored at 6 °C. Based on power analysis, five samples per group were used for CCT and ISCT.

2.2. CCT Methods

Five groups with different volume ratio mixtures of allograft and BAG were studied in CCT: pure allograft, 25% BAG, 50% BAG, 75% BAG, and pure BAG granules. Samples were prepared by measuring 3 ml (±0.1 ml) graft material using Archimedes' Principle. This material was blotted dry and inserted in a cylindrical polymethyl methacrylate (PMMA) chamber with an inner diameter of 20.4 mm.

Subsequently, samples were impacted inside the chambers using a custom-made impacting device (Fig. 1). This device consisted of a 420 g weight around a 350 mm long guide rod and a solid load distributor. The load distributor diameter was slightly smaller than the PMMA chamber inner diameter, and had three small channels (diameter 2.0 mm) at its circumference to ensure free outflow of fluids. Impaction was performed by dropping the weight 30 times from the guide rod end. This method has been reported to lead to clinically relevant impaction strains (Walschot et al., 2010). Sample height before (h_{init}) and after impaction (h_0) was measured with a marking gauge (resolution 0.05 mm) to calculate impaction strain ($\varepsilon_{impaction}$) as follows:

$$\varepsilon_{impaction} = \ln\left(\frac{h_0}{h_{init}}\right)$$

Following impaction, samples were subjected to a CCT loading regime in the PMMA chambers. This CCT setup has been used previously in other studies to determine graft layer elastic, plastic, and viscoelastic properties (Verdonschot et al., 2001; Walschot et al., 2010). The CCT test setup consisted of a chamber holder, PMMA chamber, brass filter, force distributor, and a force transducer (Fig. 1). A biomaterials testing system (858 Mini Bionix®, MTS Systems Corporation, Eden Prairie, MN, USA) was used to apply load and to record both displacement and applied force. Samples were subjected to 900 loading cycles (sinusoidal, 40–850 N, 1 Hz), followed by 300 s of unloading. The applied cyclic load is similar to physiological stress levels that may be expected around cemented implants (Walschot et al., 2010). Graft layer height was calculated with a frequency of 10 Hz during this loading regime to determine three outcome parameters: residual strain, aggregate modulus, and creep strain. Residual strain ($\varepsilon_{plastic}$) was registered as the relative height difference from the start to the end of the loading regime:

$$\varepsilon_{plastic} = \ln\left(\frac{h_{unload}}{h_0}\right)$$

In which h_{unload} is the average graft layer height during the last 50 s of unloading (Fig. 2). The aggregate modulus (H) was calculated using the elastic strain ($\varepsilon_{elastic}$) as follows:

$$\varepsilon_{elastic} = \ln\left(\frac{h_{max}}{h_{min}}\right)$$

$$H = \frac{\Delta\sigma}{\varepsilon_{elastic}}$$

In this formula, h_{max} and h_{min} are the mean maximal and mean minimal sample height during the last 50 cycles (Fig. 2). Creep strain (ε_{creep}) was calculated as the graft layer height decrease during loading that was restored after unloading:

$$\varepsilon_{creep} = \ln\left(\frac{h_{min}}{h_{unload}}\right)$$

Following CCT, each sample was scanned with a micro computed tomography (μCT) scanner (μCT80, SCANCO Medical AG, Brüttisellen, Switzerland) to measure

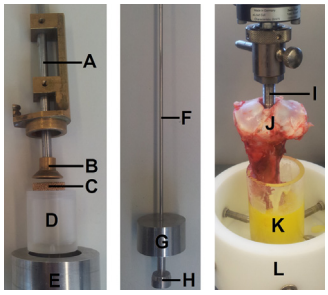

Fig. 1. Test setup, Test setup for CCT (left) and ISCT (right); and impaction device (middle). (A) Force transducer, (B) force distributor, (C) brass filter, (D) PMMA chamber, (E) chamber holder, (F) 350 mm long guide rod, (G) 420 g drop-weight, (H) load distributor, (I) force transducer and distributor, (J) sample, (K) plastic tube with resin, (L) sample holder.

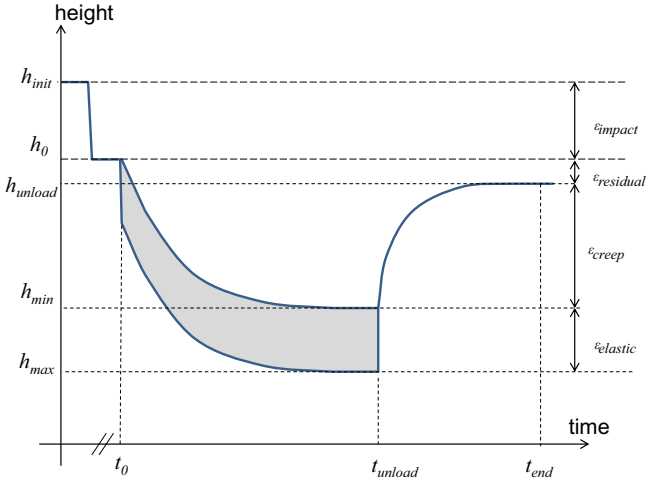

Fig. 2. CCT loading regime, Schematic representation of the height of the graft layer in CCT. Height of the graft layer is first decreased by impaction. During cyclic loading (t_0 – t_{unload}), the graft layer height decreases further. When the sample is unloaded after 900 s, it exhibits creep strain. Not all height is recovered after the loading regime, and the difference is reflected in the residual strain parameter.