UNIVERSITY OF BIRMINGHAM
University of Birmingham Research at Birmingham

The design of additively manufactured lattices to increase the functionality of medical implants

Burton, Hanna E.; Burton, Hanna E.; Eisenstein, Neil M.; Eisenstein, Neil M.; Lawless, Bernard M.; Jamshidi, Parastoo; Segarra, Miren A.; Addison, Owen; Shepherd, Duncan E.T.; Attallah, Moataz M.; Grover, Liam M.; Cox, Sophie C.

DOI:
10.1016/j.msec.2018.10.052
10.1016/j.msec.2018.10.052

License:
Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version
Peer reviewed version

Citation for published version (Harvard):
Burton, HE, Burton, HE, Eisenstein, NM, Eisenstein, NM, Lawless, BM, Jamshidi, P, Segarra, MA, Addison, O, Shepherd, DET, Attallah, MM, Grover, LM & Cox, SC 2019, 'The design of additively manufactured lattices to increase the functionality of medical implants', *Materials Science and Engineering C*, vol. 94, pp. 901-908. https://doi.org/10.1016/j.msec.2018.10.052, https://doi.org/10.1016/j.msec.2018.10.052

Link to publication on Research at Birmingham portal

Publisher Rights Statement:
https://doi.org/10.1016/j.msec.2018.10.052

General rights
Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

•Users may freely distribute the URL that is used to identify this publication.
•Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
•User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
•Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy
While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 26. Apr. 2024

The design of additively manufactured lattices to increase the functionality of medical implants

Hanna E. Burton[1,2]*, Neil M. Eisenstein[1,3], Bernard M. Lawless[4], Parastoo Jamshidi[5], Miren A. Segarra[5], Owen Addison[6], Duncan E.T. Shepherd[4], Moataz M. Attallah[5], Liam M. Grover[1], Sophie C. Cox[1]

[1] School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham, B15 2TT

[2] PDR – International Centre for Design & Research, Cardiff Metropolitan University, Cardiff, CF5 2YB

[3] Royal Centre for Defence Medicine, Birmingham Research Park, Vincent Drive, Edgbaston, Birmingham, B15 2SQ

[4] Department of Mechanical Engineering, School of Engineering, University of Birmingham, Edgbaston, Birmingham, B15 2TT

[5] School of Materials and Metallurgy, University of Birmingham, Edgbaston, Birmingham, B15 2TT

[6] School of Dentistry, University of Birmingham, Edgbaston, Birmingham, B15 2TT

*corresponding author: Hanna Burton, PDR, Cardiff Metropolitan University, Western Avenue, Cardiff, CF5 2YB

Abstract

The rise of antibiotic resistant bacterial species is driving the requirement for medical devices that minimise infection risks. Antimicrobial functionality may be achieved by modifying the implant design to incorporate a reservoir that locally releases a therapeutic. For this approach to be successful it is critical that mechanical functionality of the implant is maintained. This study explores the opportunity to exploit the design flexibilities possible using additive manufacturing to develop porous lattices that maximise the volume available for drug loading while maintaining load-bearing capacity of a hip implant.

Eight unit cell types were initially investigated and a volume fraction of 30% was identified as the lowest level at which all lattices met the design criteria in ISO 13314. Finite element analysis (FEA) identified three lattice types that exhibited significantly lower displacement (10-fold) compared with other designs; Schwartz primitive, Schwartz primitive pinched and cylinder grid. These lattices were additively manufactured in Ti-6Al-4V using selective laser melting. Each design exceeded the minimum strength requirements for orthopaedic hip implants according to ISO 7206-4. The Schwartz primitive (Pinched) lattice geometry, with 10% volume fill and a cubic unit cell period of 10, allowed the greatest void volume of all lattice designs whilst meeting the fatigue requirements for use in an orthopaedic implant (ISO 7206-4). This paper demonstrates an example of how additive manufacture may be exploited to add additional functionality to medical implants.

Keywords: additive manufacture; drug delivery; finite element analysis; lattice; mechanical testing; therapeutics

Introduction

Additive manufacture (AM) is the process of creating a three-dimensional object through layer-by-layer deposition of material. Commonly used AM techniques to melt powdered metal material to create near net shape parts are selective laser melting (SLM) and electron beam melting (EBM). Both of these approaches allow a greater design flexibility than traditional manufacturing methods to produce metallic parts (1); however, this advantage is not currently exploited to its full potential in medical applications. The possibility of new implant designs produced via AM routinely investigate osseointegration (2). However, increased functionality of implants can also be created through incorporation and controlled local release of therapeutics (3), or matching the mechanical properties of implants to the surrounding bone and tissue, for example through graded structures (4). This improvement in implant design has been possible due to the advances in additive manufacturing, where conventional subtractive methods are not capable of achieving such complex features.

Infection control of implants is a major concern in medicine, due to the increase in antibiotic resistant species. Recently, Lenguerrand et al. (5) used the National Joint Registry (NJR) for England, Wales, Northern Ireland and the Isle of Man to investigate revision surgery due to prosthetic hip joint infection. Between 2005 and 2013, the prevalence of revision surgery due to prosthetic joint infection, within three months of primary hip arthroplasty, increased 2.3-fold (5). Further, over 1000 procedures are performed due to prosthetic joint infection annually in this NJR region (5). Incorporating a therapeutic agent into a temporary cement spacer is a common solution to treat infection as it allows targeted local drug delivery with a controlled release. When revision surgery is required due to infection of a primary hip

replacement, 2-stage hip revision is chosen to treat most cases (6, 7). However, a cement hip spacer can result in poor patient quality of life during its implantation, due to its limited strength resulting in restricted mobility (8). Thus, an implant that can withstand normal loading conditions whilst eluting a desired therapeutic would be advantageous. This may be realised by using AM technologies to create an internal porous lattice structure to an implant that creates a void volume. A secondary material loaded with an antibiotic could be incorporated into this void volume, such as an antibiotic-loaded cement (9), and therapeutics released into the infected surrounding tissue. It is important to consider the mechanical effect on an implant when incorporating a lattice into a design, and ensure that fatigue and strength criteria associated with the implant are still met.

To demonstrate the potential of AM in medical implants, optimisation of an alternate 2-stage hip revision spacer with internal lattice structuring was investigated in this study, with an example design shown in Figure 1. Titanium alloy (Ti-6Al-4V) was chosen as the implant material due to its biocompatibility and suitability for orthopaedic applications (10). SLM was chosen to manufacture lattices due to the technologies capability to produce small strut diameters of 0.2 mm. It is critical for a correctly designed implant to withstand deformation, due to induced stress from the applied physiological loads, and also have a satisfactory fatigue strength. The aim of this study was to develop and additively manufacture a lattice structure that could be used in the design of a therapeutically loaded orthopaedic hip implant as an alternative to a partial-load bearing traditional cement spacer. Ultimately this approach has the potential to improve patient mobility and as such quality of life, as well as decrease the need for secondary stage surgery associated with hip revision due to infection.

Figure 1 – Computer Aided Design (CAD) of a hip implant: a) traditional implant; b) increased functionality due to integration of lattice design, providing a void space to load a therapeutic agent.

Materials and Methods

Lattice design

Lattices were designed according to ISO 13314 (11), the international standard for mechanical compression testing of porous metals, briefly explained here. A cylindrical design with diameter (D_o) of 15 mm, and height (H_o) of 15 mm was chosen for compression lattices, observing the relationship in equation 1 (11). The association between average pore size (d_a) and diameter of cylindrical specimen is specified by equation 2 (11). Notably, the resolution of the M2 Cusing® SLM system (Concept Laser, Germany) requires a minimum strut diameter of approximately 0.2 mm to achieve an acceptable part quality. Therefore, designs of lattices were kept within these parameters.

Equation 1 – Specimen height

$$H_o = D_o \sim 2D_o$$

Equation 2 – Specimen diameter

$$D_o \geq 10\ d_a$$

Compression lattice geometries were created using Simpleware ScanIP software (Synopsys, Mountain View, USA), for each appropriate unit cell type available (Figure 2). 2.5D lattices were not considered in this study due to their inappropriateness for design of AM medical implants. Resampling was set at 0.1 mm as standard, but was adjusted to 0.2 mm when the number of elements of a compression lattice exceeded 1 million. Using the Simpleware FE module

(Synopsys, Mountain View, USA), a coarse mesh was applied to the lattice geometries and these were exported for finite element analysis (FEA).

To enable incorporation of the largest volume of therapeutic agent, the target volume fraction (ratio of solid to void) of each cell type was decreased in increments of 10, until the lowest possible volume fraction was identified whilst maintaining all design parameters. The unit cell period (the number of cells that fill the image domain along an axis) was varied in steps of 5. To maintain a cubic structure, the unit cell period was identical in the *X*, *Y*, and *Z* directions.

As the volume fraction was decreased the strut diameter decreased also, compensating for the reduction in volume by removing material from the unit cell shape. Increasing the unit cell period also resulted in a decrease in strut diameter, as more unit cells were fitted along each axis length of the image domain. Thus, after determining the lowest volume fraction possible, the highest unit cell period was designed for each compression lattice. This would present the smallest strut diameter for each cell type that was within the limits of the SLM machine.

Figure 2 – CAD compression lattice cylinders (green) at 30%volume fraction, and a cubic unit cell period of 10 in the *X*, *Y* and *Z* axis. Individual unit cells (blue) with 30% volume fraction. Unit cell type below each image. Minimum strut and average pore diameters of CAD compression lattices shown for each cell type, evaluated by Simpleware software.

Finite element analysis

FEA uses computational methods to simulate applied physical conditions to a structure, and analyses the theoretical behaviour. In this study, Comsol Multiphysics® v5.2 (Comsol AB, Stockholm, Sweden) was used to perform FEA. A

tetrahedral mesh was applied to each lattice geometry (Figure 3). To simulate a comparable force across all lattices, 2300 N was applied axially, and a fixed restraint in all directions was applied to the bottom face. The 2300 N relates to the maximum force applied during fatigue testing of orthopaedic hip implants, as described in ISO 7206-4, the international standard of implants for surgery – partial and total joint prostheses (12). A stationary study was performed, using material properties for Ti-6Al-4V: Young's modulus of 113.8 GPa; Poisson's ratio of 0.342; and density of 4430 kg/m^3 (13). The maximum displacement and von Mises stress were used to evaluate the performance of each design.

Manufacture of parts

Lattice cylinders were fabricated from Ti-6Al-4V gas atomised powder (TLS Technik, Germany) sized 20-50 µm, with a M2 Cusing® SLM system (Concept Laser, Germany). Recycled powder was sieved to ensure a powder size <60 µm. Processing took place under an Argon atmosphere to limit oxygen pickup; the atmosphere was controlled to <0.1% oxygen. An Nd:YAG laser was used, with a maximum output power of 400 W, spot size of 60 µm, and wavelength of 1075 nm. The same optimised process parameters, designed to reduce residual porosity, were utilised from the authors' previous study (3). These parameters used an island scanning strategy with a scanning speed of 1750 mm/s, hatch spacing of 75 µm, 150 W laser power, and 20 µm slice thickness. To improve stability during manufacture, sacrificial support structures were built between the base substrate and each individual lattice cylinder, which were removed after manufacture.

Micro-computed tomography

Lattice cylinders were scanned using a Skyscan1172 micro-computed tomography (micro-CT) system (Bruker, Belgium) with 80 kV maximum X-ray energy, 8 W beam power, 1750 ms exposure per projection, aluminium and copper filter, and 3.38 µm pixel size. MicroCT was only employed on the Schwartz primitive (Pinched) 10% lattices since reliable results on higher volume fraction lattices was unachievable due to beam hardening and poor penetration of titanium. Reconstructed data were visualised in 3D using CTVox software (version 3.0, Bruker). A porosity analysis was performed using CTAn software (version 1.15.4.0, Bruker). Briefly, a region of interest was created within the strut material of each lattice, and this was interpolated across slices of the strut, to create a volume of interest (VOI) of approximately 0.015 mm^3. Global thresholding was applied to create a binary image, and a 3D analysis used to determine the total porosity within the VOI. The mean of 3 values taken from separate struts was calculated for each sample (n = 5).

Porosity determination using an Archimedes balance

Using an Archimedes balance, the mass of the lattice cylinders was taken in both air and ethanol, and additionally the height and diameter of each sample was measured using a Vernier calliper. The density of the lattice material was calculated from equation 3, where A is the mass of sample in air, B is the mass of sample in ethanol, ρ_O is the density of ethanol (0.79 g/cm^3), and ρ_L is the density of air (0.0012 g/cm^3). The apparent solid density (ρ_C) of the cylinder was calculated from equation 4, where the volume of the cylinder (V) was calculated from its height and diameter and ρ_T is the theoretical density of Ti-6Al-4V (4.43 g/cm^3).

Equation 3 – Material density

$$\rho = \frac{A}{A - B}\,(\rho_O - \rho_L) + \rho_L$$

Equation 4 – Apparent density

$$\rho_C = \frac{A/V}{\rho_T} \times 100$$

Strut and pore dimensions

The strut and pore dimensions could not be measured with Vernier callipers due to their geometry within the lattice. Therefore, to validate the manufactured part versus the stereolithography file (STL) sent for printing, images were taken of the specimens and the minimum strut and average pore diameters were measured using ImageJ (National Institutes of Health, Bethesda, MD, USA) (Figure 4). The photographic images allowed external features to be measured. Three repeat measurements were taken, and the mean calculated for external minimum strut and average pore diameters of manufactured lattices, with *n* = 5 for each lattice unit cell type. In addition, ImageJ was used to measure average internal strut and pore diameters for specimens scanned by micro-CT. Five repeat measurements were taken for strut and pore diameters and the mean calculated, with *n* = 5 for sample number.

Mechanical testing

Quasi-static compression tests were undertaken on *n* = 5 specimens per unit cell type using a Z030 universal mechanical tester (Zwick/Roell, USA). Testing was performed according to ISO 13314 (11). Each lattice was compressed at an initial strain rate of 10^{-2} s^{-1} to failure (0.075 mm/s). Failure strain was set to 50% of the specimen height. However, all specimens failed before the 50% maximum strain limit or reached the maximum load cell limit of 25 kN. Force and displacement were measured by the machine and from this, stress-strain curves were plotted for each

test, where stress and strain were calculated from equation 5 and equation 6, respectively. Following ISO 13314, results for quasi-elastic gradient (equation 7), plateau stress between 5-9% strain (Figure 5), first maximum compressive strength (Figure 5), energy absorption to 10% strain (equation 8) and energy absorption efficiency (equation 9) were reported (11). If specimens did not fail before the maximum load of 25 kN, the plateau stress could not be calculated. The plateau end strain could not be calculated for any of the specimens.

Equation 5 – Compressive stress (N/mm^2)

$$\sigma = \frac{F}{A}$$

Equation 6 – Strain (%)

$$e = \frac{\Delta l}{l_o} \times 100$$

Equation 7 – Quasi elastic gradient (N/mm^2)

$$E_{qe} = \frac{\sigma}{e}$$

Equation 8 – Energy absorption per unit volume (MJ/m^3)

$$W = \frac{1}{100} \int_0^{e_0} \sigma \, de$$

Equation 9 – Energy absorption efficiency (%)

$$W_e = \frac{W}{\sigma_0 \times e_0} \times 10^4$$

F is the compressive force and A is the initial cross-sectional surface area perpendicular to the loading force, in accordance with ISO 13314. Δl is the overall compressive displacement, and l_o is the initial gauge length. e_0 is the upper limit of compressive strain (%) and σ_0 is the compressive stress at the upper limit of compressive strain (N/mm^2), and e_{cr} is the initial yield point corresponding to the start of the plateau regime.

Fatigue testing was performed to emulate the testing standard ISO 7206-4 (12), which determines the endurance properties of stemmed femoral components, on an ElectroForce 3300 (Bose Corporation, ElectroForce Systems Group, Minnesota,

USA). A sinusoidally varying compressive force between 300 and 2300 N was applied at 5 Hz until failure or run-out of 5 million cycles (12). The displacement of lattices was recorded at 300 cycles (*f*), and as specified in ISO 7206-4 the test was programmed to end if the specimen displaced greater than either 5 mm or 1.25 × *f*, whichever was the greater value. Specimen sample size for fatigue testing was *n* = 3.

All mechanical testing was performed at room temperature.

Results

Eight standard lattice types available in Simpleware ScanIP (Synopsys, Mountain View, USA) were chosen for investigation. The lowest common target volume fraction across all unit cell types, whilst maintaining design parameter requirements, was 30% (Figure 2). Minimum strut diameter and average pore size were measured for each CAD (computer aided design) lattice (Figure 2) at 30% target volume fraction. The designed pore sizes varied from 0.55 mm (Neovius' surface) to 0.95 mm (Schwartz primitive (Pinched) and Schwartz diamond); and strut diameter varied from 0.30 mm (Double Schoen gyroid) to 0.60 mm (Cylinder grid).

FEA was performed on the lattices listed in Figure 3 with the von Mises stress and maximum displacement results displayed. Maximum stresses were noted at the minimum strut diameters of all lattice designs, and specifically in the vertical struts for the more cubic orientated lattices (Schwartz primitive, Schwartz primitive (Pinched) and Cylinder grid). High stresses were also noted due to partially complete unit cells at the edge of cylinder shapes. The original and displaced lattice cylinder result from FEA is shown in Figure 3, with a colour map of von Mises stress. The stiffest cell types identified were the Schwartz primitive, Schwartz primitive

(Pinched), and Cylinder grid, which all displaced ≤ 0.02 mm respectively (Figure 3; identified by *). Therefore, these cell types were chosen for manufacture and mechanical testing (Figure 4).

Figure 3 – FEA performed on Schwartz primitive (Pinched) lattice, with 30% volume fraction and a cubic cell period of 10. Deformation scale increased to 114 with original lattice ghosted, and von Mises stress displayed as a colour map with scale bar shown. FEA displacement and von Mises stress results for CAD compression lattices, with cubic unit cell structure of 10 in *X*, *Y* and *Z* axis. 30% volume fraction, except Schwartz primitive (Pinched) 10%. Number of elements of coarse model mesh at 0.1 mm resampling. If number of elements exceeded 1 million, models were resampled at 0.2 mm; where this is the case, lattices are identified with †. The stiffest lattice types chosen for manufacture are highlighted by *.

The Schwartz primitive (Pinched) lattice was capable of the lowest volume fraction (10%) whilst maintaining design parameters: D_o = 15 mm; H_o = 15 mm; strut diameter >0.2 mm. Using FEA, this lattice was identified as the strongest unit cell type at 10% volume fraction, displacing 0.05 mm. Specimens were manufactured for fatigue testing and porosity analysis with Schwartz primitive (Pinched) unit cell type, 10% volume fraction, and a cubic unit cell period of 10.

Figure 4 – AM lattices with cubic unit cell period of 10; unit cell type, volume fraction, and designed and manufactured pore and strut diameters, stated below each lattice. Height (top row) and diameter (bottom row) of specimens shown (mean ± standard deviation). Minimum strut and average pore diameters shown below each lattice, analysed with ImageJ.

Fraction of volume and material

The volume fraction and material density for specimens with the largest volume available for incorporation of a therapeutic agent were evaluated. Of the manufactured specimens, the Schwartz primitive (Pinched) lattices at 10% volume fraction, with unit cell period of 10 in the *X*, *Y* and *Z* axes, contained the highest

designed porosity. The level of defects within the manufactured specimens (i.e. porosity within the lattice struts) calculated by microCT was 99.0 ± 0.7%. The density of the lattice material was analysed using Archimedes balance measurements, as 4.24 ± 0.11 g/cm^3, comparable to the theoretical density of Ti-6Al-4V (4.43 g/cm^3). The volume fraction of the cylinder (designed to be 10%), was calculated from the Archimedes balance measurements, as 14.18 ± 0.68%. For the Schwartz primitive (Pinched) 10% lattices scanned by microCT and evaluated by ImageJ, no deviation was found (variation of 3%) between the designed and manufactured internal strut and pore diameters (Figure 4).

Mechanical testing

Schwartz primitive and Schwartz primitive (Pinched) 10% compression lattices failed (reached their first maximum compressive strength) within the quasi-static compression test limits. Two Schwartz primitive (Pinched) 30% compression lattices also failed within these test parameters. The remaining (n = 3) Schwartz primitive (Pinched) 30% lattices, and all the Cylinder grid compression lattices, did not fail before 25 kN. The first maximum compressive strength could only be calculated for specimens that failed within the test parameters. However, the stress-strain curves for each lattice type indicate the Schwartz primitive (Pinched) 30% and Cylinder grid lattices were plateauing towards the point of failure at 25 kN (Figure 5).

Figure 5 – Stress-strain curve for each AM lattice. a) Schwartz primitive 30%; b) Cylinder grid 30%; c) Schwartz primitive (Pinched) 10%; d) Schwartz primitive (Pinched) 30%. Key: 1) quasi-elastic gradient; 2) first maximum compressive strength; 3) plateau stress.

Table 1 – Mechanical testing results for AM lattices, with 30% volume fraction and cubic unit cell structure of 10. *n* = 5, except for † where *n* = 2. For ‡ energy absorption and efficiency calculated to 5% strain, otherwise calculated to 10% strain.

Cell type	Schwartz primitive 30%	Schwartz primitive (Pinched) 30%	Cylinder grid 30%	Schwartz primitive (Pinched) 10%
Plateau stress (MPa)	---	---	---	27.8 ± 3.0
First maximum compressive strength (MPa)	126.8 ± 3.8	138.1 ± 0.1†	>140.0	29.7 ± 7.7
Energy absorption (kJ/m^3)	5.11 ± 0.37	5.73 ± 0.54	6.43 ± 0.20	0.31 ± 0.04‡
Energy absorption efficiency (%)	45.8 ± 2.6	43.0 ± 2.8	46.0 ± 1.4	2.8 ± 0.4‡
Quasi-elastic gradient (GPa)	1.93 ± 0.05	2.31 ± 0.04	2.42 ± 0.09	0.92 ± 0.18

Fatigue

The Schwartz primitive (Pinched) unit cell with 10% volume fraction and a cubic unit cell function of 10 was chosen for fatigue testing, due to being the weakest mechanical structure of the 4 manufactured lattices (Table 1) and containing the greatest volume void space to incorporate a therapeutic agent. As the weakest mechanical structure but with the largest volume available for therapeutic incorporation, if the Schwartz primitive (Pinched) lattice with 10% volume fraction passed fatigue testing then the stronger lattice types should withstand with fatigue loading also in theory. Three samples completed 5 million cycles without failure (Supplementary Figure 1). The samples displaced 0.381 ± 0.115 mm after 300

cycles (*f*), and after 5 million cycles this had increased to 0.393 ± 0.113 mm, thus all samples passed the fatigue criteria (< 1.25 × *f*) set in ISO 7206-4.

Discussion

This paper describes a potential use of lattice design in orthopaedic implants, with the 2-stage hip replacement spacer identified as a possible selection for redesign due to its current limited life span and the inability for full patient load bearing. The results of this study showed that the fatigue life of a Schwartz primitive (Pinched) unit cell type, with 10% volume fraction and cubic cell function of 10, manufactured in Ti-6Al-4V by SLM, was suitable for use in the design of an orthopaedic hip implant. Use of such a lattice design would allow for the incorporation of a therapeutic agent, such as a resorbable antibiotic-loaded cement, to allow the targeted release of a drug. This could reduce the overall amount of antibiotics required, as the targeted delivery would allow release of the antibiotics locally rather than if administered by alternative methods. Whilst the Schwartz primitive (Pinched) 10% lattice design reduces the mechanical strength of the implant, this study demonstrates that the structure was capable of meeting the axial load requirements of an orthopaedic hip implant, as described by ISO 7206-4. A major advantage of this design would be the increased mobility of a patient during a 2-stage hip revision. There is even the potential to use the implant as a permanent prosthesis, which is especially beneficial in cases where further surgery is undesirable, for example in elderly patients (14) or high risk surgical cases (15). Although this study assessed the capability of designed lattice structures to meet the axial load conditions of an orthopaedic hip implant, further work would study the associated torsion and bending forces.

A total of 8 reticulated lattice types were designed using CAD, with a possible common minimum volume fraction of 30%. The Double Schoen gyroid, evaluated by FEA, was the weakest lattice design (Figure 3; 1.23 GPa von Mises stress), with a predicted displacement of 0.7 mm; this was approximately ten times weaker than other lattice designs. Another notably weak lattice was the Neovius' surface, with von Mises stress of 1.05 GPa. The common design feature of these cell types is their organic shape structure, compared to the more cubic design of other cells (Figure 2). As reported in other studies, stretch dominated structures are generally stiffer than bending dominated structures, lending themselves as more suitable for weight efficiency in structural applications (16). Since this study aimed to maximise the void space available to determine the maximum volume of therapeutic agent that could be incorporated, stretch dominated structures are an attractive solution to maintain implant stiffness whilst removing material. This enables targeted drug delivery within an orthopaedic implant and reduces the amount of antibiotics required to treat an infection. Further, it provides a long-term implantable for when it is undesirable to perform secondary surgery to remove a temporary cement spacer. The strongest lattice types were the Schwartz primitive (Pinched) and Cylinder grid, with von Mises stresses of 0.17 and 0.15 GPa, respectively (displacing 0.01 mm each). The FEA results calculated in this study were used to inform the selection of lattice geometry for AM and subsequently mechanical testing. Future work would involve validating the FEA model to consider manufacturing defects and the influence of deviation from the CAD model.

FEA was performed under identical conditions for all lattice types to provide a comparison between designs. When evaluating lattice designs by FEA, stress concentrations were noted at the edge of all specimens due to part cubic cells (cells

that were sectioned to fit within the cylindrical body). As noted in other studies, the edge effect in FEA models of lattices makes it difficult to accurately model these geometries (17). The displacement of Schwartz primitive (Pinched) manufactured lattices (10% volume fraction) during fatigue testing was greater than predicted during FEA (0.05 mm), due to specimens bedding in. Ultimately, although FEA influenced the choice of which lattice geometries to manufacture, mechanical testing of the lattices proved their validity as a choice for orthopaedic hip implants. The compressive displacement of the Schwartz primitive (Pinched) lattices increased during fatigue testing by 0.012 mm to 0.393 ± 0.113 mm, thus samples passed the fatigue criteria (1.25 × *f*) set in ISO 7206-4.

The density of the printed titanium alloy, calculated within struts as 4.24 ± 0.11 g/cm^3, is similar to the theoretical density of Ti-6Al-4V (4.43 g/cm^3). This result, accompanied by the low level of porosity (1.0 ± 0.7%) calculated from microCT data, confirms minimum defects within the solid material of the structure, even with small strut diameters of 0.37 mm.

Notably, the accuracy of the manufactured specimens was close to the designed parts as evidenced by dimensional measurements. Specifically, the average pore size for Schwartz primitive, Schwartz primitive (Pinched) and Cylinder grid for the designed and manufactured parts were similar; 6%; -2%; -3%; variation from design respectively. Furthermore, the minimum strut diameters for the same cell types measured from the manufactured parts exhibited 29%, -4% and 6% variation from design respectively. Similarly, the designed strut and pore diameters of Schwartz primitive (Pinched) 10% lattices were designed as 0.29 mm and 1.18 mm. The external strut and pore diameters measured by photography and ImageJ varied by

28% and -3%, while the internal diameters (0.30 ± 0.03 mm and 1.22 ± 0.03 mm) measured by microCT and ImageJ varied by 3% and 3%. Although the greatest variability of strut diameter may appear high at 29% (Schwartz primitive (Pinched)), it is worth noting that the standard deviation of measurements for the minimum struts manufactured diameter deviated a maximum of 0.17 mm from the designed geometry, and the average pore size a maximum of 0.11 mm. These values are beyond the resolution of the SLM machine used (0.2 mm), and therefore it can be assumed that the predominant cause of measurement variation is most likely due to the triangulation process when creating an STL file.

Traditionally, AM implants are finished through polishing techniques, therefore, further investigation to assess the challenges associated with finishing lattice structures would be beneficial. Although the example in this paper has investigated the potential of lattices in the design of orthopaedic hip spacers, another use of lattices is to mechanically match an implant to surrounding tissue (18). Titanium alloys are the traditional material of choice for manufacture of implants due to their biocompatibility, corrosion resistance and mechanical properties (10, 19, 20). However, stress shielding is commonly cited as a barrier to titanium implants (19, 21, 22), since the material is significantly stiffer than that of the surrounding bone. The elastic modulus of cortical and cancellous bone varies from 3 to 30 GPa and 0.02 to 0.3 GPa, respectively (23, 24), whereas the elastic modulus of Ti-6Al-4V is significantly greater at 113 GPa (13). It is hypothesised that a lower Young's modulus for the implant material results in more deformation of the implant and therefore better bone ingrowth (25). A study by Schouman showed that by reducing the overall stiffness of an implant through increased porosity, resulted in better bone formation compared to a rigid design (21). By mechanically matching an implant to

surrounding bone, it is possible to prevent stress shielding and promote improved osseointegration. The results of this study found that the quasi-elastic modulus of the investigated lattices ranged from 0.92 ± 0.18 to 2.42 ± 0.09 MPa. These results are within the range of those presented elsewhere: 2-6 GPa, with strut and pore diameters of 400 µm and 650 µm, and relative density of 0.3 (26); and 0.5-1.5 GPa, with 0.4 mm and 0.6 mm strut and pore diameter, and relative density 14% (27). Notably, the results of this study are similar to the lower elastic modulus range of cortical bone. Assuming a solid titanium structure would have an elastic modulus of 113 GPa, by varying the lattice geometry through an increase in volume fraction it is predicted the modulus of the lattice structures could be designed to match the variation in cortical bone. The manufactured specimens within this study failed at, or around, a strain of 0.1 due to vertical struts within a layer fracturing. This strain range is similar to that achieved in other studies (26). As vertical struts fractured at high loads, the machine experienced rapid unloading (evident in Figure 5a), and therefore tests were automatically stopped at this point due to the machine safety mechanism. These lattices, therefore, did not reach the plateau stage. The exception to this is the Schwartz primitive (Pinched) 10% lattice, which failed before a strain of 0.1 but at a much lower load (Figure 5c), therefore plateau strength could be calculated for this lattice type (Table 1).

Although this study demonstrates the suitability of lattice geometries for use in load bearing orthopaedic applications, their design was limited to cylindrical geometry with constant cross-sectional area to comply with ISO 13314. The final geometry of lattices is still to be determined. Future work would involve further testing to evaluate the effect of cross sectional area over which the lattice was applied. A similar approach could be adopted to this study, which iterates between FEA and

experimental analysis, to assess the design envelope in which this lattice could be employed.

The use of AM is not currently being exploited to its full potential in medical devices. This study assesses the potential of a lattice design as an alternative for a cement hip spacer, notably this approach could add value to other orthopaedic cases. Implementation could decrease complications such as stress shielding by matching implant strength to patient-specific bone properties, or to allow targeted delivery of drugs by incorporating a chamber within an implant whilst maintaining associated strength and fatigue requirements.

Conclusions

The design of implants can be redefined to increase functionality due to advances in additive manufacture, with orthopaedic implants no longer restricted to simply mechanically replacing or supporting damaged joints and bones. Here, we explore the potential to exploit the void volume of porous lattice structures as a reservoir for a secondary material containing a therapeutic agent. There is also the potential to design implants containing lattice structures to mechanically match surrounding bone and reduce stress shielding. This study assessed the suitability of additively manufactured titanium lattices as an alternative design for hip cement spacers, to decrease associated morbidity and further surgery. The weakest lattice design (Schwartz primitive (Pinched) 10%), with the greatest volume void, withstood 5 million cycles of loading between 300 and 2300 N. In summary, this study confirms that AM methods can produce a lattice design for use in a titanium implant that could allow targeted drug delivery of a loaded therapeutic, without compromising the fatigue life of a load bearing orthopaedic hip implant.

Acknowledgments

This work was supported by the Engineering and Physical Sciences Research Council [grant number EP/L020815/1]. The Bose materials testing machine used in the study was funded by the Engineering and Physical Sciences Research Council [grant number EP/F014562/1]. The Zwick mechanical tester used in this work was funded by Birmingham Science City: Innovative Uses for Advanced Materials in the Modern World (West Midlands Centre for Advanced Materials Project 2), with support from Advantage West Midlands and part funded by the European Regional Development Fund.

Declarations of interest: none.

1. Vandenbroucke B, Kruth JP. Selective laser melting of biocompatible metals for rapid manufacturing of medical parts. Rapid Prototyping Journal. 2007;13(4):196-203.
2. Perez RA, Mestres G. Role of pore size and morphology in musculo-skeletal tissue regeneration. Materials Science and Engineering: C. 2016;61:922-39.
3. Cox SC, Jamshidi P, Eisenstein NM, Webber MA, Hassanin H, Attallah MM, et al. Adding functionality with additive manufacturing: Fabrication of titanium-based antibiotic eluting implants. Materials Science and Engineering: C. 2016;64:407-15.
4. Choy SY, Sun C-N, Leong KF, Wei J. Compressive properties of functionally graded lattice structures manufactured by selective laser melting. Materials & Design. 2017.
5. Lenguerrand E, Whitehouse M, Beswick A, Jones S, Blom A. Revision for prosthetic joint infection following hip arthroplasty. Bone. 2017;3:R1.
6. Board TNE. 12th Annual Report National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. 2015.
7. Castellani L, Daneman N, Mubareka S, Jenkinson R. Factors Associated with Choice and Success of One- Versus Two-Stage Revision Arthroplasty for Infected Hip and Knee Prostheses. HSS Journal. 2017:1-8.
8. Leunig M, Chosa E, Speck M, Ganz R. A cement spacer for two-stage revision of infected implants of the hip joint. International orthopaedics. 1998;22(4):209-14.
9. Cox SC, Jamshidi P, Eisenstein NM, Webber MA, Hassanin H, Attallah MM, et al. Adding functionality with additive manufacturing: Fabrication of titanium-based antibiotic eluting implants. Materials Science and Engineering: C. 2016;64(Supplement C):407-15.
10. Attar H, Calin M, Zhang L, Scudino S, Eckert J. Manufacture by selective laser melting and mechanical behavior of commercially pure titanium. Materials Science and Engineering: A. 2014;593:170-7.
11. ISO E. 13314.
12. ISO E. 7206-4.
13. Welsch G, Boyer R, Collings E. Materials properties handbook: titanium alloys: ASM international; 1993.
14. Lee WY, Hwang DS, Kang C, Shin BK, Zheng L. Usefulness of Prosthesis Made of Antibiotic-Loaded Acrylic Cement as an Alternative Implant in Older Patients With Medical Problems and Periprosthetic Hip Infections: A 2- to 10-Year Follow-Up Study. Journal of Arthroplasty. 2017;32(1):228-33.
15. Scharfenberger A, Clark M, Lavoie G, O'connor G, Masson E, Beaupre L. Treatment of an infected total hip replacement with the PROSTALAC system.: Part 2: Health-related quality of life and function with the PROSTALAC implant in situ. Canadian journal of surgery. 2007;50(1):29.
16. Fleck N, Ashby M, Deshpande V. The Topology of Cellular Structures. New Approaches to Structural Mechanics, Shells and Biological Structures: Springer; 2002. p. 81-9.
17. Wieding J, Wolf A, Bader R. Numerical optimization of open-porous bone scaffold structures to match the elastic properties of human cortical bone. Journal of the Mechanical Behavior of Biomedical Materials. 2014;37:56-68.
18. Harrysson O, Cansizoglu O, Marcellin-Little DJ, Cormier DR, West HA. Direct metal fabrication of titanium implants with tailored materials and mechanical properties using electron beam melting technology. Materials Science and Engineering: C. 2008;28(3):366-73.

19. Deing A, Luthringer B, Laipple D, Ebel T, Willumeit R. A porous TiAl6V4 implant material for medical application. International journal of biomaterials. 2014;2014.
20. Matena J, Petersen S, Gieseke M, Kampmann A, Teske M, Beyerbach M, et al. SLM produced porous titanium implant improvements for enhanced vascularization and osteoblast seeding. International Journal of Molecular Sciences. 2015;16(4):7478-92.
21. Schouman T, Schmitt M, Adam C, Dubois G, Rouch P. Influence of the overall stiffness of a load-bearing porous titanium implant on bone ingrowth in critical-size mandibular bone defects in sheep. Journal of the Mechanical Behavior of Biomedical Materials. 2016;59:484-96.
22. Arabnejad S, Johnston B, Tanzer M, Pasini D. Fully porous 3D printed titanium femoral stem to reduce stress-shielding following total hip arthroplasty. Journal of Orthopaedic Research. 2016.
23. Wang X, Xu S, Zhou S, Xu W, Leary M, Choong P, et al. Topological design and additive manufacturing of porous metals for bone scaffolds and orthopaedic implants: a review. Biomaterials. 2016;83:127-41.
24. Li B, Aspden RM. Composition and mechanical properties of cancellous bone from the femoral head of patients with osteoporosis or osteoarthritis. Journal of Bone and Mineral Research. 1997;12(4):641-51.
25. Van der Stok J, Van der Jagt OP, Amin Yavari S, De Haas MF, Waarsing JH, Jahr H, et al. Selective laser melting-produced porous titanium scaffolds regenerate bone in critical size cortical bone defects. Journal of Orthopaedic Research. 2013;31(5):792-9.
26. Wauthle R, Vrancken B, Beynaerts B, Jorissen K, Schrooten J, Kruth J-P, et al. Effects of build orientation and heat treatment on the microstructure and mechanical properties of selective laser melted Ti6Al4V lattice structures. Addit Manuf. 2015;5:77-84.
27. Choy SY, Sun C-N, Leong KF, Wei J. Compressive properties of Ti-6Al-4V lattice structures fabricated by selective laser melting: Design, orientation and density. Addit Manuf. 2017;16:213-24.

Supplementary information

Supplementary Figure 1: Fatigue test data to 5 million cycles for Schwartz primitive (Pinched) unit cell with 10% volume fraction and a cubic unit cell function of 10. Applied peak and trough load over 5 million cycles (a). Strain (%) versus number of cycles for specimen 1 (b), specimen 2 (c), and specimen 3 (d).